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Editorial

OPPORTUNISTIC INFECTIONS IN HIV/AIDS AND OUR ALERTNESS

B.L. Parija*, M.R. Behera**

HIV/AIDS, is a global epidemic with approximately 40 million people are living with HIV/AIDS worldwide[1]. Of all HIV infected people, 95% are living in developing countries. About 5.134 million HIV infected cases are present in India which comprises of 65% cases of south east Asia. In India, HIV pandemic no longer belongs to the high risk group but now it is commoner among general population.[2,3]

Opportunistic infections (OIs), have been recognised as common complications of HIV infection which detoriates both the standard of life and life expectancy of HIV infected people. Oral candidiasis (OC) emerged as the most frequent OI associated with HIV infected patients. OC was found to be present in 88% of these patients. Tuberculosis, emerged as the second most prevalent infection developing in 57% of patients in a study done by N.Chakraborty[4], both pulmonary 69.4% and extrapulmonary 16.6% were found to be prevalent. According to A.A Takalka et al[5] commonly observed Opportunistic Infections are Pulmonary TB(52.3%), Candidiasis(39%), Cryptosporidial diarrhea(30.1%) and Pneumocystis Carinii Pneumonia in 14.2% cases. In 46.4% cases CD4 count was <200.

In the present study done by Choudhary et al, they have found Tuberculosis as the commonest opportunistic infection(51%) with most of the patients having pleural effusion. The second most common OI was Candidiasis (43%) occurs at higher CD4 counts than Tuberculosis. Next common OI being Cryptosporidiosis (9.3%). Among viral OIs, CMV infection was most predominant followed by HSV infection and HBV. In this study other OIs found in descending order of their prevalence were CNS Toxoplasmosis (6.9%), Pneumocystis Jeroveci Pneumonia (5.8%), Mucocutaneous Herpes Simplex infection (4.6%), Cryptococcal meningitis (2.3%), Molluscum Contagiosum and Progressive Multifocal Leukoencephalopathy 1.1% each. These infections were found in CD4 count less than 200/microlitre.

With an extensive knowledge of OIs in HIV with various level of CD4 count, it helps in early diagnosis and prompt treatment of OIs. It will definitely contribute to increased life expectancy among infected patients and also delays the progression of AIDS. As the free ART roll out programme is extended to many states in India many long term studies will have to be undertaken to assess the effect of this programme on the incidence of various OI. With the background knowledge of OI health care professional should improve their decision regarding prophylaxis for prevention and appropriate therapeutic intervention for OIs along with ART. The detection and awareness towards OIs related to HIV is of immense importance especially in Indian perspective. A high level of alertness is needed at both laboratory and clinical level and routine surveillance studies need to be undertaken. Institutions in Odisha and other states of our country need to be equipped to face the emerging challenge in the form of updating the present knowledge, by way of education and training of the personnel, acquisition of skills of improved procedures, and their implementation in appropriate settings with adequate administrative support.

*Associate Professor, **Assistant Professor, Dept. of Medicine, SCB Medical College, Cuttack, Odisha.

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Original Article

CLINICO-EPIDEMIOLOGICAL PROFILE OF OPPORTUNISTIC INFECTIONS IN HOSPITALISED HIV INFECTED ADULTS / ADOLESCENTS IN WESTERN ODISHA WITH A CORRELATION TO CD4+T CELL COUNT

S.P.S. Choudhury*, P. K. Mohanty, M. K. Mohapatra***, L. K. Dash******

ABSTRACT

Background: *Opportunistic Infections (OIs) are important determinants of morbidity and mortality in HIV infected persons. The spectrum of OIs varies in different regions and appear at different thresholds of CD4+T cell count.* ***Method:*** *Eighty six hospitalized patients with HIV infections confirmed as per National AIDS Control Organization (NACO) guidelines were studied prospectively for evaluation of opportunistic infections and their co-relation with CD4+T cell count between July 2010 to September 2012.* ***Results:*** *Of the cases under study 62 patients (72%) were male and 24 patients (28%) were female. Forty five cases (52.3%) were in age group of 31 to 45 years followed by 28% between 15 to 30 years and 19.7% between 46 to 65 year. Heterosexual transmission was the commonest mode in 63 cases (73.3%). In nineteen cases (22%) mode of transmission could not be known. Among the patient studied, 36 cases (42%) had a CD4+T cell count between 101 – 200/µl followed by 29 cases (33%) with 200-400/µl,15 cases (18%) with 51 – 100/µl and 6 cases (7%) with ≤ 50/ µl. Fifty seven cases (66%) had single OI while rest had multiple OIs. Tuberculosis was the most common OI (51%) with pleural effusion in 23 cases, pulmonary tuberculosis in 18 cases, lymphadenitis in 7 cases, meningitis in 4 cases tuberculous peritonitis and disseminated tuberculosis in 2 cases each and spinal tuberculosis in one case. Median CD4+T cell count was 218/µl in those with tuberculosis. Candidiasis was the second most common OI (43%) with oral candidiasis in 36%, oral and oesophageal candidiasis in 5% and vulvo-vaginal candidiasis in 2% cases. Median CD4+ T cell count was 272/µl. Among other OIs it is observed that Cryptosporidiosis seen in 9.3% cases with median CD4 count of 142/µl, CNS Toxoplasmosis seen in 7% cases with median CD4 count 76/µl, Pneumocystis jiroveci pneumonia were seen in 5.8% cases with median CD4 count of 123/µl, Herpes simplex infection was found in 4.6% cases with median CD4 count of 109/µl, Cryptococcal meningitis seen in 2 cases with median CD4 count 92/µl, Molluscum contagiosum and Progressive Multifocal Leucoencephalopathy seen in one case each with median CD4 count of 35/µl and 28/µl respectively.* ***Conclusion:*** *Most common OI in the study was tuberculosis, of which pleural effusion is commonest manifestation. Other OIs are candidiasis second most common followed by cryptosporidium, toxoplasma, pneumocystis jiroveci, herpes simplex, cryptococcus, molluscum contagiosum and JC virus infection.* ***Keywords:*** *HIV infection, Opportunistic infections, CD4+T cell count.*

INTRODUCTION

HIV infections/AIDS is a global health problem with cases reported virtually from every country. According to 2011 estimates from UNAIDS, WHO and UNICEF around 30.6 million adults and 3.4 million children are living with HIV infection at the end of 2010.[1],[2],[3]

Though India is a country with low HIV prevalence, it has the third largest number of people living with HIV/AIDS. Based on HIV Sentinel Surveillance 2008-09, it is estimated that 23.9 lakhs people are infected with HIV of which 39% are female and 3.5% are children. The four high prevalence states (Andhra Pradesh – 5 lakhs, Maharashtra – 4.2 lakhs, Karnataka – 2.5 lakhs, Tamil Nadu – 1.5 lakhs) account for 55 percent of all HIV infections in the country. The estimated adult prevalence is 0.31%. Among the states Manipur has shown the highest adult prevalence (1.4%),

* Post Graduate Student, ** Associate Professor, *** HOD and Professor, **** Professor, Department of General Medicine, V.S.S. Medical College, Burla, Sambalpur, Odisha.

followed by Andhra Pradesh (0.9%), Mizoram (0.81%), Nagaland (0.78%), Karnataka (0.63%) & Maharashtra (0.55%).[4]

Although Odisha is a state among low HIV prevalence (0.29%), the prevalence is on rise. There are 26127 people living with HIV infection, among which 35.2% are female and 6.6% are children. Death due to AIDS in our state estimated to be 1347 till August, 2012 according to Odisha State AIDS Control Society (OSACS).

The Human Immunodeficiency Virus (HIV) destroys the CD4+ T cells repertoire progressively and relentlessly thus making the HIV infected persons susceptible to a number of opportunistic infections(OIs). It was also noted that certain OIs manifest below a particular threshold of CD4+T cell count, many of these in a advanced stage of the HIV infection. Since the beginning of HIV epidemic , OIs have been recognized as common complications of HIV infection. OIs cause substantial morbidity and hospitalization, necessitate toxic and expensive therapies and shorten the survival of PLHA (People Living with HIV/AIDS).[5] The right diagnosis and proper treatment will improve the quality of life and survival in PLHA. The relative frequencies of specific OIs vary in different countries and even in different areas within the same country. While *Pneumocystis jiroveci* is the commonest in the Western part of world, *Tuberculosis* and *Candidiasis* are the common OIs in India supported by various studies.

The present study was carried out with an aim to study the spectrum of OIs and their correlation with CD4 count in hospitalized patients of Western Odisha.

MATERIAL & METHODS

It is an observational, analytical and prospective study. The study included all HIV infected patients with OIs admitted to the Department of Medicine, V.S.S. Medical College and Hospital, Burla from July 2010 to September 2012 (a period of 26 months in total). Patients with known HIV positive status having OIs or patients with different OIs admitted to the hospital and later found to have HIV positive status were included in the study.

Diagnosis of HIV infection in the included cases was done at ICTC (Integrated Counseling and Testing Centre) as per the NACO guidelines by three different methods *Dot blot (comb AIDs), Immunochromatographic test (Pareekshak) and Immunoblot (Pareekshak)*. Those having reactive test results at other laboratories were sent to the ICTC for confirmation. Informed consent was taken in each case as per NACO ethical guidelines. Children below the age of 15 years were excluded from this study. [6],[7]

Detailed history , clinical examination and investigations were done as necessary like CD4+T cell count, CBC, ESR, Blood culture, Arterial Blood Gas analysis, HBsAg, Anti-HCV antibody, Urine routine and culture, Stool routine and culture, Mantoux Test, Sputum AFB & Microscopy, Chest X-ray, USG Abdomen & Pelvis, CT scan Brain, CT Thorax, MRI Brain, MRI Spine, Fundoscopy, Peritoneal fluid/Pleural fluid/CSF analysis, CSF for Indian Ink staining,CSF PCR, FNAC of lymphnode, ELISA for Toxoplasma IgG & IgM, Latex Agglutination for Cryptococcal antigen, Oral Scraping for Microscopy of fungal element, UGI endoscopy. CD4+T cell count was done by *Partec CD4 flow cytometer using flow cytometry.* [8],[9],[10],[11],[12]

RESULTS

Eighty six (86) HIV infected patients with OIs were studied out of which 62 cases (72%) are male and 24 cases (28%) are female with male: female ratio of 2.6:1. The patients were mostly in the age group of 31-45 years(45cases ,i.e., 52.3% of total number of cases), followed by 24 cases (28%) in the age group of 15-30 years and 17 cases (19.7%) in the age group of 41-65 years.

The various occupations among the studied patients are mentioned in Table-1. Majority of the patients were labourers (32.5 %) working in the nearby industries on a daily wage basis.

Table-1: Occupation of the patients.

Occupation	
	Num
Labourer	16
Driver	19
Farmer	14
Employee (government)	6
Student (upto graduation)	2
Housewife	0

*Others include private employees, businessmen, contractors, shopkeepers, commercial sex workers etc.

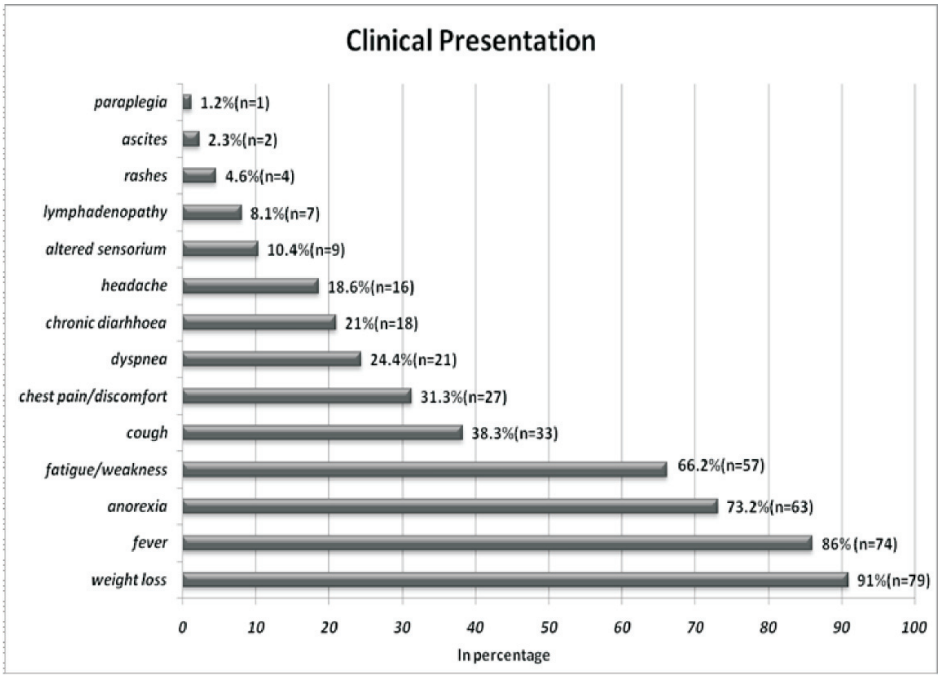
Different modes of transmission among males and females are as depicted in Table-2. The commonest mode of transmission is the heterosexual mode of transmission i.e., 73.3%. One case of thalassemia with repeated blood transfusion had possible transmission by blood. In nineteen cases (22%) modes of transmission could not be ascertained.

Table- 2: Modes of transmission

Modes of transmission	***Male***(n=
	Number
Heterosexual	48
Homosexual	0
Blood Transfusion	1
I.V. Drug Abuse	3
Frequent needle prick	0
Vertical transmission	0

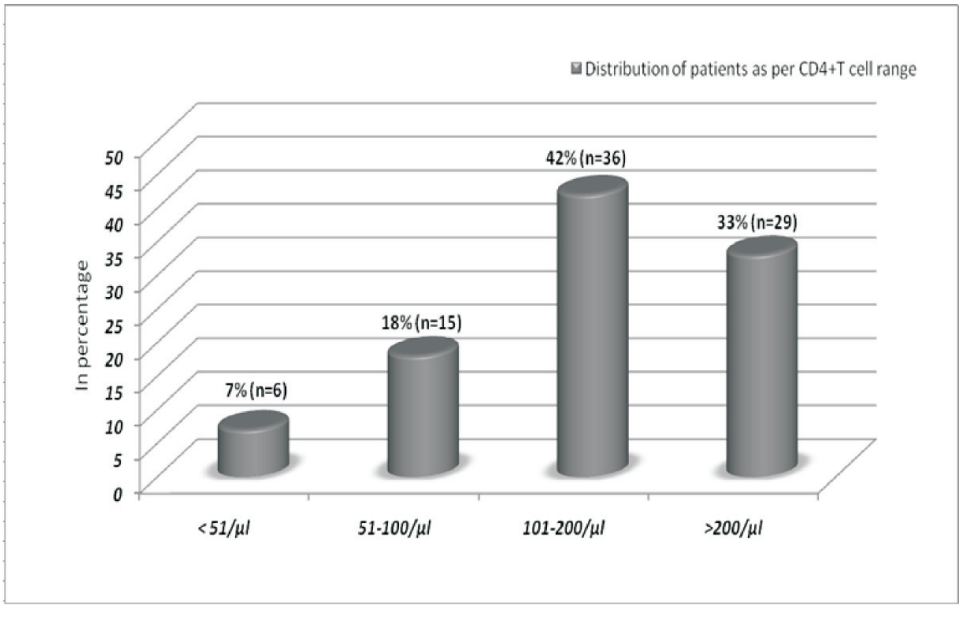
The various clinical manifestations in patient presenting with OIs are depicted in Figure- 1. The most common symptoms was noted to be weight loss, fever and anorexia.

Figure-1: clinical presentations of hospitalised patients.



The maximum CD4 count in the patients was 387/µl and minimum CD4 count is 28/µl. Figure- 2 shows the distribution of patients according to CD4 cell range.

Figure-2: Distribution of patients as per CD4+ T cell range.



The maximum number of patients i.e., 42% cases (n=36) belonged to CD4+T cell count of 101-200/µl, followed by 33% cases (n=29) having a CD4+ T cell count of > 200/µl. 18% of cases (n=15) had a count between 51-100/µl and 7% cases (n=6) had a very low CD4+ T cell count of < 51/µl. Thus 57 cases (66.2%) had a CD4 count below 200/µl. The *Median CD4 Count* of the study population was observed to be *183/µl*.

In the study population out of 86 cases in toto, single OI were seen in 57 cases (66%), while multiple OIs were found in 29 cases (34%). Table–3 describes the different combinations of OIs. Tuberculosis and candidiasis was the most common type of combination in patient admitted with multiple OIs.

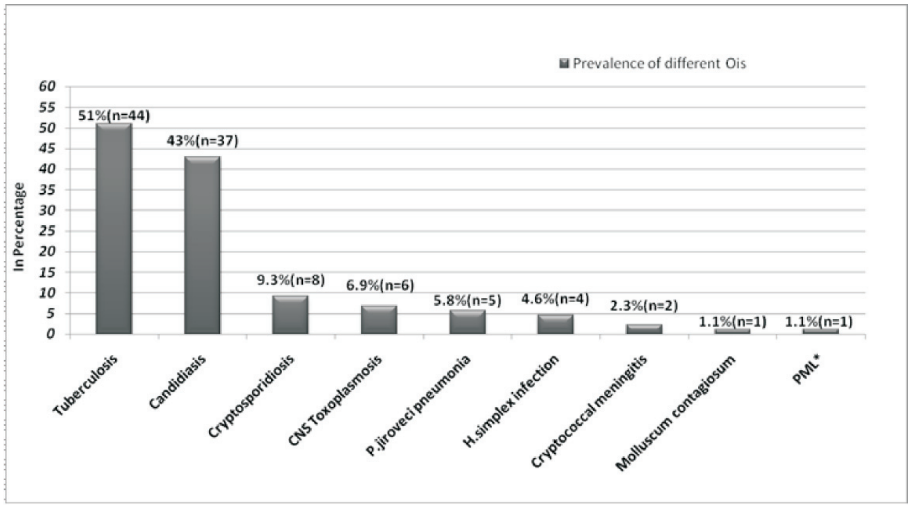
Table-3: Different combinations of OIs.

Differe
Tubercul
Cryptospor
Toxoplası
PCP*
Molluscum co
Cryptospori
Herpes sin

* Pneumocystis jiroveci pneumonia (formerly called as pneumocystis carinii pneumonia).

The prevalence of different OIs are depicted in Figure- 3. Tuberculosis is the most common OI (51% cases, n=44). Candidiasis is the second most common infection seen in 43% cases (n=37), followed by Cryptosporidial diarrhea, CNS Toxoplasmosis, Pneumocystis jiroveci pneumonia (PCP), Herpes simplex infection, Cryptococcal meningitis, Molluscum contagiosum and Progressive multifocal leukoencephalopathy (PML).

Figure-3: Prevalence of different OIs in the study population



* Progressive multifocal leukoencephalopathy.

The most common manifestation of tuberculosis (TB) in HIV infected patients is Pleural effusion seen in 52.2% cases(n=23) followed by Pulmonary TB, including a case of military TB noted in 41% cases(n=18). Among these, 6 cases presented with both pleural effusion with parenchymal involvement of TB. Tubercular lymphadenitis, TB meningitis, TB peritonitis and TB spine were seen in 31.8% cases, both as isolated and associated entities in cases having Pulmonary TB and/or Pleural effusion. 2 cases presented with Disseminated TB as shown in Table- 4.

Table- 4: Distribution of tubercular manifestations among cases of TB.

Tubercular manifestatic
Pleural Effusion
Pulmonary TB *including M*
TB lymphadenitis
TB meningitis
TB peritonitis
TB spine
Disseminated TB

Among the 37 cases (43%) patients suffering from Candidiasis, Oral Candidiasis was noted to be the most common type seen in 31cases(83.3%), followed by Oroesophageal Candidiasis seen in 4 cases (10.8%) , and Vulvovaginal Candidiasis in 2 cases (5.4%).

The distribution of median CD4 count in various OIs are shown in Table- 5. In case of tuberculosis median CD4 count was 218/µl, which is lower than that of candidiasis i.e., 272/µl.

Table- 5. Median CD4 count for different OIs in study population.

OIs
Candidiasis
Tuberculosis
Cryptosporidiasis
PCP*
Herpes simplex infec
Cryptococcal mening
CNS Toxoplasmosis
Molluscum contagio

* Pneumocystis jiroveci pneumonia (formerly known as pneumocystis carinii pneumonia).
**Progressive multifocal leukoencephalopathy.

DISCUSSION

During 26 months study and among 86 hospitalised patients 72% were male and 28% female which is comparable with other studies conducted by Chakravarty J. et al [13] (80.8% male) and Kumarasamy N. et al [16] (68% male). Most of the patient belonged to the age group 31-45 (52.3%) as compared to Chakraborty N. et al [17] (55% were in 31-40 yr) and Singh A. et al [18] (54% were in 31-40 yr). Majority of the studied population were labourer (Table-1) which is comparable to that reported by Chakravarty J. et al[13] (majority were migrant worker).This could be due to illiteracy and low level of awareness about transmission of HIV amongst them. The distribution of male patients was noted to be almost homogenous amongst labourers, drivers and farmers, whereas almost half of female patients are daily labourers by occupation. Most of the male patients were drivers by occupation (30.7%) and had a past history of emigration to nearby states like Andhra Pradesh, Chhattisgarh and West Bengal. The commonest mode of transmission, as depicted by this study (Table-2) as well as other studies of national (including NACO)[7] and international cadre (including WHO)[6] is the heterosexual mode of transmission, (73.3% in this study) like Chakravarty J. et al[13] (80.4%), Kumarasamy N. et al [16] (90%), Chakraborty N. et al [17] (80%). Mode of transmission could not be ascertained in a significant number of cases (22%) like that reported by Chakravarty J. et al[13] in which risk factor for HIV transmission could not be elicited in 14.1% . This could be ascribed to various reasons like insufficient history and embarssment or unwillingness of the patient to come clear about their sexual behaviour. At the time of hospitalization majority of patients were presented with more than one symptom like fever, weight loss and anorexia seen in more than 73% (Figure-1) which is similar to study done by Sharma SK et al[15] that most common presentation was fever (71%) and weight loss (65%). But study done by Chakravarty J. et al[13] is different in which majority patient were presented with fever (70.6%), weight loss (53.3%), chronic diarrhea (43.9%) & cough (40.3%).

A significant number of cases (42%) belonged to the CD4+ Tcell count range of 101-200/µl, with a median CD4 count of 183/µl (Figure-2). But the study by Chakraborty N. et al [17] shows 36.8% belonged to CD4 range of 101-200/µl, with lower median CD4 count i.e., 120/µl. The study by Chakravarty J. et al[13] shows a different scenario, in which the mean CD4 count in male was 179±9.3/µl where as CD4 count in female was 323±28.26/µl. In another study by Sharma SK et al[15] it was observed that 82.6% had CD4 count <200/µl from which 46% had CD4 count <50/µl.

The opportunistic infections may be found singly or in combinations. In our study single OI was found in 66% cases and multiple OIs in 34% of cases (Table-3).

The most common OI was tuberculosis (*51%*) with pleural effusion as its commonest manifestation. The second most common OI was candidiasis (*43%*) with most cases suffering from oral candidiasis which was seen to occur at higher CD4 counts than tuberculosis.The other OIs found in descending order of their prevalence were cryptosporidiosis, CNS toxoplasmosis, Pneumocystis jiroveci pneumonia, Mucocutaneous herpes simplex infection, Cryptococcal meningitis, Molluscum contagiosum and Progressive multifocal leucoencephalopathy due to JC virus infection (Table-4). The prevalence of different OIs varies in different studies. Table-6 shows a comparative analysis of prevalence of OIs in different Indian studies including the present study. [19],[20]

The relatively low prevalence of candidiasis in present study could be due to exclusion of HIV infected persons who are not hospitalized.

The median CD4 count for different OIs in this study was observed to be 272/µl for candidiasis, 218/µl for tuberculosis and 142/µl for cryptosporidiosis. But this observation was different than the study conducted by Vajpayee M. et al that median CD4 count

Table-6 : Comparison of prevalence of OIs in different studies.

Different OIs	Chakrabc N. et al[17 (2006-07 ICMR, Kolkata
Tuberculosis	57%
Candidiasis	88%
Cryptosporidiasis	43%
CNS toxoplasmosis	-

for candidiasis was 189/µl, tuberculosis was also 189/µl and for cryptosporidiosis was 227/µl [14]. In the present study the CD4 count is found to be below 100/µl in cases of Cryptococcal meningitis and CNS toxoplasmosis where as it is below 50/µl in each case of Molluscum contagiosum and Progressive multifocal leucoencephalopathy.

CONCLUSION

The spectrum of OIs in the present study in descending order of frequency are Tuberculosis, Candidiasis, Cryptosporidiosis, CNS toxoplasmosis, Pneumocystis jiroveci pneumonia, Herpes simplex infection, Cryptococcal meningitis , Molluscum

contagiosum and Progressive multifocal leucoencephalopathy, with a median CD4 count of 183/µl, i.e., < 200/µl. So there is increased chance of hospitalization in patients having CD4 count below 200/µl. The study is limited by the fact that many cases of OIs treated outpatients might not have been represented.

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Original Article

LUNG RECRUITMENT IN PATIENTS WITH THE ACUTE RESPIRATORY DISTRESS SYNDROME: A COMPARISON OF TWO RECRUITMENT MANEUVERS

R. Padhi* B. N. Panda S. Jagati*** S. C. Patra******

ABSTRACT

Background : *Recruitment Maneuver (RM) is a procedure where a sustained positive pressure is applied to an injured lung, over an increment of time, to recruit, open and keep open closed alveoli. The aim of this study was to compare two recruitment maneuvers, a high continuous positive airway pressure (CPAP), and an extended sigh (**eSigh**) in patients with Acute Respiratory Distress Syndrome (ARDS) during lung protective ventilation.* ***Material and Methods:*** *Thirty patients with acute respiratory distress syndrome were randomly divided into two groups, 15 patients each. Group A received a CPAP of 40 cmH_2O for 40 seconds and group B received **eSigh**. We assessed the effects of both recruitment maneuvers on respiratory mechanics and gas exchange. Binary end points were analyzed by means of a Fisher's exact test. Continuous variables were compared with the use of unpaired t-tests, Mann-Whitney test (independent samples), or Wilcoxon ranksum tests (paired samples). $P < 0.05$ was considered statistically significant.* ***Results:*** *Both methods improved the compliance, increased partial pressure of arterial oxygenation (PaO_2), and increased the partial pressure of arterial oxygen / fraction of inspired oxygen (**PaO_2/FiO_2**)ratio. However, the extended sigh improved both PaO_2 and PaO_2/FiO_2 ratios more than continuous positive airway pressure.* ***Conclusion:*** *Both RMs are useful adjuncts in management of mechanically ventilated ARDS patients during lung protective ventilation. Extended sigh (eSigh) is more effective than CPAP as a recruitment maneuver.* ***Keywords****: Recruitment maneuvers, acute respiratory distress syndrome, lung protective ventilation.*

INTRODUCTION

Acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS) represent a continuum of severity for the same pathologic condition, both defined by noncardiogenic pulmonary edema and hypoxemia in the setting of direct or indirect lung injury. Inappropriate ventilation strategies can lead to ventilator-induced lung injury (VILI) which can worsen lung damage in ARDS. [1] The largest randomized, multicenter trial to date demonstrated a significant benefit in mortality of lung protective ventilation by using a tidal volume (V_T) of 6 mL per kg of predicted ideal body weight and a target plateau pressure 30 cm H_2O or less (mortality, 31.0%) as opposed to V_T of 12 mL per kg and a target plateau pressure (P_{plat}) less than 50 cm H_2O (mortality, 39.8%). [2] However, this lung protective ventilation which uses small V_T can cause alveolar derecruitment and arterial hypoxemia. In the ARDSNet trial, patients randomized to the low tidal volume group had lower PO_2 levels, possibly due to alveolar derecruitment. [2] A Recruitment Maneuver (RM) is a procedure where a sustained positive pressure is applied, to an injured lung, over an increment of time, to recruit, open and keep open closed alveoli. Strategies to recruit closed lung units and prevent derecruitment might be beneficial in improving gas exchange as well as reduce the incidence of VILI. Classically, a lung RM requires briefly increasing the

*Asso. Professor, **Prof. & HOD, *** Jr. Resident, Dept of Medicine (ICU) and ****Asst. Prof Dept of Anaesthesia, IMS AND SUM HOSPITAL, Bhubaneswar, Odisha.

alveolar pressure to a level above that recommended during ongoing management of ALI/ARDS, so as to aerate lung units filled with edema or inflammatory cells. Amato et al. [3] employed both lower tidal volumes and RMs followed by optimal positive end-expiratory pressure (PEEP) designed to limit both overdistention at peak inflation and shear injury at end-exhalation. The data on the safety and efficacy of different RMs are not enough till date. [4] The aim of this study was to compare the effects of two recruitment maneuvers, a high continuous positive airway pressure (CPAP) and an extended sigh (***eSigh***) as an adjunct to lung protective ventilation in patients with ARDS.

MATERIAL AND METHODS

An observational prospective study of thirty patients with acute respiratory distress syndrome who were randomly divided into two groups, of fifteen patients each. Group A received a CPAP of 40 cmH_2O for 40 seconds and group B received an extended sigh (eSigh) as an adjunct to lung protective ventilation. The study was conducted in the intensive care unit of a teaching medical college of Eastern India between January 2009 and March 2012. All patients fulfilled the ARDS criteria of the American European Consensus Conference on ARDS [5] which include the following: identifiable associated condition, acute onset, bilateral infiltrates on chest radiography, pulmonary artery wedge pressure $\leq$18 mmHg or absence of signs suggesting left atrial hypertension, and partial pressure of arterial oxygen / fraction of inspired oxygen (PaO_2 /FiO_2) ratio $\leq$200. Patients with hypotension (systolic blood pressure <100 mmHg), significant arrhythmia, or gross baro-trauma in any form (subcutaneous emphysema, pneumo-mediastinum, or pneumo-thorax) were excluded from the study. Also, patients who were having ARDS of more than 3 days duration were excluded from the study. All the patients were intubated with a cuffed tracheal tube and were ventilated with Maquet Servo-i adult ventilators which are equipped with a display screen and software capable of plotting and analyzing the pressure-volume (P-V) curves, pH, partial pressure of arterial oxygen (PaO_2), and partial pressure of arterial carbon dioxide ($PaCO_2$) were measured using the Cobas b 121 POC system blood gas analyzer. The patients were sedated with fentanyl and midazolam during lung protective ventilation and paralyzed with vecuronium during the recruitment maneuvers (RMs). The study was approved by the local Ethics Committee and informed written consent was obtained from the patients or guardians.

Tidal volume (V_T) was set at 6 ml/kg and respiratory rate at 15 per minute in volume control mode (VCV). The PEEP and fraction of inspired oxygen (FiO_2) were set to obtain arterial oxygen saturation (SaO_2) value of 90-95% or partial pressure arterial oxygen (PaO_2) of 60-80 mmHg (baseline). Patients were randomly divided into two groups. Each group contained 15 patients. Randomization was done by an independent statistician using a random number generated by computer. The investigator who was responsible for the collection of the data was blinded in respect to the study protocol during the whole process of data evaluation.

Recruitment maneuvers

CPAP was performed by imposition of a sustained pressure of 40 cm H_2O for 40 seconds without delivering tidal volume (V_T) for this the ventilator was set on the CPAP mode. The ventilator was then set back to its baseline values.

Extended sigh (eSigh), consisted of increasing PEEP 10 cm H_2O above the lower inflection point (LIP) for 15 minutes, the patient being on volume-controlled ventilation. eSigh was performed twice with one minute of baseline ventilation in between. If necessary, V_T was decreased to maintain P_{plat} below the upper inflection point (UIP) or below 35 cm H_2O if UIP could not be identified on the zero end-expiratory pressure (ZEEP), pressure volume (P-V) curve. During the RM, the maximum peak airway pressure was limited to 50 cm H_2O. In case of severe arterial hypotension (systolic arterial pressure of less than 70 mm Hg) or severe hypoxemia (SpO_2 of less than 80%), the RM was immediately stopped. The outcome measures were

changes in the pulmonary mechanics and arterial blood gas parameters.

Pulmonary mechanics

Static and dynamic compliance of the respiratory system (C_{st} and C_{dyn}) were recorded from the display on the ventilator digital monitor at baseline, 5, and 60 minutes after application of the recruitment maneuver. Airway pressures (peak, mean, plateau) (P_{peak}, P_{mean}, and P_{plat}) were also read from the display on the ventilator digital monitor at baseline, 5, and 60 minutes after application of the recruitment maneuver. Pressure volume curves were obtained by the quasistatic method[6] at baseline, 5, and 60 minutes after recruitment; analysis of the pressure-volume (P-V) curve of the respiratory system was done as follows: the P-V curve was displayed on the screen of the ventilator, the obtained P-V curve was frozen on the screen, and controlled mechanical ventilation was resumed. Two cursors present on the screen were used to determine the lower and the upper inflection points of the P-V. The parameters were calculated automatically by the ventilator after positioning the cursors. The whole maneuver took 2 minutes at the bedside without requiring any special equipment. Values of pressures at the upper and lower inflection points of the P-V curve were quantified.

Arterial blood gas parameters

Arterial blood gas analysis was done baseline, 5, and 60 minutes after application of the recruitment maneuver. The PaO_2/FiO_2 at ratio was calculated at baseline, 5, and 60 minutes after application of the RMs.

Bedside chest X-ray films were taken at baseline and one hour following recruitment to note the presence of any pneumo-thorax, pneumo-mediastinum, or pneumatocoeles for assessment of the safety of the RMs.

STATISTICAL ANALYSIS

Data are expressed as mean ± standard deviation. Binary end points were analyzed by means of a Fisher's exact test. Continuous variables were compared with the use of unpaired t-tests, Mann-Whitney test (independent samples), or Wilcoxon ranksum tests (paired samples). All odds ratios and their corresponding 95% confidence intervals were calculated according to the profile-likelihood method. All p values were 2-tailed and p values of < 0.05 were considered statistically significant.

RESULTS

After the recruitment maneuvers the static compliance (C_{st}) and the dynamic compliance (C_{dyn}) increased both increased after 5 minutes and also after 60 minutes compaired to baseline. However the magnitude of change was not significant when both groups were compaired statistically.

Peak inspiratory, mean airway, and plateau pressures decreased slightly in both groups but there was no significant difference between both groups [Table 2.].

In group A, the upper inflection point (UIP) disappeared in three patients following the recruitment maneuver; in the remaining 12 patients, there was an increase in the UIP following the recruitment maneuver. In group B, the UIP disappeared in six patients following the recruitment maneuver; in the remaining 9 patients, there was an increase in the UIP following the recruitment maneuver. There was no significant difference between both groups [Table 2.].

In group A, the LIP could not be detected at the baseline in five patients; in the remaining 10 patients, the LIP did not show significant change. In group B, the LIP could not be detected at the baseline in two patients. In the remaining patients, the LIP did not show significant change. There was no significant difference between both groups before or after recruitment maneuvers [Table 2.]

Both methods improved arterial oxygenation, increased the PaO_2/FiO_2 ratio, and decreased the pulmonary shunt fraction. The extended sigh improved both arterial oxygenation and PaO_2/FiO_2 ratio more than the CPAP method. MAP in the CPAP group was

Table 1. Baseline Characteristics of the Study Patients *

Table 1. Baseline Ch
Variable
Age — yr
Female sex — no./tot
Weight — kg
Body-mass index†
Reason for ICU admi
Operative
Nonoperative
Location before ICU
Emergency departm
Hospital floor (or w
Without previous ICU

* Plus–minus values are means ± SD. Acute Physiology and Chronic Health Evaluation II (APACHE II) scores can range from 0 to 71, with higher scores indicating more severe illness, and Sequential Organ Failure Assessment (SOFA) scores can range from 0 to 4 for each organ system, with higher scores indicating more severe organ dysfunction. Severe sepsis was defined according to the consensus-conference criteria of the American College of Chest Physicians–Society of Critical Care Medicine.[12] ICU denotes intensive care unit, PEEP is positive end-expiratory pressure, PaO_2/FIO_2 is partial pressure of arterial oxygen / fraction of inspired oxygen ratio and I:E is inspiratory : expiratory time ratio.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

Table 2: Respiratory mechanics and arterial blood gas parameters in both groups.*

Table 2 : Respiratory mechani	
Variable	**G**
C_{st} (ml/cmH_2O) Baseline After 5 min. After 60 min.	
C_{dyn} (ml/cmH_2O) Baseline After 5 min. After 60 min.	
PIP (cmH_2O) Baseline After 5 min	

* Plus–minus values are means ± SD. ǃ indicates P value < 0.5. CPAP = continous positive airway pressure , Cst =static compliance, Cdyn = dynamic compliance, PIP = peak inspiratory pressure, P_{aw}= mean airway pressure, P_{plat}= plateau pressure, UIP = upper inflection point, LIP = lower inflection point; PaO_2 is partial pressure arterial oxygen; PaO_2/FIO_2 is partial pressure of arterial oxygen / fraction of inspired oxygen ratio.

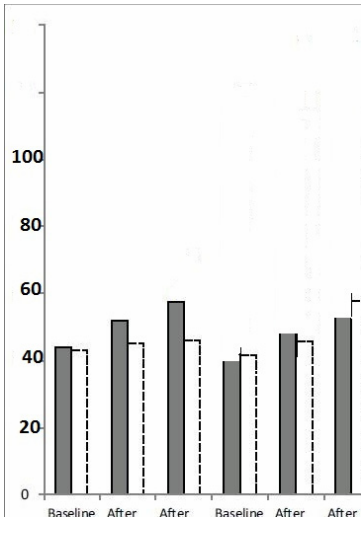
Table 3. Outcomes and Adverse Events.*

Table 3. Outcomes and A	
Outcome Measure	G (((me *n*=15
Death — no. of patients/total no. (%) ; all cause 30-day	3/15
Days in ICU — median (IQR)	16 (1
Days in hospital —	23 (1

* Plus–minus values are means ± SD. ICU intensive care unit, and IQR interquartile range.

† Absolute differences (percentage points) are given for median days in the ICU or hospital, and mean ± SD days of mechanical ventilation; for all other measures, odds ratios are given.

Graph 1. Respiratory mechanics and arterial blood gas parameters in both groups.*



*Cst =static compliance, Cdyn = dynamic compliance, PaO_2 is partial pressure arterial oxygen, PaO_2 is partial pressure arterial oxygen, CPAP is continuous positive airway pressure.

significantly lower than in the extended sigh group.

In both groups no baro-trauma, pneumo-thorax, or any other complications were found in the chest X-rays. There was no difference in all-cause 30 day mortality, ICU length of stay, days of hospitalization or duration of mechanical ventilation in the two groups. [Table 3.]

DISCUSSION

The present study showed that both CPAP and extended sigh methods of recruitment maneuvers improved the static and dynamic lung compliance. The arterial oxygenation increased and the PaO_2/FiO_2 ratio improved, and reduced the pulmonary shunt fraction. However, the extended sigh improved arterial oxygenation and PaO_2/FiO_2 ratio more than CPAP. No pneumo-thorax or baro-trauma was detected.

Several methods have been employed to carry out RMs in the clinical setting as well as in experimental models. The ideal timing, duration, pressure, and mode of recruitment maneuvers have not yet been clearly identified. Rothen *et al.* showed that a sustained inflation maneuver of 40cm of H_2O, for 7-8 seconds might re-expand all collapsed lung units as evident on CT scans of the chest and improve oxygenation in anesthetized subjects. [7] In another study, three consecutive sighs of plateau pressure 45cm of H_2O were applied every minute for an hour. This resulted in an increase in the end- expiratory lung volume, reduction in the intrapulmonary shunt, and improvement in oxygenation. [8] Lapinsky *et al.* applied a sustained inflation maneuver of 45cm of H_2O or the peak pressure at a tidal volume of 12mls/kg, whichever was lower, for a period of 20 seconds. An improvement in oxygen saturation was noted in all patients; in 10 out of 14 patients, this was sustained for up to four hours. No significant adverse effects were noted. [9] Lim *et al.* used an 'extended sigh' (e-sigh) as an RM. [10] This involved gradually reducing tidal volumes from 8-2mls/ kg and increasing the PEEP from 10-25cm of H_2O in a stepwise manner, each step lasting 30 seconds. When a tidal volume of 2mls/kg and a PEEP of 25cm of H_2O were reached, a Continuous Positive Airway Pressure (CPAP) level of 30cm of H_2O was applied for 30 seconds following which a reverse sequence was applied till the baseline settings were reached. The authors could demonstrate a statistically significant increase in PO_2 and static compliance with this maneuver. RMs may also be practicable in spontaneously breathing patients.

The patient should be monitored for hypotension and fall in oxygen saturation during the RM. It is also important to emphasize that an RM should be followed up with an appropriate PEEP level, set in a decremental fashion; otherwise derecruitment may occur.

Amato *et al.*, in their landmark paper, studied 53 patients with ARDS using a low tidal volume of 6mls/ kg on one arm combined with RMs and compared this with a tidal volume of 12mls/kg on the other arm. They found a significant mortality reduction in the low tidal volume group - 38 vs 71%. [3]

Gattinoni *et al.* studied 67 patients with ALI or ARDS using CT scans to assess recruitability. [11] Whole lung CT scans were done at an inspiratory plateau pressure of 45cm of H_2O followed by PEEP levels of 5 and 15cm of H_2O. The extent of recruitable lung was highly variable, with a mean of 13 ± 11% of the total lung weight. Progressive increase of airway pressure resulted in an increase of hyperinflated and normally aerated lung. More recruitable lung correlated with a higher fraction of nonaerated lung tissue, a lower P/F ratio, lower compliance, higher PCO_2, greater shunt fraction, and increased mortality. Physiological variables such as improved P/F ratio, compliance, and reduced PCO_2 predicted recruitability with a sensitivity of 71% and specificity of 59%.

Recently, Lowhagen *et al.* [12] performed the SLRM "slow moderate pressure recruitment maneuver" and compared it against a vital capacity recruitment maneuver (VICM). The two recruitment maneuvers were performed on patients with early ALI/ARDS followed by decremental PEEP titration. SLRM provided the best response in compliance, PaO_2/FiO_2 and venous admixture at significantly lower PEEP and plateau pressure.

CONCLUSION

Recruitment maneuvers may prevent lung derecruitment and fall in oxygenation associated with low tidal volume ventilation strategies employed in ARDS. The extended sigh was more effective than CPAP as a recruitment strategy. Although both RMs have shown to improve gas exchange, there is no evidence that suggests improved morbidity or mortality. The primary role of RMs may be as rescue therapy in refractory hypoxia in patients with severe ARDS.

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Original Article

EPIDEMIOLOGY OF BETA THALASSAEMIA TRAIT IN EASTERN INDIA

S. Meher*, D.K. Patel*, S. Patel*, S. Dehury*, P. Purohit*, K. Das*

ABSTRACT

Aim : *To report the findings on Betathalassaemia Trait (BTT) and its epidemiology in Eastern India.* ***Results :*** *Of the 5690 samples tested, 213 individuals (101 female), were found to have BTT. The frequency was 3.74%. The mean age of male was 31.1 ± 14.1 years and that of female was 31.7±14.6 years. Highest frequency of cases were from Bargarh and Jharsuguda districts (17.31% each), followed by Sambalpur, Sundargarh and Bolangir districts (15.87, 15.38, 12.50% respectively) of western Odisha. Lower no. of cases were from Sonepur & Deogarh districts (6.73% & 4.81% respectively). 97.65% cases were Hindu, 0.94% cases were Muslim, 1.41% cases were Christian by religion. 44.6% Hindu BTT were OBC by category followed by 24.88% SCs, 14.08% each were found to be from General Caste & STs.* ***Keywords :*** *Beta Thalassaemia, Eipidemiology, Haemoglobinopathy.*

Introduction:

Beta Thalassaemia is a single recessive gene haemoglobinopathy, which in homozygote condition leads to fatal thalassaemia disease causing severe anaemia necessitating periodical blood transfusion, leading to progressive Iron overload, significant hepato-splenomegaly and even causes death if not treated adequately [1,2]. On the other hand the heterozygote state of thalassaemia (Beta thalassaemia trait, mentioned as BTT here) is benign and presents no clinical severity. Nevertheless detection of BTT has been very important in knowing the epidemiology of the gene and in effort of prevention of the disease by prenatal diagnosis. The only way to detect BTT is by its exclusive presentation of typical microcytic hypochromic CBC finding and a hallmark elevation in % HbA2 fraction [3].

There have been different strategies recommended for prevention in countries with higher risk for â-thalassaemia. Most of them include carrier screening programme followed by either PND or retrospective social counselling discouraging high risk marriages at community level [2,4,5]. However, explicit epidemiological data is quite essential in revealing the risk associated with higher prevalence of the disorder as well as in earmarking the zone and communities to be given priorities on implementing preventive strategies. Even countries like Iran, where specific cultural practices proscribe PND and other preventive measures for genetic disorders, have initiated community and government level preventive measures in practice lately. The instances of Cyprus, Sardinia and Greece have demonstrated that baseline information on the epidemiology of thalassemia helps in strategic implementation of preventive measures [6,7].

In India, numbers of studies have been done on the distribution of BTT and the prevalence of its disease state. Almost all the communities and ethic groups of India have this gene with a wide variation of occurrence [8,9,10]. Recent data on the heterogeneity of molecular spectrum of â-thalassaemia also have been used to explain the gene flow and localisation of mutations responsible for the disorder among certain high risk populations and regions [11,12,13]. Among all the Eastern Indian states, Odisha, inhabited by over 36.8 million people comprising 22.13% Scheduled Tribes and 16.52% Scheduled Castes, is home to a large

* Sickle Cell Clinic & Molecular Biology Laboratory, V.S.S. Medical College & Hospital, Burla, Odisha.

number of communities who still adhere to restricted mating boundaries and hence give way to a very shallow gene flow. Over generations, though there have been admixtures between and within regions of Odisha, but till date most ethnic groups are localised with respect to their genetic composition. Though the state is already been highlighted for its high frequency of HbS gene and the number of thriving Sickle Cell Disease patients, only a few studies on the prevalence of â-thalassaemia gene are undertaken.

Now it is well known that the prevalence of BTT ranges from 1-17% in the Indian sub continent [14,15,16] with an overall frequency of 3-4% [17,18]. In the Eastern Indian states the frequency of BTT has been reported to vary from 0 to 12% [19,20,21,22]. There have been sporadic reports of â-thalassaemia from Odisha, either in heterozygote state [23,24] or in double heterozygote state with HbS [25]. Even though few studies done on â-thalassaemia have reported prevalence of BTT among many communities from Odisha, the data does not essentially represent the epidemiology of BTT in the state, primarily because almost all the studies are on patients either referred to a tertiary hospital or are from retrospective screening of â-thalassaemia disease families [26].

In the Sickle Cell clinic established at the V.S.S.Medical College, Burla, Odisha, we accommodate a huge number of patients with severe Sickle Cell haemoglobinopathies since 2005. During the routine community based blood screening and periodically organized health camps in various places of six districts of Odisha, we have detected a large number of individuals with BTT. It is pertinent to mention here that a significant number of individuals from other states like Chhattisgarh, Jharkhand and West Bengal also attend and voluntarily participate in these blood screening camps. We present here the outcome of our study on BTT from this centre.

Objective:

To report the findings on BTT and its epidemiology in eastern India.

Material and Method:

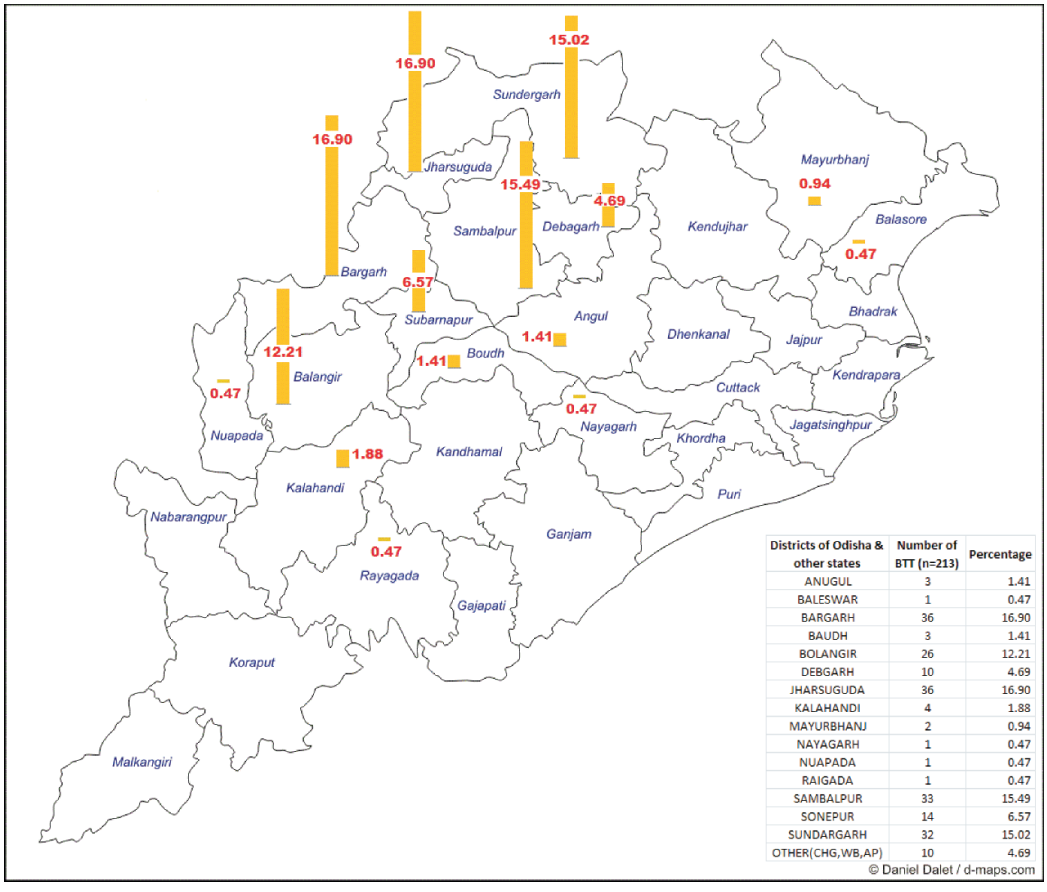
Total of 5690 individuals volunteering to participate in the blood screening camps or referred for ANC routine check up were tested for their BTT status in the Sickle Cell clinic and Molecular biology Laboratory, V.S.S.Medical College, Burla, Odisha, India between November 2010 and July 2012. 2-3 mL of venous blood was collected in EDTA vaccutainers and were transported to the laboratory under recommended condition. All samples were subjected to Complete Blood Count by automated cell counter (Sysmex KX-21; Kobe, Japan) within 8 hours of collection, alkaline agarose haemoglobin electrophoresis at pH 8.6 and quantification of haemoglobin fractions by HPLC (Variant II â-Thalassaemia short program, Bio-Rad, Herculus, CA, USA). We have used below 80fl cut off for MCV and below 27 pg for MCH as the inclusion criteria for suspecting BTT as illustrated [3]. Cases with HbA2 above 3.5% [27] and HbF below 3.0% were considered as BTT [28]. Data detailing on place of residence, ethnic group, parental origin, any family history of beta thalassaemic individuals and other relevant information were recorded from all individuals.

Results:

Of the 5690 samples tested, 213 individuals (101 females) were found with BTT who had no apparent clinical presentation. The mean age of male was 32.1±14.1 years and that of female was 31.7±14.6 year. It is noteworthy to mention here that three (1.16%) cases of BTT were found among a total of 259 cases of pregnant women attending to this clinic. The age and sex distribution of BTT cases are presented in Table-1. Overall the BTT occurrence seems to be on a par among the males and females. However, the figure of Male children (aged below 10 years) with

Table-1: Age and sex distribution of BTT in Odisha

Fig 1: District wise frequency of â-thalassaemia trait in Odisha



Districts of Odisha & other states	Number of BTT (n=213)	Percentage
ANUGUL	3	1.41
BALESWAR	1	0.47
BARGARH	36	16.90
BAUDH	3	1.41
BOLANGIR	26	12.21
DEBGARH	10	4.69
JHARSUGUDA	36	16.90
KALAHANDI	4	1.88
MAYURBHANJ	2	0.94
NAYAGARH	1	0.47
NUAPADA	1	0.47
RAIGADA	1	0.47
SAMBALPUR	33	15.49
SONEPUR	14	6.57
SUNDARGARH	32	15.02
OTHER(CHG,WB,AP)	10	4.69

Table-2: Caste-wise distribution of beta Thalassemia Trait cases

Religious communit
Hindu (N=208)
Christian
Muslim

Table-3: Haematological presentation of 213 BTT Cases from Odisha

Haemtalogical parameters	M
Hb (g/dl)	1
RBC ($\times 10^{12}$/l)	5
MCV (fl)	7
MCH (pg)	2
MCHC (g/dl)	2
HbA2 (%)	4
HbF (%)	0

BTT is almost double to that observed in the females. It is apparent from the figures in Table-1 that almost 23% of males detected to be BTT are below 17 years of age, whereas in females almost 65% of BTT detected cases are in their child bearing and pre-menopausal age group (20-40 years).

Sizeable number of individuals from Odisha were included in the present study. Highest frequency of cases were from Bargarh and Jharsuguda districts (17.31% each), followed by Sambalpur, Sundergarh and Bolangir districts (15.87, 15.38, 12.50 % respectively) of Western Odisha. Interestingly a lower number of cases were there from Sonepur and Deogarh districts (6.73 & 4.81% respectively). The study also included cases from adjacent states. Ten cases of BTT were detected among individuals from Andhra Pradesh, west Bengal and Chhattisgarh states. Map showing the frequency distribution of BTT in different districts of Odisha is presented in Fig-1.

Caste/ethnic group wise prevalence of BTT in Odisha (Table-2) reveals that, 97.65 % (208/213) BTT cases in our data were Hindu by religion. Two cases of Muslims (0.94%) and 3 cases of Christians (1.41%) had been found to have BTT. 44.6% Hindu BTT were OBC by category followed by 24.88% SCs. 30 cases each (14.08%) were found to be from the general caste and STs.

It is well understood that the MCV and MCH cut offs are significantly affected by the selection of %HbA2 cut off in predicting success of BTT in population based screenings, especially where higher methods like HPLC of DNA based confirmation are not available. However, MCH has been suggested to be better marker in association with %HbA2 between 3.5 (lower cut off) and 4.0 (higher cut off) [29]. As anticipated, with increase MCV and MCH value, % HbA2 decreases and with an increase in the % HbA2, RBC count increases among the BTT cases in our study. The statistical constants of the haematological presentation of BTT are depicted in Table-3.

Conclusion:

In our study all the cases with a microcytic hypochromic CBC and HbA2 more than 3.5% were confirmed against presence of â-thalassaemia mutation by ARMS PCR at the Sickle Cell Clinic. MCV as low as 56.5 fL and %HbA2 as high as 6.5 among the 213 BTT suggests high frequency of severe â-thalassaemia mutations in the populations and the area. This was confirmed by the molecular study on mutational profiling of â-thalassaemia of all cases. About 97% of â-thalassaemia mutations were found to be IVS-1-5-G>c, cd41/42 (-4 bp) and cd15 G>A mutations (data not presented).

It was also found that HPLC based detection of BTT by considering an elevated HbA2 (above 3.5%) is highly sensitive and moderately specific which was in conformity to earlier studies [3]. Moreover the automated system allows high throughput of samples. Our experience with HPLC recommends that this system can be used efficiently in large scale population

based surveys on BTT detection and reporting, thus making it convenient for epidemiological studies on widely distributed sub-structured ethnic compositions suiting Indian scenario.

The present study depicts the BTT frequency in Odisha to be 3.74% (213/5690) which is in agreement to the reported BTT frequency from Eastern India [30,31,32,33,34,35]. Looking at this high frequency of BTT in this part of the country and appreciating that only a few studies have addressed to the epidemiological depiction of the gene, the present study, as a bench-mark approach, attempts to exemplify the general trend of BTT frequency and its distribution over different regions and ethnic groups of Odisha.

It is noteworthy here to mention that, though the ST population of Odisha is only one fifth of that of the total population whereas the general castes prevail in number over the STs many folds, still a finding of 14.08% cases each from STs and general population in our study indicates high frequency of BTT in the tribes of Odisha. The finding that the other religious groups like Muslims and Christians have lower frequency of BTT in our study differs from the observation from West Bengal [19].

The trend observed in this study though is unique in its reporting of BTT from Odisha, in order to avail a definitive depiction on the â-thalassaemia gene in Eastern India especially in such a high risk belt for HbS, more effective and in-depth population based surveys are of much importance to mark the distribution and epidemiology of the gene in this part of the country.

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Original Article

PROFILE OF SELF-POISONING AMONG ADULTS: STUDY FROM A TERTIARY CARE HOSPITAL IN EASTERN ODISHA

***P.K. Behera, *K.P. Tripathy, *C. Das, **A. Devi**

ABSTRACT

Objectives: *The aim of the present study is to find out the current trend and pattern of self poisoning in regard to socio-demographic profile of patients, type of poison and outcomes in hospitalised patients in Eastern Odisha.* **Material and Methods**: *The Present study is a hospital based observational study with prospective data collection. The subject population included all adult patients admitted to the Medicine ward or ICU of Hi-Tech Medical College and Hospital, Bhubaneswar with history of poisoning, during the period from March 2010 to March 2012.Snake bites and insect stings were excluded. Detailed history regarding poison substance used, apparent cause of poisoning, demographic profile of patients were collected either from the family members or from the patient .All the data were collected in a format and were analysed at the end.* **Results :** *Total of 163 cases were included in the study with a male to female ratio of 1:1.29. 20-39 yrs was the most common age group (61.3%) followed by 14-19 yrs (21.4%). Most of the patients were unmarried (55.2%) and were from low or middle income group (89%). Patients were almost equally from urban (31.5%), semi urban (32.5%) or rural (36%) areas. Most of the patients were educated either attended school (44.3%) or college (50.3%). Among various poison substances used, pesticides were the most common poison to be used (41.3%). Significant number of patients used commonly prescribed medicines (31.2%) or household products for poisoning. Irritant poisons and caustics which mostly included house hold products were 22%. Most of the cases suicide was the main intention behind self poisoning (87.1%). Mean hospital stay was 5.4 days and overall mortality was 2.4%.* ***Conclusion:*** *There is a change in the socio demographic profile in self poisoning in adults as well as the poison substance used in comparison to the trend observed one decade ago. Young, educated, unmarried people from urban and semi urban areas with increasing number of females with a low socioeconomic background are the most common victims of self poisoning. Commonly prescribed medicines and house hold products are increasingly being used as the poison substance.* **Key words**: Self –poisoning, pesticides, literacy, un-employment, college students, house hold products.

INTRODUCTION:

Rapid industrialisation, advancing science and technology, increasing literacy, growing economy has brought a lot of hope and expectation in social life. At the same time unemployment, ever increasing stress in work place, academics and business with fragile family and personal relationship has brought frustration and despair. The inability to balance these expectations and frustrations has resulted in increasing number of suicides. Massive use of pesticides in agriculture, increasing alcohol and substance abuse, use of hazardous chemical products in domestic life, increasing and easy availability of pharmaceutical products has widened the spectrum of toxic products to which people has been exposed as compared to earlier days and has resulted in increasing suicidal as well as accidental poisoning.[1,2.]

*Asso. Professor, **Prof & HOD, Dept. Of Medicine, Hi-Tech Medical College, Bhubaneswar, Odisha.

Easy availability and low cost of hazardous chemicals plays a major role in both accidental and suicidal poisoning in developing countries like India, Sri Lanka ,South Africa etc.[2,3,5.] Lack of specialised toxicological services in developing countries like India has further contributed to the higher rate of morbidity and mortality.[3,4.]

WHO estimated 6.3 million people die every year due to various poisoning agents.[6] High doses of analgesics, tranquilisers and antidepressants are the commonly used agents for intentional poisoning in industrialised countries whereas agricultural pesticides are used in Asian region for self poisoning particularly in rural areas with a fatality range of 10-20%. [9,10] A comparative data revealed that in developed countries the mortality rate due to poisoning is only 1-2% but in developing countries like India it varies between 15-30%and is the fourth most common cause of mortality in rural India. [7,8.]

So this study has been aimed to determine various parameters and socio –demographic profile of poisoning.

MATERIAL AND METHODS:

This study was undertaken as a hospital based observational study with prospective data collection and analysis. All the adult cases with a diagnosis of poisoning admitted to the Medicine ward or ICU of Hi-Tech Medical College and Hospital between March, 2010 to March, 2012 were included in our study. Hi-Tech Medical College and Hospital is a 600 bedded, private Medical college & hospital with 20 bedded central ICU, well equipped Central Laboratory and all super speciality services, located in Bhubaneswar, Odisha. Patients mostly come from adjacent districts of eastern Odisha . Cases of snake bite or insect sting were not included in the study. Information and data were collected both from the patient as well as family members regarding age, education, marital status, employment, annual income, disharmony in family, personal relation or work place including academic stress and apparent cause of poisoning. In all cases proof of the poison substance was sought but only in few cases the poison bottle or the medicine strips were available and the substance identified .In other cases patients or family member's claim of a poison was corroborated with the patients' clinical feature. All the above data were collected in a Performa and were analysed.

RESULTS:

During the study period total of 163 patients with history of poisoning were admitted and were included in the study. Out of them 71(43.5%) were male and 92(56.5%) were female with a ratio of 1:1.29. The median age of patients was 24 yrs. Majority of them were in the age group of 20-39 yrs (61.3%) followed by 10-19 yrs(21.4%), and 40-59 yrs(14.1%). Patients above 60 yrs were only 3.2%. When age and sex were considered all patients above 60 yrs were male while below 60 yrs, females (65%) out -numbered males (35%).The route of exposure was oral in all cases .No case of inhalational or dermal exposure was admitted. Out of 163 cases 142 cases (87.1%) were intentional self poisoning, 18(11%) were accidental poisoning and 3(1.9%) were apparently for robbery or homicidal purpose. Patients were almost equally from rural (36%) urban (31.5%) and semi urban (32.5%) areas. Out of 163 patients 90 (55.2%) were unmarried and 73 (44.8%) were married. When literacy was considered 82 patients (50.3%) were having above 10^{th} standard but below masters degree. 71 cases (44.3%) were below 10^{th} standard and only 5.4% patients were illiterate. None of the patients were having masters degree or above. Majority of our patients were students (41.1%). 37.4% cases were unemployed and only 21.5% patients were having some form of employment. When family income was considered, majority (50%) were having annual income of less than 1 lac. only 11% were having annual income of more than 3 lacs. Rest 39% were having annual income between 1-3 lacs. Pesticides were the most common poison consumed (41.3%) followed by pharmaceutical products like commonly prescribed medicines and sedatives (31.2%). Irritant poisons (both organic and inorganic) were used in 14.1%cases and caustics (acids and alkalis) in 7.9% cases. Cases of substance overdose like alcohol and cannabis were 5.5%.The average hospital stay was 5.4 days .Most of them were discharged home in stable condition after treatment in wards. 14 patients (8.5%) were shifted to ICU either from casualty or subsequently from wards for severity of the condition and overall mortality was only 2.4%.

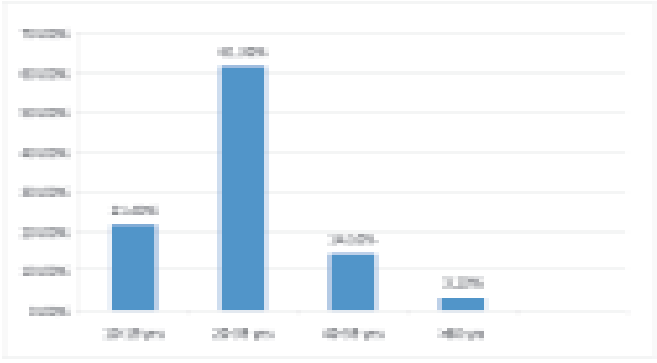

Fig 1: Age wise distribution of cases

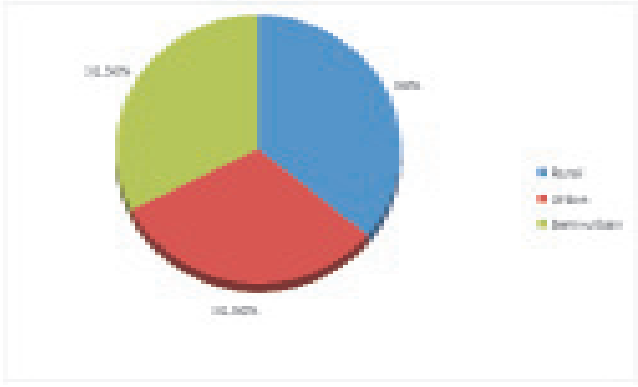

Fig 3: Distribution of patient according to residence

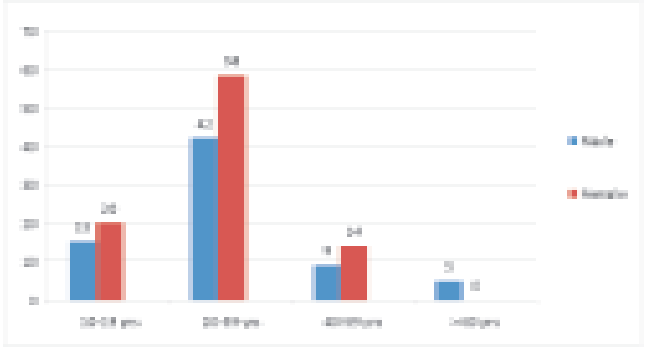

Fig 2 Age & Sex distribution of cases (In numbers)

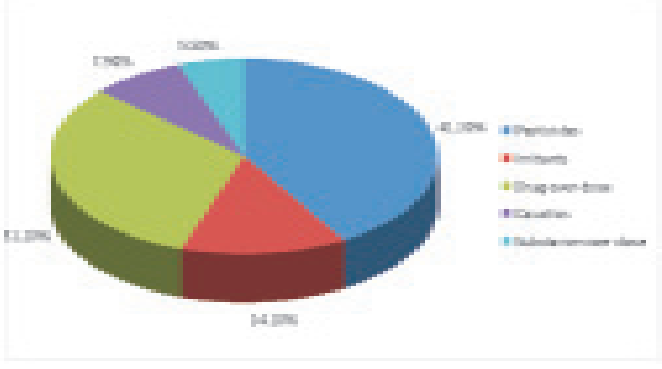

Fig 4: Distribution of various poison substances in percentage.

Table 1: Distribution of patients according to literacy

DISCUSSION:

Various national and international studies have projected the rise in incidence of intentional poisoning cases[11]. During our study period of 24 months 163 cases were admitted with average admissions of 6-7 cases per month. Though this is a lower value in comparison to the observation of Dash et al[3] from MKCG Medical college, Berhampur, who observed 12-13 cases of poisoning admitted per month. This may be due to the fact that poisoning is more prevalent in low socioeconomic groups who prefer Govt. Hospitals over private hospitals. In our study females outnumbered the males with a male to female ratio of 1:1.29 in contrast to many other studies where poisoning was more common in males.[3,12,13, 14]. High incidence of male patients in earlier studies was thought of due to the fact that males were facing more stress and strain of life as family heads and exposed to outside world. But with a change in the status of females in family and society and their active participation in public life they are equally vulnerable to mental stress and strain which has led to increase in proportion of female poisoning. The age group with maximum incidence of poisoning in our study was between 20-39 yrs followed by 14- 19 yrs and was significantly less in the age group above 60 yrs. This is in accordance with the observations of many other previous studies done in our country and abroad. [3,14, 15, 16] Increased incidence of poisoning in this young and active age group is of great concern. This is mostly due to failure of academic performance, break-ups in personal affairs, not able to maintain a life style at par with the peers because of financial constraints or unemployment. Immature minds with expectations out of proportion to realty end up in suicides from poisoning. There is an urgent need of an intervention programme for these young adults and adolescents.

In our study we found unmarried persons were more often victims of poisoning than married people. This is in contrast to the observation of many other similar studies where poisoning was more prevalent among married people. [3,14,15]This change in trend may be due to a late age of marriage in present days or young unmarried people staying away from home frequently getting into multiple love affairs and break ups ending in suicides.

Studies by Agarwal R et al [15], Das et al [3] and Dhattarwal SK et al [19] has shown that most patients were from rural areas but the patients in our study were mostly equally from rural, semi urban and urban areas. This trend is probably due to increased immigration from rural areas to semi urban and urban areas, increased population density in urban areas with more stress in urban life. In our study patients were more from lower and medium income group as compared to high income groups. Similar trend was observed by many other authors in similar studies. [3,17,18] The vulnerability of lower and middle income group may be due to that fact that they are under continued financial and other stresses in life. In respect to literacy status, previous studies by Dhattarwal SK et al [19] from Rohtak, Haryana and Dash et al[3] from Berhampur , Odisha showed poisoning was more prevalent among illiterates or lower educational level. It was presumed that failure in life and tolerance to problems were better understood by literates than illiterates .In contrast our study showed higher rates of poisoning among literates. Most of our patients were having minimum of high school education and significant number were college students or college passed. This change may be due to increasing literacy in the society as well as this group of people are active in life , trying for a good academic carrier or job and are under mental pressure.

Several studies [16,17,18] have reported that pesticides are the most commonly used agents for self poisoning, particularly in Asia-Pacific Region including India, which was also observed in our study. Pesticides are commonly used in rural and semi urban areas for use in farm lands or preserving crops. Because of lack of stringent regulation in its sale and low cost these are easily procured and consumed for suicide purpose. There is an increasing trend in use of commonly used medicines and house hold products (irritant poisons) as observed in our study. Medicines like anti-cold preparations, sleeping pills, anti-malarials, anti-amoebic preparations which are often stored in houses were frequently used for self poisoning. In many cases drugs like antidepressants or anti epileptics which are frequently bought on monthly basis were used. Similar observations were also found by Jesslin J et al [20] and McClure GM et al[9]. Poisoning from household products like phenyl, floor cleaner, car wash , Hair dye etc

which were more common in childhood poisonings are now common among adults, as noted in our study as well as many other studies.

The hospital stay of patients with poisoning ranged between 1 to 30 days with mean hospital stay of 5.4 days which coincides with the observation of Kiran N et al[21]. The overall mortality rate was 2.4% which is significantly lower in comparison to many other studies.(Singh B et al[22] 15% and Kiran N et al[21]-14.86%). This may be due to development of infrastructure leading to early transport of patients to hospitals and improvement in health care services like emergency and ICU services.

CONCLUSION:

The incidence of self poisoning is increasing and there is a shift in the socio-demographic profile of patients from what was observed one decade before. At present self poisoning is more prevalent among females and among educated mass. More patients are from urban or semi urban areas. Unmarried, college going or college passed out people from low or middle income group are more vulnerable for self poisoning. The high prevalence of poisoning among young and educated people in the society needs urgent attention and intervention. Programs for educating young people against harmful outcomes of poisoning should be planned. School and colleges should take extra care to reduce academic stress from adolescents and young adults, should teach and motivate to cope with increasing stress and strain in life. Parents should not put extra pressure regarding academic or carrier, rather help the young minds to cope with ever increasing pressure .The print and electronic media has also some role in reducing this emerging problem in the society. All these efforts may bring down the incidence, morbidity and mortality of self poisoning.

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Original Article

AETIOLOGY OF ACUTE VIRAL HEPATITIS (AVH) WITH PARTICULAR EMPHASIS ON MAGNITUDE OF HEPATITIS A VIRUS (HAV) INFECTION AND ITS CLINICAL COURSE IN ADULTS

U.C. Patra[*], M. Nayak[**], C.R. Sarangee[***], A Devi[****]

ABSTRACT

In this prospective study, two hundred and fifty four patients diagnosed to be having AVH were analyzed with reference to clinical profile & viral markers and statistical analysis was done. Isolated viral infection was documented in 102 (40.1%) patients where as more than one hepatotrophic viruses caused AVH in 27(10.6%) patients. Non A-E Virus was the major case of sporadic AVH (40.1%), HBV & HEV were the etiological agent in 23.6% & 25.1% respectively. HAV was detected in 16.5% of the patients and the HCV was incriminated rarely as cause of sporadic AVH. The demographic, clinical and biochemical profile amongst isolated & mixed viral infection were found to be similar. However, HBV-AVH had significant prolonged course ($p<0.001$) and HAV-AVH was found to have significantly higher number of patients pursing a course of relapsing hepatitis. However HAV infection amongst adults in the present study was not found to cause severe liver disease except in few cases. ***KEY WORDS:*** *AVH - Acute Viral Hepatitis, HAV-AVH - Hepatitis A virus induced AVH, HBV-AVH - Hepatitis B virus induced AVH, HEV-AVH - Hepatitis E virus induced AVH, HCV-AVH - Hepatitis C virus induced AVH*

INTRODUCTION:

Viral Hepatitis, caused by hepatitis viruses A through E, is a major public health problem in India[1], since 1955, several epidemics of hepatitis have been reported[2-8]. Although hepatitis A Virus (HAV) and hepatitis E Virus (HEV) both enterically transmitted are highly endemic in India, HEV has been responsible for most of these epidemics[2,8,10]. In India, HEV infection is responsible for 30-70% of cases of acute sporadic hepatitis & the major cause of Acute Liver Failure (ALF)[11]. Amongst children, HAV is the predominant cause of acute hepatitis and dual infection with HAV & HEV have been more frequently reported amongst children with ALF[12]. There are no published data in Eastern India especially in the State of Odisha. Further our clinical impression indicates rise in frequency of HAV Infection amongst adults causing severe and atypical form of hepatitis. In view of paucity of data on the aetiology and clinical profile of AVH due to different hepatotrophic viruses, the present study was undertaken to prospectively evaluate.

1) The aetiology of AVH in a tertiary care referral center in Eastern India, especially in the State of Odisha.

2) The clinical course of the HAV induced acute hepatitis amongst adults and to compare the clinical course of AVH due to HAV, HBV, HEV and Mixed Infection.

MATERIAL AND METHODS:

Acute Viral Hepatitis (AVH) was diagnosed if a patient presented with following clinical & biochemical characteristics -

a) Acute onset clinical symptoms characteristics of AVH such as prodrome followed by onset of overt icterus or biochemical evidence of hepatitis.

* Prof. & HOD, Department of Hepatology, **Asso. Prof., Dept. of Pathology, ***Asso. Prof. Dept. of Experimental Surgery, SCB medical College & Hospital, Cuttack, Odisha, ****Prof. & HOD, Department of Medicine, Hi-tech Medical College & Hospital, Bhubaneswar, Odisha.

b) Alanine transaminase (ALT) elevation of more than 2.5 times normal documented at least twice during the first two weeks of presentation.

c) Absence of ingestion of known hepatotoxins such as alcohol, indigenous medicines and known hepatotoxic drugs.

d) Absence of history suggestive of previous liver disease.

Inclusion Criteria:

Consecutive patients diagnosed as AVH and attending the Hepatology department at SCBMCH, Cuttack Odisha, India from January 2010 to December 2011 were included in this study.

Exclusion Criteria

Patients in whom history is unreliable or alcoholic and patients in whom other diseases like congestive cardiac failure were excluded from the study.

Methods:

All patients had a detailed clinical evaluation followed by routine relevant investigations.

Clinical Evaluation:

A detailed history with special reference to etiology was taken. Also a complete general and systemic examination was done to look for tender, liver span hepatomegaly, splenomegaly and other signs of liver failure.

Investigations:

Various biochemical, hematological, serological, microbiological investigations were undertaken in each patients as an outpatient basis on the first visit and then at regular intervals (10 days to 2 weeks) till recovery.

A) **Biochemical**

LFT-Serum bilirubin, Serum transaminase (AST & ALT), Serum protein & albumin, Prothrombin time

Others-Blood urea, serum creatinine, blood glucose, serum electrolytes.

B) **Hematological**:

CBC/Peripheral smear / ESR / Coagulation profile / Malaria Parasite & Leptospira

C) **Serological** : Serum was collected at the time of initial examination to establish the etiological diagnosis of AVH. The following test were done.

Hepatitis B Surface Antigen (HBsAg)

lgM Antibody to Hepatis A Virus (lgM HAV)

lgM Antibody to hepatitis E Virus (lgM HEV)

lgM Antibody to hepatitis B Core antigen (lgM anti-HBc)

Anti Hepatitis C virus antibody (Anti HCV)

Markers of autoimmune Hepatitis (ANA, SMA, Anti LKM) were performed only in a selected group of patients diagnosed as non A-E AVH with prolonged course.

HBsAg, lgM anti HBc, lgM anti HAV and anti HEV tests were performed using commercial Elisa kits (Organon Teknika, Netherlands) according to manufacturers instruction.

Criteria for etiological diagnosis of AVH:

HAV - AVH - lgM anti HAV +Ve

HBV - AVH - lgM anti HBc +Ve

HEV - AVH - lgM anti HEV +Ve

HCV - AVH - anti HCV +Ve

Non A-Non-E - AVH - Absence of all above markers in the sera.

D) **Radiological Study**-Chest X-ray was done in few cases to look for associated lesion.

FOLLOW-UP:

Patients were followed up every 10 days to two weeks to evaluate their clinical and biochemical improvement.

Cholestatic hepatitis is used to refer to a clinical picture ,in which the course of the disease and the laboratory finding simulate those associated with mechanical obstruction of the bile ducts. It is also used to describe the characteristic set of histological findings in the liver.

Prolonged viral hepatitis refers to rare cases of viral hepatitis that are atypically lengthy, laboratory abnormalities persist and symptoms and physical findings continue for more than 16 weeks.

Relapsing hepatitis refers to an illness in which the patient who has apparently had complete recovery after an acute episode of viral hepatitis manifests a recurrence of the original symptoms and finding on one or more occasions usually within six months of the original illness.

STATISTICS:

Discrete variables amongst various etiologies of AVH were compared using Chi-square test continuous and rating variables were compared using L test, Wilcoxson rankusum test, and Mann Whitney's test.

RESULTS:

Two hundred and fifty four consecutive patients over the age of 15 years diagnosed as AVH attending the Hepatology department at SCB Medical College & Hospital, Cuttack, Odisha from January 2010 to December 2011 were included in the present study. Their mean age was 29.7 12.4 with a male : female ratio of 1.8:1. All the patients had distinct prodrome, hepatitic phase and convalescence. There were only 11 (4.3%) anicteric hepatitis and the remaining patients (n=243) had overt jaundice. There liver function profile has been depicted in Table-1. This depicted liver function profile indicated the value at the time of maximum level of serum biliurbin in individual patients.

The etiological distribution of AVH has been depicted in table 2. Isolated viral infection was documented in 102 (40.1) patients. Mixed acute viral infection was documented in 27 (10.6%) patients and super infection of one of the hepatotrophic viral infection over hepatitis B virus carrier was documented in 23(9.0%) of the patients. Non A-E viral hepatitis (patients without any of known hepatotrophic viral marker) was documented in 102 (40.1%) of the patients and 22 (21.5%) of these non A-E patients were HBV carriers. The over all frequency of HAV, HBV, HCV and HEV amongst these patients was 42(16.5%), 60(23.6%), 13(5.1%) and 64(25.1%) respectively. Isolated HAV, HBV, HCV and HEV infection was documented in 28(11%), 43(16.9%) 1(0.3%) and 30(11.8%) patients respectively. Amongst 23(9.0%) patients of HBV carrier with super infection, HEV was super infecting agent in 16 patients.

Table 3 depicts the details of acute mixed viral infection (co-infection) amongst patients with AVH. The commonest form of acute mixed viral infection was due to Hepatitis B+E & Hepatitis A+E Co-infection.

To detect the difference in clinical and biochemical dynamics amongst various etiological agent induced AVH, they were grouped into following six groups:

Group-I : Isolated HAV Infection (n=28)
Group-II : Isolated HBV infection (n=43)
Group-III : Isolated HEV Infection (n=30)
Group-IV : HAV with HBV or HEV or HCV (n=11)
Group-V : HBV with HEV & HCV (n-=17)*
Group-VI : Non A-E AVH (n=102)

(* Details of clinical & Biochemical information were available only in these number of patients.)

Isolated HCV infection was documented only in one patient and hence was not taken as separate Group. The remaining 12 patients with HCV Infection were associated with another viral infection which was included in either group IV & group V. Twenty two patients (87.5%) in group I, 34(79%) in Group-II, 24(80%) in group-III, 6(54.5%) in group IV, 10(58.82%) in group V and 78(76.4%) in group VI could be followed up till they had complete clinical & biochemical recovery.

Table 4 depicts the demographic profile of AVH amongst various etiological group. The frequency of blood transfusion and needle prick amongst HBV-AVH was significantly ($P<0.05$) higher than other group of AVH. The age and sex distribution however was similar amongst the groups.

Table 5 denotes the important clinical features amongst various group of AVH. However the types of

Table-1

Liver Function Profile

Liver Function	± Mean SD	Range
S Bilirubin(mg/dl)	7.9±8.6	0.3 - 41.9
ALT (iu/dl)	207.2± 389.9	100-2130
AST (iu/dl)	155.1 ± 277.2	80-1900
SAP (iu/dl)	333.3 ± 211.5	23-1360
T. Pr. (g/dl)	7.4 ± 0.9	4.4-11.8
S.Alb(g/dl)	3.8 ± 1.1	0.5-5.7
Proth. Time Prolongation over control in seconds	1.2 ± 2.9	0-24

Table-2
Etiology of AVH n=254

Viral etiology	Isolated infection	Mixed infection	Super infection	Total
HAV	28(11.05)	11	3	42(16.5%)
HBV	43(16.92%)	17	-	60(23.6%)
HEV	30 (11.8%)	18	16	64 (25.1%)
HCV	1 (0.3%)	8	4	13 (5.1%)
Total	**102 (40.1%)**		**23(9.0%)**	

No viral marker 102(40.1%), (22 had only HBsAg)
Under each etiology few patients had been common viz. acute HAV+HEV infection has been included both under HAV with another viral infection and HEV with another viral infection. Mixed viral infection occurred in 27(10.6%) patients.

Table-3
Etiological distribution of Acute Mixed viral infection

Serological markers	No. of Patients	Percent Positivity	
		(Of total patients) (n=254)	Of mixed infection (n=27)
IgMAnti HBc + IgM Anti HAV	3	1.18%	11.1%
IgMAnti HBc + IgM Anti HEV	10	3.93%	37.0%
IgMAnti HBc + IgM Anti HCV	4	1.5%	14.8%
IgMAnti HAV + IgM Anti HEV	6	2.3%	22.2%
IgMAnti HAV + Anti HEV	2	0.7%	7.4%
IgMAnti HEV + IgM Anti HCV	2	0.7%	7.4%
Total	**27(10.6%)**		

Table-4
Demographic profile amongst various etiological types of AVH

Demographic Profile	HAV Alone (n=28)	HBV Alone (n=43)	HEV Alone (n=30)	HAV with other viruses (n=11)	HBV with other viruses (n=17)	Non A-E (n=102)
Age (Mean Yrs ± SD)	19.1 ± 8.8	35.3 ± 12.3	30.4 ± 12.3	30.2 ± 18.6	35 ± 9.7	29 ± 11.4
Range	15-42	15-65	15-70	15-77	24-52	16-65
Sex M:F	14:14	29:14	20:10	5:4	7:5	71:31
Transfusion	1	7*	1	0	2	0
Needle Pricks	2	8+	0	2	0	-
H/o of surgery	2	5	5	0	3	18

* P=0.02 (when compared with other groups) + P=0.04
Remaining parameter were similar between each individual groups

Table-5
Clinical feature among various etiological types of AVH

Clinical Profile	HAV Alone (n=28)	HBV Alone (n=43)	HEV Alone (n=30)	HAV with other viruses (n=11)	HBV with other viruses (n=17)	Non A-E (n=102)
Types of prodrome						
Fever	26	34	26	8	10	87
Anorexia & Nausea	27	38	29	8	12	95
Abd. Pain	5	4	11	1	5	14
Arthralgia	4	14	0	0	1	8
Duration of prodromme (days)						
Means ± SD	5.4 ± 3	6.2 ± 4.6	6.6 ± 8.2	4.6 ± 2.3	5.2 ± 4.4	7.5 ± 7.3
Range	1-14	1-22	2-24	1-7	1-17	1-36
Duration of icterus (Days)						
Means ± SD	39.2 ± 34	68.9 ± 42.4	44.3 ± 40.6	60.1 ± 60.2	60.9 ± 55.9	42.3 ± 36.9
Range	2-135	11-180	11-180	13-210	13-233	15-180
Hepatomegaly (cm)						
Means ± SD	2.4 ± 1.2	2.2 ± 1.1	3.3 ± 1.7	2.5 ± 0.5	3.1 ± 1.5	2.5 ± 1.3
Range	0-5	0-6	0-7	0-3	0-5	0-8

None of the above parameters were significantly different from each other (P>0.1)

Table-6
Liver function profile amongst various etiological types of AVH

Liver Function	HAV Alone (n=28)	HBV Alone (n=43)	HEV Alone (n=30)	HAV with other viruses (n=11)	HBV with other viruses (n=17)	Non A-E (n=102)
S.bil (mg/dl)						
Means ± SD	7.5 ± 7.4	12.6 ± 11.3	8.7 ± 8.2	4.1 ± 3.4	6.6 ± 3.1	6.1 ± 7.1
AST(iu/dl)						
Means ± SD	322 ± 567.8	236 ± 417.2	126.8 ± 254.6	92.6 ± 45.1	111.4 ± 59.5	112.9 ± 172.3
ALT (iu/dl)						
Means ± SD	322 ± 567.8	298.6 ± 422.7	124.7 ± 232.9	217 ± 135.3	130 ± 69.9	173.8 ± 39.3
Alk.phos (iu/dl)						
Means ± SD	373.3 ± 231.5	325.8 ± 214.9	194.7 ± 125.8	362.7 ± 152.8	383.8 ± 311.6	329.9 ± 214.5
T.Protein(g/dl)						
Means ± SD	7.5 ± 0.7	7.7 ± 0.8	7.3 ± 1.1	8.0 ± 0.6	6.9 ± 1.1	7.2 ± 1.0
S.albumin(g/dl)						
Means ± SD	4.1 ± 0.7	3.9 ± 0.8	3.8 ± 0.8	3.3 ± 0.6	3.6 ± 2.1	3.8 ± 1.3
Pro-time prolongation over control (Second)						
Means ± SD	0.6 ± 1.1	1.7 ± 3.7	0.4 ± 1.0	0.1 ± 0.3	0.6 ± 1.7	1.5 ± 3.3

There was no significant difference between the groups.

prodrome, duration of prodrome, duration of icterus & degree of hepatomegaly were similar amongst various groups.

Table 6 outline the various liver function profile amongst the six groups of AVH. It is obvious that the mean (SD) and ranges of the various liver functions were similar amongst the different groups of AVH.

HBV-AVH in comparison to other types of AVH had significantly prolonged course (table 7). About 70% of patients with AVH-B had icteric hepatitis more than 6 weeks where as only about 30% of AVH due to other etiologies had icteric hepatitis of more than 6 weeks.

Two peaks of ALT could be documented amongst about 14% of HAV-AVH (Table-7) where as similar phenomenon was rarely observed amongst AVH patients due to other etiologies. Severe prolongation of prothrombine time was not a usual feature in any types AVH. Only two of the 254 patients developed complication in the form of fulminant hepatitis. One patients belonged to non A-E AVH and the other belonged to HAV-AVH. 4(four) patients developed sub-acute hepatic failure (HBV-2, Non A-E -2).

DISCUSSION

The present study revealed four important events regarding the etiology of AVH in one of the

Table-7
Unusual characteristics amongst various etiological types of AVH

Characteristics	HAV Alone (n=28)	HBV Alone (n=43)	HEV Alone (n=30)	HAV with other viruses (n=11)	HBV with other viruses (n=17)	Non A-E (n=102)
Duration of Icterus more Than 6 wks	**8(28.5)**	**30(69.7%)***	**10(33.3%)**	**3(27.2%)**	**7(41.1%)**	**32(31.3%)**
Two peaks of ALT	**3+**	**1**	**0**	**2+**	**0**	**5**
Proth. time Prolongation of >20 seconds	**0**	**3**	**0**	**0**	**0**	**2**

* P<0.001(Significantly higher proportion of HBV-AVH had prolonged course of AVH than any other groups of AVH. The remaining group had similar number of patients with prolonged hepatic illness.

+ 5(12.8%) patients out of total 39 patients with HAV infection had two peak ALT which was significantly higher (p=0.04) than similar events in any other group.

large tertiary care centre in Eastern India in the State of Odisha.

First the major etiological agents of sporadic AVH was found to be HBV (23.6%) as well as HEV (25.1%) and hepatitis C virus is an infrequent cause of sporadic AVH (Table-2). This is in sharp contrast to developed nations where HEV is unusual and HBV as well as HCV constitutes the major viral etiologies of sporadic AVH. In the present study none of our patients with sporadic HCV-AVH which can be termed as community acquired HCV-AVH had history of any identifiable parenteral exposure such as blood transfusion or needle prick. None of them were drug addicts, alcoholic and neither had multiple sex partners. The source of such HCV infection needs evaluation.

Secondly, it was seen that about one tenth (10.6%) of our patients had serological evidence of acute infection due to more than one hepatotrophic viruses. The commonest type of mixed infection encountered was due to hepatitis B+E and hepatitis A+E (Table-3). Such high frequency of mixed infection has not been reported previously from any part of the country and dual infection amongst sporadic AVH in developed nation is extremely rare and in English literature such reports are lacking. However despite having multiple hepatotrophic viral infection, their demographic (Table-4), clinical (Table-5), liver function profile (Table-6) was similar to isolated viral infection. None of these multiple viral infected AVH developed severe acute hepatitis in the form of fulminant and subacute hepatic failure. This factor emphasizes that host factor possibly plays a major role in determining the severity of acute hepatitic illness.

Third important fact noted in the present study was the frequency of HAV-AVH amongst adult (>15yrs). In the present study about 15% of the adults AVH were due to HAV. This fact assumes importance particularly in India because India is supposed to be endemic for HAV and by the age of 15 yrs 90% of population are reported to be protected against HAV due to sub-clinical exposure to HAV in childhood

resulting in development of protective antibody against HAV in them.[13]

This observation indicate that in India, due to developmental progress certain population pockets are not exposed to sub-clinical HAV infection in childhood. Such observation also indicate the need to re-evaluate the seroepidemiology of HAV infection in population to identify the high risk group to develop HAV infection. Such information may influence vaccination strategy for HAV in this country. Further a recent report indicate that combined infection of HAV & HEV amongst children was responsible for 40% of fulminant hepatitis in this Country[14]. Both these studies may be indicating a serious problem due to Hepatitis A Virus that this country may face in the ensuing decade.

Fourthly the previous reports on sporadic AVH indicated non A, non B, as the etiological agent in about 60% of the patients. In the present study however non A-E Virus was found to be the cause in 40% of patient. Obviously this reduction in frequency of unidentified viral etiology of AVH is due to identification of HEV & HCV. Further it also indicates the possibility of existence of more than one non A-E viruses. In 1995 hepatitis G virus has been identified as the third major non A, non B virus, however its role in causation of acute sporadic AVH is yet to be evaluated. Recently it has been reported regarding the presence of HGV in one patient in acute liver failure[15]. Evaluation for presence of HGV among these sporadic non A-E patients may provide beneficial information.

The clinical and liver function profiles of isolated hepatotropic viral infection and acute mixed viral infection was found to be similar in the present study. However, patients with Hepatitis A virus infection were not infrequently found to have two peak ALT elevation. Recently in the Western country two forms of clinical course was described amongst patients with HAV infection viz. Cholestatic hepatitis and relapsing hepatitis (two peak ALT elevation). Even though we documented relapsing hepatitis amongst 15% of our HAV-AVH patients the frequency of prolonged hepatitis amongst HAV patients was similar to HEV-AVH & mixed viral infection. In contrast HBV-AVH in the present study frequently had prolonged course (table-7). Unlike Western report clinical course of adult HAV-AVH in the present study was relatively benign and severe form of hepatitic illness was encountered in few cases only. We will like to conclude that non A-E followed by HBV & HEV are the major etiological agents of AVH at our centre. Despite endemicity of HAV in this country 15% of the adults AVH are due to HAV infection. More than one hepatotrophic viral infection was encountered in about 10% of the patients. Fifteen percent of HAV-AVH had relapsing Hepatitis. The demographic clinical and liver function profile of isolated & mixed viral infection was similar. HBV-AVH patient however had much more prolonged course than all other etiological types of AVH.

SUMMARY :

In this prospective study two hundred and fifty four patients diagnosed to be having AVH were analyzed with reference to clinical profile & viral markers and statistical analysis was done. Isolated viral infection was documented in 102 (40.1%) patients where as more than one hepatotrophic viruses caused AVH in 27(10.6%) patients. Non A-E Virus was the major case of sporadic AVH (40.1%), HBV & HEV were the etiological agent in 23.6% & 25.1% respectively. HAV was detected in 16.5% of the patients and the HCV was incriminated rarely as cause of sporadic AVH. The demographic, clinical and biochemical profile amongst isolated & mixed viral infection were found to be similar. However, HBV-AVH had significant prolonged course ($p<0.001$) and HAV-AVH was found to have significantly higher number of patients pursing a course of relapsing hepatitis. However HAV infection amongst adults in the present study was not found to cause severe liver disease except in few cases.

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BEST PAPERS OF 2012

The following original article and case report are selected as best papers of 2012 by the following refrees and are to be awarded on 10th November, 32nd APICON Odisha Branch, 2012.

Refrees : Prof. J.P. Das (Cuttack), Prof. M. Kar (Burla), Dr. S.K. Kar (Bhubaneswar)

Original Article

Title : Clinico Epidemiological Profile and Outcome in Posterior Circulation Stroke

Authors : P.K. Mohanty, L.K. Dash, G.P. Nayak, L.K. Singh, C.R. Khatua

Case Report :

* *Title :* Pulmonary Metastasis of Giant Cell Tumour of Bone Diagnosed by Image Guided FNAC

Authors : K.P. Tripathy, P.K. Behera, R. Panigrahi, A. Devi

Original Article

CLINICO-ETIOLOGICAL PROFILE OF SEIZURE DISORDER : AN OBSERVATIONAL STUDY IN A REFERRAL HOSPITAL IN ODISHA

C. Raghuram*, M.R. Behera, B.L. Parija***, A. Acharya****, S. Mohanta*****, J. Narayan*, P. Panda***

ABSTRACT

Seizures are paroxysmal events arising from abnormal excessive hypersynchronous discharges from central nervous system neurons. The impact of seizure on morbidity and mortality are substantial. The present study was undertaken with the aim of determining clinico-aetiological profile of seizure in hospitalized patients.Out of 181 patients, 136 (75.14%) cases were males and 45 (24.86%) cases were females. The mean age of onset of seizure was 42.93 years, the most common presentation was loss of consciousness 111 (61.33%). The most common type of seizure in present study was generalized tonic clonic seizure. The unpredictability and recurrence were most disability, leading to life threatening complications with high mortality. Appropriate treatment should be started as early as possible to treat the primary disease to prevent status epilepticus.
Key Words : *Seizure, Status epilepticus.*

INTRODUCTION :

Seizure, is defined as paroxysmal events arising from abnormal, hypersynchronous diseases from central nervous system neurons[1,2]. Epilepsy, describes a clinical phenomenon in which a person has recurrent seizures due to a chronic underlying process[1,2]. Convulsion, refer to an intense paroxysm of involuntary repetitive muscular contractions and consists only of an alteration of consciousness[3]. The Brain attempts to repair itself after a head injury, stroke, or other problem may inadvertently generate abnormal nerve connection that lead to seizure[4]. The World Health Organization (WHO, 2010) estimates that 80% of people living with epilepsy live in low middle income countries which is five times more than high income countries[5]. In 60-70% of patients no specific cause of their seizures can be identified known as Idiopathic Epilepsy[6]. In infants / children, congenital malformations, perinatal injuries or hypoxia, developmental neurologic disorders, metabolic defects, injury and infections are common causes of seizures. In young adults : head trauma, brain tumors, infection and arteriovenous malformations are common causes of seizure.

In elderly patients, cerebrovascular disease, degenerative diseases of CNS and brain tumor are common causes.

AIM OF THE STUDY :

To find the etiological profile of patients presenting with seizure and to find the clinical profile of patients with seizure disorder.

MATERIAL & METHODS :

Patients of seizure disorder admitted to Department of Medicine & Neurology in S.C.B. Medical College, Cuttack during the period August 2010 to September 2011 were taken. All the patients were evaluated clinically and all the relevant investigations were done.

OBSERVATION & DISCUSSION :

The present study was done with the patients of seizure disorder admitted to Department of Medicine and Neurology in S.C.B. Medical College, Cuttack during the period of August 2010 to September 2011. Out of 181 patients taken into study 136 (75.10%) were male and 45 (24.86%) were female with a male : female ratio being 3:1. The mean age of presentation was 4th decade between (40-50 years).

* PG Student, ** Asst. Professor, *** Asso. Professor, ***** Sr. Resident, Dept. of Medicine, SCB Medical College, Cuttack, **** Asst. Surgeon, CHC, Harichandanpur, Govt. of Odisha.

In this study all 181 patients presented with seizures or developed seizure following admission. Out of 181 patients 111 (61.33%) presented with loss of consciousness. 63 (34.81%) patients presented with fever, 44 (24.31%) patients presented with vomiting, headache in 17 (9.39%), meningeal signs were present in 19 (10.5%) cases and 23 (12.71%) patients presented clinically as hemiplegia or hemiparesis. Loss of consciousness was the most common presentation of seizure followed by fever & vomiting. (Table-1)

TABLE-1
CLINICAL PROFILE OF PATIENTS WITH SEIZURE

CLINICAL PRESENTATION	MALE	FEMALE	TOTAL
LOSS OF CONSCIOUSNESS	91 (81.98%)	20 (18.02%)	111 (61.33%)
FEVER	45 (71.43%)	18 (28.57%)	63 (34.81%)
VOMITING	31 (70.45%)	13 (29.55%)	44 (24.31%)
HEMATEMESIS	1 (100%)	0	0
EARACHE	12 (70.59%)	5 (29.41%)	17 (9.39%)
ICTERUS	5 (71.43%)	2 (28.57%)	7 (3.87%)
LOOSE STOOLS	2 (40%)	3 (60%)	5 (2.76%)
MENINGEAL SIGNS	15 (78.95%)	4 (21.05%)	19 (10.5%)
HEMIPLEGIA/HEMIPARESIS	18 (78.26%)	5 (21.74%)	23 (12.71%)

In this study 45 (24.86%) patients had GCS score < 8, 33 (18.23%) patients had solitary seizure, 125 (69.06%) had multiple seizure and 23 (12.71%) patients presented with status epilepticus. CT scan / MRI of brain was done in 138 (75.24%) cases (rest of the patients could not afford to do CT/MRI of brain) out of which 66 (47.83%) patients presented with seizure had CT scan or MRI abnormalities. Out of 181 patients with seizures abnormal EEG was recorded in 128 (70.17%) patients, and in 33 (18.23%) patients no abnormality was detected on both EEG and CT Scan / MRI.

TABLE-2
CORELATION OF ETIOLOGY WITH CT SCAN/MRI ABNORMALITY

	CTSCAN/MRI ABNORMALITY
HTN CVA (hemorrhage)	12 (18.18%)
HTN CVA (infarct)	5 (7.58%)
VIRAL ENCEPHALITIS	7(10.61%)
GLIOMA	5 (7.58%)
TUBERCULOMA	5 (7.58%)
SECONDARIES TO BRAIN	4 (6.06%)
NEUROCYSTICERCOSIS (Central dot representing scolex or single enhancing lesion on CECT).	4 (6.06%)
ALZHEIMER'S DISEASE (age related atrophic changes with dilated ventricles)	4 (6.06%)
ASTROCYTOMA	3 (4.55%)
CEREBRAL PALSY (Periventricular Leukomalacia)	3 (4.55%)
RHD CARDIOEMBOLIC STROKE (Infarct)	3 (4.55%)
SUB-DURAL HEMORRHAGE	2 (3.03%)
VASCULOTOXIC SNALE BITE WITH DIC	2 (3.03%)
SSPE	1 (1.52%)
PARTIAL HANGING	1 (1.52%)
CHRONIC RENAL FAILURE WITH UREMIC ENCEPHALOPATHY (Cerebral edema)	1 (1.52%)
CIRROSIS OF LIVER WITH HEPATIC ENCEPHALOPATHY (Cerebral edema).	1 (1.52%)
DM WITH HYPONATREMIA WITH CVA (Infarct)	1 (1.52%)
ALL – L2 WITH ICH	1 (1.52%)
CNS LUPUS WITH ICH	1 (1.52%)

Most common CT scan/MRI abnormality was cerebrovascular accident (ICH & infarction) 25.5% followed by viral encephalitis (10.61%), Tuberculoma & Glioma (7.5%) each. (Table-2).

TABLE-3
ETIOLOGY OF SEIZURES

ETIOLOGY OF SEIZURES	MALE	FEMALE	TOTAL
Infections (severe malaria, viral encephalitis, neurocyticercosis, tuberculoma, HIV, SSPE).	41(70.69%)	17(29.31%)	58(32.04%)
Idiopathic	34(87.18%)	5(12.82%)	39(21.55%)
Central nervous system (CVAMAKZGEUNER'S disease, cerebral palsy)	21(87.5%)	3(12.5%)	24(13.26%)
Metabolic (hypoglycemia, hyponatremia, hyperglycemia).	15(71.43%)	6(28.57%)	21(11.60%)
Malignancies (primary CNS tumor secondaries to brain)	9(75%)	3(25%)	12(6.63%)
Poisoning (organo-phosphorus, organochlorine poisoning)	4(44.44%)	5(55.56%)	9(4.97%)
Envenomation (Snake bite)	2(66.67%)	1(33.33%)	3(1.66%)
Renal (CRF)	2(66.67%)	1(33.33%)	3(1.66%)
Hanging	1(33.33%)	2(66.67%)	3 (1.66%)
Head Injury	2(100%)	0	2(1.1%)
Cardiovascular (RHD)	2(66.67%)	1(33.33%)	3(1.66%)
Hepato-biliary	2(100%)	0	2(1.1%)
Connective tissue disorder	0	1(100%)	1(0.55%)
Hematological	1(100%)	0	1(0.55%)
TOTAL :	136(75.13%)	45(24.86%)	181

TABLE-4
ETIOLOGY OF MULTIPLE SEIZURES THEIR DISTRIBUTION
(Excluding STATUS EPILEPTICUS)

DIAGNOSIS	MALE	FEMALE	TOTAL	DEATH
SEVERE MALARIA	12(60%)	8(40%)	20(16%)	4(20%)
VIRAL ENCEPHALITIS	14(80%)	4(20%)	18(12%)	4(26.67%)
SEIZURE DISORDER	12(85.71%)	2(14.29%)	14(11.2%)	0
HTN CVA(INFARCT/ICH)	3/6(75%)	2/1(25%)	12(9.6%)	4(33.33%)
PRIMARY CNS TIMOR	6(100%)	0	6(4.8%)	2(33.33%)
ORGANO PHOSPHORUS POISOINING	2(28.57%)	5(71.43%)	7(5.6%)	3(42.86%)
HYPONATREMIA	2(33.3%)	4(66.67%)	6(4.8%)	3(50%)
DM with HYPOGLYCEMIA	4(80%)	1(20%)	5(4%)	0
IDIOPATHIC	4(80%)	1(20%)	5(4%)	0
ALZHEIMER'S DISEASE	4(100%)	0	4(3.2%)	0
TUBERCULOMA	5(100%)	0	5(3.2%)	1(20%)
NEUROCYTICERCOSIS	2(50%)	2(50%)	4(3.2%)	0
SECONDARIES TO BRAIN	2(66.67%1)	1(33.33%)	3(2.4%)	1(33.33%)
RHD with CARDIOEMBOLIC STROKE	2(66.67%)	1(33.33%)	3(2.4%)	1(33.33%)
CRF WITH UREMIC ENCERHALOPATHY	2(66.67%)	1(33.33%)	3(2.4%)	1(33.33%)
HANGING	1(50%)	1(50%)	2(1.6%)	0
CEREBRAL PALSY	2(100%)	0	2(1.6%)	0
SUB-DURAL HEMATOMA (HEAD INJURY)	2(100%)	0	2(1.6%)	0
SNAKE BITE	1(50%)	1(50%)	2(1.6%)	1(50%)
ORGANOCHLORINE POISOINING	1(100%)	0	1(0.8%)	0
SSPE	1(0.55%)	0	1(0.55%)	1(100%)
CNS LUPUS WITH ICH	0	1(100%)	1(0.55%)	1(100%)
TOTAL	89(71.2%)	36(28.8%)	125(69.06%)	29(23.2%)

TABLE-5
ETIOLOGY & DISTRIBUTION OF STATUS EPILEPTICUS

DIAGNOSIS	MALE	FEMALE	TOTAL
HTN CVA	2(66.67%)	1(33.33%)	3(13.43%)
HYPONATREMIA	2(66.67%)	1(33.33%)	3(13.43%)
SEVERE MALARIA	1(50%)	1(50%)	2(8.7%)
DM WITH HYPOGLYCEMIA	1(50%)	1(50%)	2(8.7%)
IMMUNOCOMPROMISED WITH CRYPTOCOCCAL MENINGOENCEPHALITIS	1(50%)	1(50%)	2(8.7%)
CNS TUMOUR	2(100%)	0(0%)	2(8.7%)
CEREBRAL PALSY	1(100%)	0(0%)	1(4.35%)
CIRRHOSIS OF LIVER WITH HEPATIC COMA	1(100%)	0(0%)	1(4.35%)
SNAKE BITE WITH DIC	1(100%)	0(0%)	1(4.35%)
DM WITH HYPERGLYCEMIA	0(0%)	1(100%)	1(4.35%)
SECONDARIES TO BRAIN	0(0%)	1(100%)	1(4.35%)
HANGING	0(0%)	1(100%)	1(4.35%)
TOTAL	14(60.87%)	9(39.13%)	23(12.71%)

TABLE-6
MORTALITY OF SEIZURES

SEIZURE TYPE	TOTAL PATIENTS	TOTAL DEATHS	DISCHARGED
SOLITARY SEIZURE	33(18.23%)	1(3.03%)	32(96.67%)
MULITIPLE SEIZURE (more than >1 seizure)	125(69.06%)	31(24.8%)	94(75.2%)
STATUS EPILEPTICUS	23(12.71%)	13(56.52%)	10(43.48%)
TOTAL	181	45(24.86%)	136(75.13%)

Out of 181 patients, only in 142 (78.45%) patients, etiology could be identified. In 58 (32.04%) patients had infectious etiology which include 28 (48.28%) cases of severe malaria, 18 (32.14%) cases of viral encephalitis (14 cases were HSV-1, 3 CASES HSV-2 and 1 case of Japanese B Encephalitis), 5 cases of tuberculoma (8.93%), 4 (7.14%) cases had neurocysticercosis, 2 (3.57%) cases of HIV with cryptococal meningoencephalitis and 1 (1.79%) case of subacute sclerosing panencephalitis. The most common etiology of seizure in our study was infections 32.04%. (Table-3).

125 (68.51%) patients out of 181 had multiple seizures. Severe malaria was responsible for multiple seizures in 20 (16%) cases followed by CVA, viral encephalitis, primary CNS tumor, organophosphorous poisoning and hyponatremia accounting for majority cases of multiple seizure. Out of 125 cases of multiple seizures 29 (23.2%) died. (Table-4).

Idiopathic epilepsy accounts for 16 (48.49%) cases of solitary seizure (includes known epileptic who discontinued medicine or mixed dose or inadequate dosage with breakthrough seizure) 6 (18.18%) cases of severe malaria with complications like acute renal failure, icterus etc. Cerebrovascular accident accounts for 2 (6.06%) cases and diabetes mellitus with hyperglycemia accounts for 2 (6.06%) cases of solitary seizure.

In this study, 125 (69.06%) patients presented with multiple seizure 33 (18.23%) presented with solitary seizures and 23 (12.71%) had status epilepticus. Combined mortality was 45 (24.86%) patients out of 181. Highest mortality was found in 31 (24.80%) patients with multiple seizures. (Table-6)

DISCUSSION :

In our study of 181 patients presenting with history of seizure or who subsequently developed seizure admitted to Medicine & Neurology ward taken into the study. Mean age of the patient at the onset of seizure was in the 4th decade (between 40-50 years) of life and with male : female 3:1. Patients who presented with seizure or developed seizure, following admission had overlapping clinical features such as fever, loss of consciousness, vomiting, headache, icterus, loose stool, hematemesis, meningeal signs, hemiplegia/heparesis, etc.

128 patients had EEG abnormality and 53 patients had no EEG abnormality, 66 patient had abnormal CTSCAN/MRI findings in the form of Hemorrhage, Infarction, Tuberculoma, Neurocysticercosis, Secondaries to brain. Etiology of seizures in our study was infections (32.04%), idiopathic (21.55%), metabolic conditions such as uncontrolled diabetes mellitus with hypoglycemia/hyperglycemia, hyponatremia, accounting for 11.60% patients, Involvement of central nervous system (19.89%) in the form of cerbrovascular accidents, cerebral palsy & Alzheimer's disease. Malignancies such as Primary CNS tumors & secondaries to brain (carcinoma breast, bronchogenic carcinoma, carcinoma testis)causing seizures in (6.63%) patients. Uncommon etiologies were found like poisoining in 4.9% patients, Envenomation (snake bite) in 1.6% cases, hanging in 1.66% patients, head injury in 1.1% cases, connective tissue disorder such as systemic lupus erythematosis in 0.55% patients & hematological malignancies in 0.55% patients. Chronic renal failure with uremic encephalopathy, cirrhosis of liver with hepatic encephalopathy, rheumatic heart disease with cardio-embolic stroke were other minor causes of seizure.

Out of 181 patients taken for the study, with all available laboratory investigations etiology was found in 142 (78.45%) patients and in 39 (21.55%) etiology of seizure could not be identified, even though some patients were showing abnormal EEG and hence grouped into ldiopathic epilepsy (patients who had seizure before and discontinued medicine or missed dose or inadequate dose of medicine – break through seizure) or seizure disorder (patients presenting with seizure for the 1st time in life without any risk factors). All patients with normal EEG recording serum prolactin was done to confirm the occurrence of seizure.

Majority 125 (69.06%) of patients had more than 1 seizure and subsequently 23 (12.71%) developed status epliepticus & they were associated with high mortality (56.52%) and patients with solitary seizure had less mortality. Generalized tonic clonic seizures were found in 156 (86.19%) patients & focal seizure in 25 (13.81%) patients. Generalized tonic clonic seizure were associated with 29.92% mortality and focal seizure with 12% mortality. 87 patients of the total (46.07%) had Autonomic dysfunction. 87.29% of patients had a GCS score $\geq$ 9 & 12.71% had GCS score below $\leq$ 8, lower GCS score was predictor of higher mortality in the present study.

CONCLUSION :

Seizure is a common neurological problem in many medical diseases, its unpredictability and recurrence are most disabling leading, to life threatening, complications with high mortality. But in majority of patients, etiology of seizure is preventable like infections, metabolic abnormalities (hypoglycemia, hyponatremia, hyperglycemia). Appropriate treatment should be started as early as possible to treat the primary disease to prevent status epilepticus, as untreated seizures become difficult to treat later on and hence associated with high mortality. Patient and their family education regarding their attitude and belief about seizure is another important factor that may prevent the occurrence of seizure and their subsequent life threatening complications.

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Original Article

STUDY OF ETIOLOGY AND CLINICAL PROFILE OF ACUTE CONFUSIONAL STATES IN ELDERLY

S.N. Das*, B. Bharani**

ABSTRACT

Objective : *To study etiology and clinical profile of Acute confusional states in elderly admitted to Department of Medicine, SCBMCH, Cuttack during the period of September 2011 to September 2012.* ***Result :*** *Total number of patients included in the study were 100. Male to female ratio was 3:2. The most common age group presenting with acute confusional state (Delirium) in elderly was 66-70yrs (Total-34%). Hemorrhagic stroke was the most common cause of delirium in elderly(22%), followed by Hyponatremia(16%).Etiology was multifactorial in 68% of cases.* ***Keywords :*** *Acute Confusional State, Elderly People, Delirium, Coma.*

INTRODUCTION-

The term Delirium is synonymous to Acute confusional state[1] . Elderly age group according to WHO criteria is age more than 60 yrs[2].

The criteria for diagnosing delirium is DSM IV Criteria[3]. The prevalence of delirium in hospitalized older patients is 14% to 60%.This estimate would be higher in intensive care units[4]. In a study conducted male gender is identified as independent risk factor for delirium in elderly. In most cases, the cause of delirium is multifactorial. Nearly half of elderly patients with delirium have more than one cause.

Delirium develops rapidly over hours or days but rarely more than a week[5]. Fluctuations occur throughout the day. Delirium is associated with major mortality and morbidity .Patients suffering from delirium have initial mortality rate upto 26% and as high as 75% three years after an episode of delirium. The best available evidence suggests that prevention of delirium is more effective than its treatment. Multifactorial intervention programmes can reduce the duration of delirium, length of hospital stay and mortality rate.

AIM AND OBJECTIVES

To study etiology and clinical profile of Acute confusional states in elderly, admitted to Department of Medicine, SCBMCH, Cuttack between September 2011 to September 2012 fulfilling DSM IV Criteria were taken into study.

MATERIALS & METHODS

100 consecutive elderly patients with acute confusional state admitted to Department of medicine, were studied .Detailed history ,physical examination and investigations were done to know the etiology causing delirium in elderly.

OBSERVATION

100 patients admitted between 01-09-2011 to 30-09-2012 were studied. The most common age group presented with delirium was 66-70yrs (Total-34%). The male to female ratio is 3:2.

*Associate Professor, ** Post graduate, Dept. of Medicine, SCB Medical College, Cuttack, Odisha.

The most common cause of delirium in elderly was found to be hemorrhagic stroke(22%). Second most common was Hyponatremia(16%).

The most common presenting symptom apart from delirium was vomiting(36%) followed by fever (35%) and breathlessness(32%). The most common cause of delirium in elderly with diabetics-mellitus was Hypoglycemia(29.7%). Second most common was stroke.(18.9 %). The commonest cause of delirium in elderly with hypertension was hemorrhagic stroke(3.2%) and hypertensive encephalopathy(3.2%). The commonest predisposing factor for hyponatremia was diuretic use(50%). Other causes were vomiting and stroke. Out of 100 cases ,40 cases(40%) showed abnormality in imaging modalities.

TABLE-1

AGE AND SEX DISTRIBUTION OF PATIENTS WITH DELIRIUM IN ELDERLY

Age in group years	Male(n=58)	%	Female(n=42)	%	Total(n=100)	%
60-65	8	6.6	6	5	14	14
66-70	22	37.9	12	10	30	34
71-75	7	5.8	3	2.5	10	10
76-80	10	8.3	13	11.2	23	23
81-85	6	5	4	3.1	10	10
86-90	5	4.1	3	2.5	9	9

TABLE-2

CAUSES OF ACUTE CONFUSIONAL STATES AMONG ELDERLY

CAUSE	No of cases(n=100)	%
Hemorrhagic stroke	22	22
Hyponatremia	16	16
Infarction	9	9
Hypoglycemia	11	11
Hypertensive encephalopathy	10	10
Septicemia	3	3
Uremic encephalopathy	6	6
Hypercapnia	4	4
Hyperglycemia	4	4
ICSOL	6	6
Cerebral malaria	4	4
Hypovolemic shock	1	1
Viral encephalitis	2	2
Tuberculous meningitis	2	2

TABLE-3
PRESENTING FEATURES OTHER THAN DELIRIUM IN ELDERLY

SYMPTOMS	No of cases(n=100)	%
Fever	28	28
Vomiting	36	36
Breathlesness	10	10
Seizures	8	8
Decreased urination	8	8
Headache	10	10

TABLE-4
CAUSES OF DELIRIUM IN PATIENTS WITH DIABETES MELLITUS

CAUSE	NO OF CASES(n=37)	%
Hyponatremia	2	5.4
Hemorrhagic stroke	4	10.8
Infarction	7	18.9
Hypoglycemia	11	29.7
Septicemia	3	8.1
Uremic encephalopathy	5	13.5
Hyperglycemia	4	10.8
Hypovolemic shock	1	2.7

TABLE-5
HYPERTENSIVES WITH DELIRIUM

CAUSE	NO OF CASES(n=32)
Hyponatremia	3
Hemorrhagic stroke	10
Infarction	1
Hypoglycemia	5
Hypertensive encephalopathy	10
Uremic encephalopathy	3

TABLE-6
PREDISPOSING FACTORS OF HYPONATREMIA

PREDISPOSING FACTOR	NO OF CASES(n=16)
Diuretic use	8
Vomiting	6
Stroke	2

TABLE-7
CT SCAN/MRI ABNORMALITIES IN PATIENTS WITH DELIRIUM

IMAGING FINDINGS	NO OF CASES(n=40)
Infarction	20
Hemorrhagic stroke	32
ICSOL	6
Hydrocephalus	2
Temporal lobe enhancement	1

DISCUSSION

In a study conducted by Grover et al over 6 years (2000-2005) among 3092 elderly patients showed that acute confusional state forms the largest diagnostic category in elderly admitted patients and metabolic disturbances are the most common cause of delirium in elderly[7].

In another study by chrisphal A et al on the clinical profile and association of confusional state in geriatric patients showed that it is multifactorial[8].

Inouye and Charper 1996 showed that medications contribute upto 39% of elderly patient with delirium[9].

In our study done from September 2011-september 2012, Out of 100 patients ,58 patients were male, 42 were female. The most common age group presenting with delirium is 66-70yrs of age. The most common cause was found to be hemorrhagic stroke(22%).second common is hyponatrmia(16%).In patients with diabetics mellitus the most common cause of delirium was hypoglycemia(27.%) and in hypertensives was hemorrhagic stroke and hypertensive encephalopathy(10%).The etiology is multifactorial in 68% of cases.

In most cases of delirium etiology was easy to recognize once it is suspected and an adequate history has been obtained. Although a diagnostic work up and therapy is indicated for specific brain injury is always important, this situation is rare. More commonly , multiple possible etiological factors are identified and attention needs to be directed to each of these. Masterly management of delirium seldom requires a single clever diagnosis; more commonly management requires insightful clinical practice that can detect multiple potential contributors and ameliorate each of these.A collaborative team approach is key to success.

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Original Article

A STUDY OF INFLAMMATORY MARKERS LIKE FIBRINOGEN AND C-REACTIVE PROTEIN IN TYPE 2 DIABETES MELLITUS

Krishnakumar K[*], Tity P[*], Deepak Dash[*], N T Minz[**], N Mohanty[***]

ABSTRACT

Diabetics are more vulnerable to cardiovascular diseases and so there is a need for new markers to assess the risk. ***Aim:*** *The present study is contemplated to estimate plasma fibrinogen and CRP levels in patients with type 2 diabetes mellitus and to assess the prognostic relation between these two factors and mortality in patients with type 2 diabetes mellitus with coronary artery disease.* ***Material and Methods :*** *We compared the serum CRP and fibrinogen levels in 100 diabetics cases versus 100 non diabetic controls (age and sex matched) Serum fibrinogen and CRP levels were measured and statistical analysis was done.* ***Results:*** *The mean fibrinogen levels in diabetics with CAD with mortality (274.2 ±16.52) was higher than the serum fibrinogen levels in those without mortality(256.5 ±17.37).Diabetics with cardiovascular morbidity do have higher fibrinogen levels (264.3±17.037) in comparison with those without cardiovascular morbidity(253.0 ±15.684).(.p 0.001) .Correlating CRP levels in diabetics with CAD between those with mortality and those without mortality, the mean CRP levels were 1.865± 1.16 in the first group and 1.273 ±0.332 in the second group. p value of 0.0064 suggests the finding to be very significant.The mean CRP values in diabetics with CAD was higher (1.501 ±0.81) than the mean CRP levels in diabetics without CAD (1.169±0.47). p value of 0.0186 showed the result can be considered significant. In the comparison of the CRP levels between cases and controls, p <0.0001 showed the result (that mean CRP levels 1.358± 0.70 , higher in cases compared to that in control 0.892± 0.34), was extremely significant.* ***Conclusion :*** *Both fibrinogen and c-reactive protein levels were significantly higher in diabetics with coronary artery disease (especially those with mortality) than those without accompanying coronary artery disease.* ***Key words :*** *CRP creactive protein, diabetes mellitus, coronary artery disease.*

INTRODUCTION

Diabetes Mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia[1].It is a chronic disorder resulting from a number of factors in which an absolute or relative deficiency .of insulin or its function occurs . Irrespective of the ethnic background the risk for coronary heart disease among diabetic subjects is greater by a factor of 2 to 4 compared to non-diabetic subjects[2].

The diabetic condition contributes for initiation and progression of micro and macrorovascular complication in diabetes. As diabetics are at risk of cardiovascular disease, there is a need to identify markers which would help in prognosis and diagnosis of the disease.

Basic research studies have revealed that inflammatory markers like CRP (c-reactive protein) are high among subjects with insulin resistance and diabetes .(4) Inflammation is considered to be a part of insulin resistance syndrome and this to some extent explains the high risk for coronary artery disease among diabetic subjects.

Recent studies have identified defects in coagulation and fibrinolytic cascade to play a major role in the pathological mechanisms leading to CAD (5)

*P.G. Student, **Asst. Prof., *** Asso. Prof., Dept. of Medicine, MKCG Medical College, Berhampur, Odisha.

These two cascades consist of activators and inhibitors which regulate clot formation and vascular potency. Fibrinogen is one of the key elements of this cascade, which is also an inflammatory marker.

Fibrinogen is the major coagulation protein in blood by mass , the precursor of fibrin and an important determinant of blood viscosity, platelet aggregation and smooth muscle cell proliferation. Fibrinogen has also been shown to be involved in the development of atherosclerotic lesion beginning with the early stages of plaque formation[6].Furthermore fibrinogen is also a prominent acute phase reactant . It augments the degranulation of platelets in response to adenosine diphosphate, when taken by the granules [7]. Thus fibrinogen plays a vital role in a number of pathophysiological processes in the body including inflammation, atherogenesis and thrombogenesis .

Thus in this study CRP and fibrinogen levels are estimated in type 2 diabetes mellitus patients .

MATERIAL & METHODS:

A prospective case control study was conducted to compare the serum CRP and fibrinogen levels in diabetic cases versus non diabetic controls.100 cases of type 2 DM who came to the OPD and indoor of general medicine department of mkcg medical college and hospital Brahmapur Odisha during the period from August 2010 to August 2012 constituted the material of the present study.100 age and sex matched healthy subjects, comprising of the relatives of the patients constituted the control group.

The 100 cases were further subdivided into 57 cases(who are diabetics with ACS-C)and 43 cases(diabetics without any cardiovascular problems-D). Among the 57 cases of diabetics with cardiovascular problems ,22(m) had died during the course of our study.

Cases were those who satisfy the criteria for diabetes mellitus (as per the criteria for diagnosis of DM American diabetes association 2007) . Persons with traditional cardiovascular risk factors like hypertension, hypercholesterolemia ,smoking and obesity were excluded from the study. Serum fibrinogen assays were done using the clauss method and the latex CRP reagent method was used to assay the CRP levels.

Data were collected and analyzed with the students t–test using Microsoft excel and graphpad prism for windows version 4.2 .

RESULTS AND DISCUSSION

Out of the total cases, 78% were males and 22 % females, and maximum number of cases (51%) were in the age group of 50-60years, which is supported by the work done by *D E Fentol et al*, who had the maximum no of cases in the age group of 40-60 years.

Majority of the patients (64%) were from a rural background. The higher percentage of rural population in the study could be due to their preference to avail medical facilities from tertiary care hospitals, rather than private nursing homes, besides rural population is higher in our country. The majority (62%) belonged to the average socioeconomic status.

Among the diabetics with CAD ,out of a total of 57 ,there were 30 patients (53%)with STEMI,16 (28%) with NSTEMI and 11 (19%) patients with unstable angina.(Table 1)

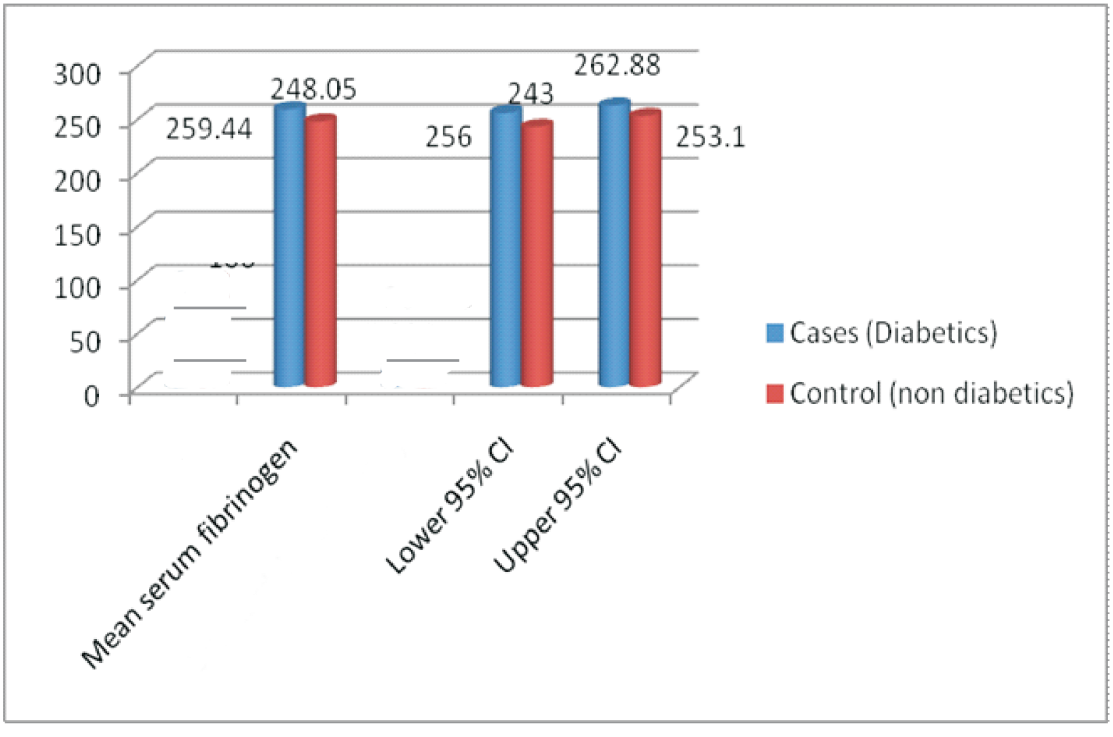
Cardinal presenting symptoms of the diabetics with CAD were breathlessness in 56% cases, chest pain in 19% cases ,diaphoresis in 12%, nausea & vomiting in 9% and syncope in 4% cases. Haematological examination revealed that the total leucocyte count was normal in 70% cases and high in 30 % cases. Cardinal symptoms of the diabetics without ACS in our study were asymptomatic presentation in 28%, numbness/ paresthesia in 8%, polyuria in 5% cases and non healing ulcers in 2% cases.

Among the different groups of DM with CAD, STEMI cases (30) had higher mean CRP values (1.627) and higher mean fibrinogen (268.96) values as compared to the other two groups(NSTEMI and unstable angina).

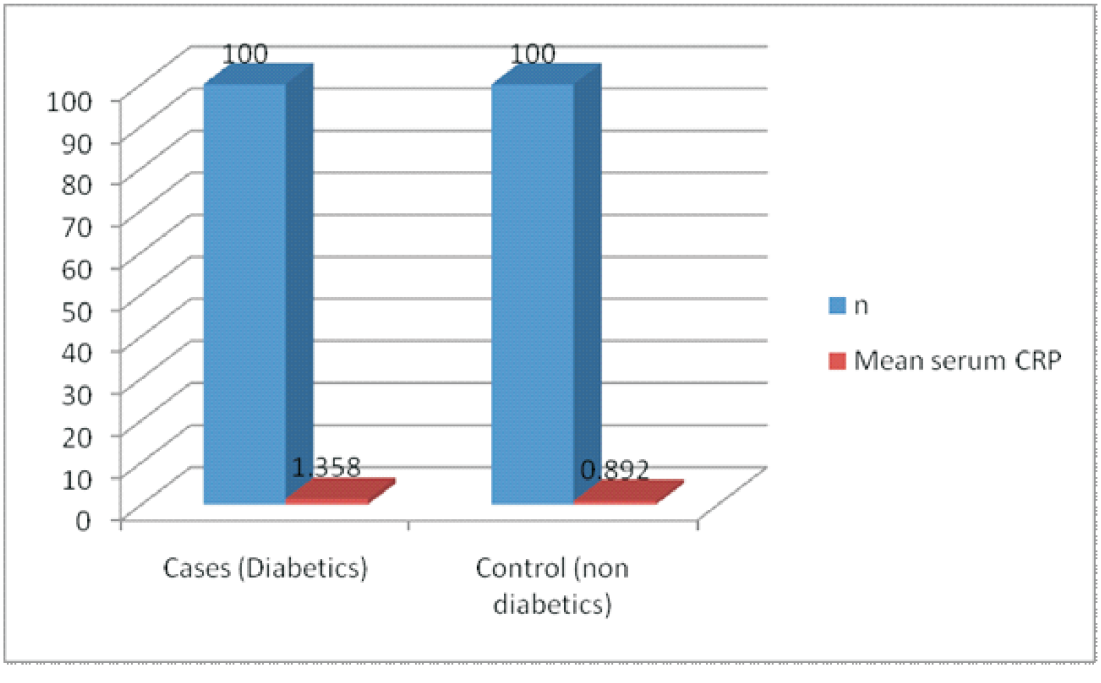
The mean fibrinogen levels in diabetics with CAD with mortality (274.2±16.52) was higher than the serum fibrinogen levels in those without mortality. (256.5±1 7.37).(p 0.0003). This result in our study is comparable to the the study of Sanchez et al.(Table 2)

Diabetics with cardiovascular morbidity do have higher fibrinogen levels (264.3 ±17.037) in comparison with those without cardiovascular morbidity. (253.0±15.684).(p 0.001) (Table 3)

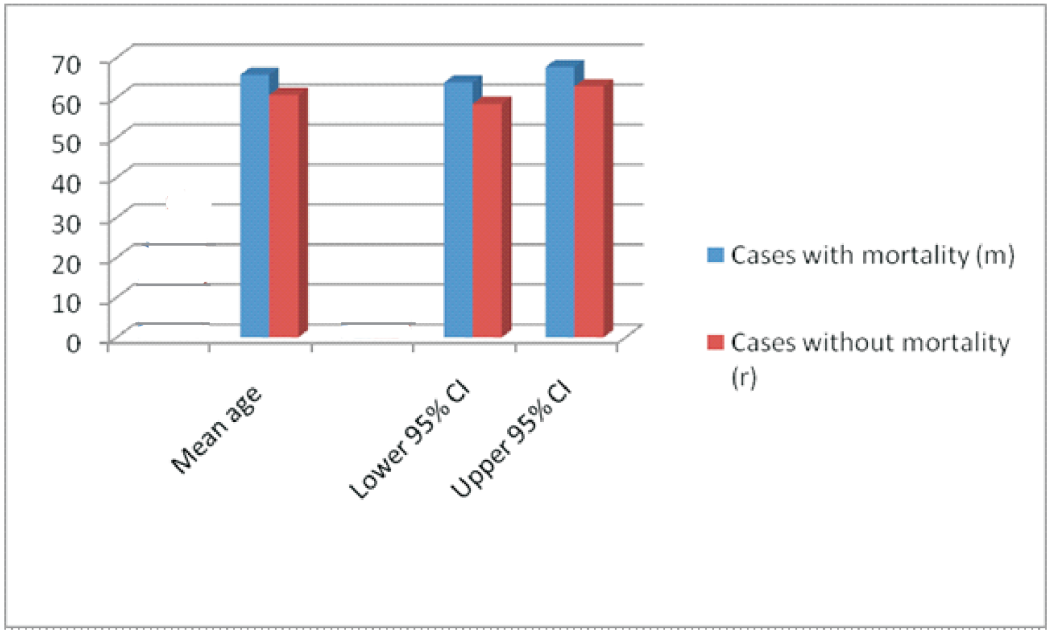
COMPARISON OF SERUM FIBRINOGEN LEVELS BETWEEN CASES AND CONTROLS (fig 1)



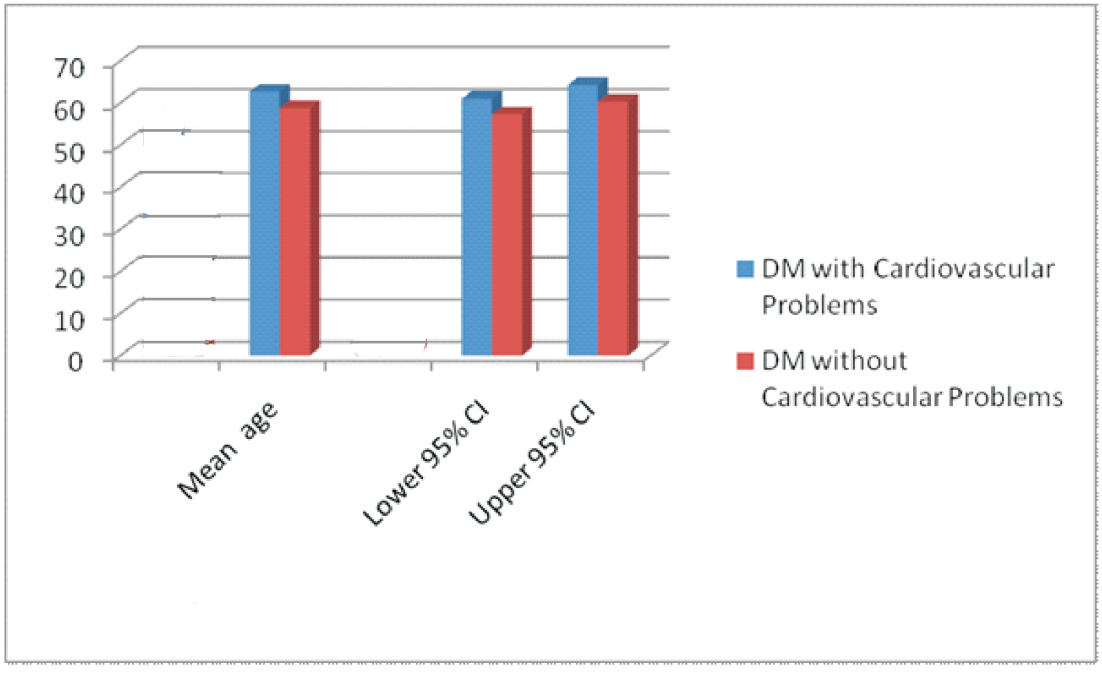
COMPARISON OF SERUM CRP LEVELS BETWEEN CASES AND CONTROLS (fig 2)



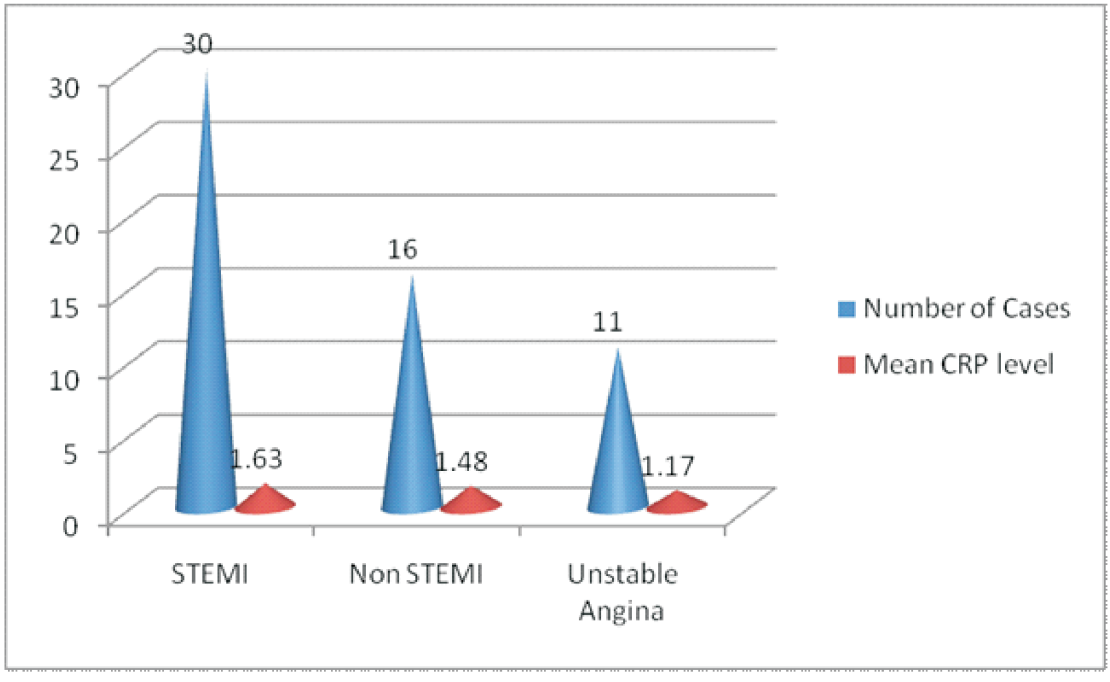
COMPARISON OF AGE DISTRIBUTION IN DIABETICS WITH CARDIOVASCULAR PROBLEMS (between those with mortality (m) and those without mortality (r) (fig 3)



COMPARISON OF AGE DISTRIBUTION IN DIABETICS WITH CARDIOVASCULAR PROBLEMS AND THOSE WITHOUT CARDIOVASCULAR PROBLEMS (fig 4)



CRP LEVELS AMONG DIABETICS WITH CARDIOVASCULAR MORBIDITY(fig 5)



FIBRINOGEN LEVELS AMONG DIABETICS WITH CARDIOVASCULAR MORBIDITY (fig 6)

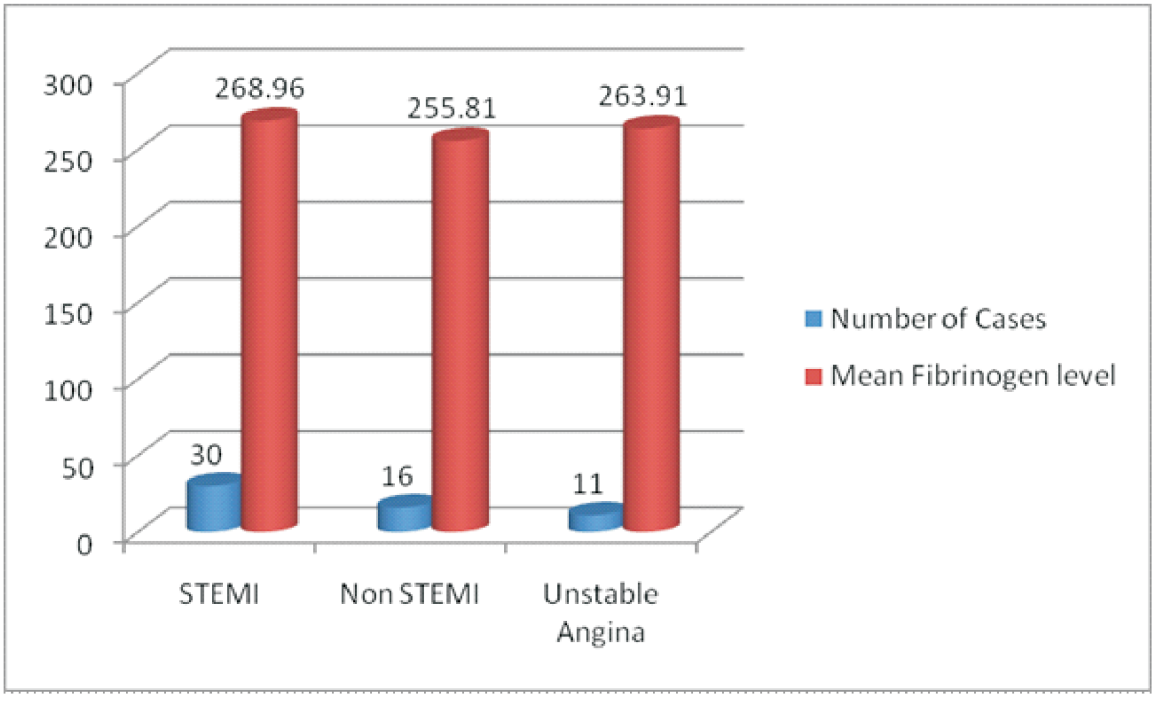


Table-1
SPECTRUM OF CARDIOVASCULAR MORBIDITY AMONG THE DIABETICS (n-57)

Type		No. of Cases	Percentage
AMI	ST elevation	30	53%
	Non ST elevation	16	28%
Unstable Angina		11	19%
Total		57	100%

Table-2
COMPARISON OF FIBRINOGEN LEVELS IN DIABETICS WITH CARDIOVASCULAR PROBLEMS (between those with mortality (m) and those without mortality (r) (n=57)

	Cases with mortality (m)	Cases without mortality (r)
n	22	35
Mean serum fibrinogen	274.2	256.5
Standard deviation (SD)	16.52	17.37
Lower 95% CI	266.9	250.54
Upper 95% CI	281.55	262.49

Table-3
COMPARISON OF FIBRINOGEN LEVELS IN DIABETICS WITH ACS AND THOSE WITHOUT CARDIOVASCULAR PROBLEMS (n=100)

	DM with Cardiovascular Problems	DM without Cardiovascular Problems
n	57	43
Mean serum fibrinogen	264.3	253.0
Standard deviation (SD)	17.037	15.684
Lower 95% CI	259.78	248.17
Upper 95% CI	268.82	257.83

Table-4
COMPARISON OF CRP LEVELS IN DIABETICS WITH CARDIOVASCULAR PROBLEMS
(between those with mortality (m) and those without mortality (r)
(n=57)

	Cases with mortality (m)	Cases without mortality (r)
n	22	35
Mean serum CRP	1.865	1.273
Standard deviation (SD)	1.166	0.33
Lower 95% CI	1.347	1.159
Upper 95% CI	2.38	1.38

Table-5
COMPARISON OF CRP LEVELS IN DIABETICS WITH CARDIOVASCULAR PROBLEMS AND THOSE WITHOUT CARDIOVASCULAR PROBLEMS
(n=100)

	DM with Cardiovascular Problems	DM without Cardiovascular Problems
n	57	43
Mean serum CRP	1.501	1.169
Standard deviation (SD)	0.813	0.471
Lower 95% CI	1.285	1.024
Upper 95% CI	1.717	1.314

Between the cases and controls, the mean serum fibrinogen levels in those with DM was 259.44 ±17.325 and in non diabetics was 248.05 ± 25.41. The p value of 0.0003 showed that this result was extremely significant.(Fig.1)

Correlating CRP levels in diabetics with CAD between those with mortality and those without mortality, the mean CRP levels were 1.865± 1.166 in the first group and 1.273 ± 0.332 in the second group. p value of 0.0064 suggests the finding to be very significant.(Table 4)

The mean CRP values in diabetics with ACS was higher (1.501 ± 0.813) than the mean CRP levels in DM without ACS (1.169 ±0.47). p value of 0.0186 showed the result can be considered significant.(Table 5)

In the comparison of the CRP levels between cases and controls , p <0.0001 showed the result(that mean CRP levels 1.358 ± 0.70 , higher in cases compared to that in control 0.892 ± 0.34), was extremely significant.(fig 2)

While comparing the age group of those diabetics with ACS those with mortality and those without mortality ,it was found the mean age was 65.72 ± 4.39 in the former group and 60.65 ±6.39 in the latter group.(p value 0.0019) (Fig 3).

Comparing the age groups of those DM with CAD and DM without CAD , the mean age was 62.614 ± 6.187 in the former group and 58.74 ± 4.86 in the latter .p value 0.001 showing the result to be very significant.(fig 4)

While comparing the age distribution of cases versus controls, the mean age in the case group was 60.95 ± 5.948 versus 60.98 ± 5.919 in the control group. p value 0.9715 showed the difference was not significant ,showing that the age was correctly matched when diabetics and non diabetics were enrolled for the study.

In our study the mean serum CRP levels were found to be 1.63mg/dl in STEMI ,1.48 mg/dl in NSTEMI and 1.17 mg/dl in the unstable angina group (fig 5). Sanchez PL et al study on kinetics of C reactive protein in different forms of ACS shows that the mean crp level was 6.7 mg/dl in STEMI, 2.9 mg/dl in NSTEMI, and 1.8mg/dl in unstable angina. The maximum CRP elevation was observed in STEMI. The mean fibrinogen levels in STEMI was 268.96, NSTEMI 255.81 and unstable angina 263.91 in our study (fig 6). Although the mean levels of CRP in different forms of ACS of our study and the above mentioned study are different, but the finding of maximum CRP elevation in STEMI is comparable. This may be due to the difference in the time interval between the onset of attack and estimation of serum CRP. Also this may be due to the fact that other significant contributors to atherogenesis (thereby contributing to CAD in diabetics moresoever than non diabetics) like hypertension, hypercholesterolemia, obesity and smoking had been excluded from our study.

Conclusion:

The results of our study showed both fibrinogen and creactive protein levels to be significantly higher in diabetics compared to nondiabetics. Furthermore our study came to the conclusion that both fibrinogen and C-reactive protein levels were significantly higher in diabetics with coronary artery disease (especially those with mortality) than those without accompanying coronary artery disease. But there is a need to validate the results on a much larger sample size.

In view of these observations we recommend that along with the traditional markers of cardiac morbidity which should be monitored regularly in diabetics, serum levels of fibrinogen and C-reactive protein also be regularly monitored for assessing the cardiovascular risk. This strategy may help to identify and monitor high risk diabetic subjects for any cardiovascular events thereby reducing the economic burden and improving the quality of life.

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Original Article

HEPATOBILIARY ASCARIASIS: STUDY OF 34 CASES FROM RURAL AREA OF ANGUL DISTRICT OF ODISHA.

B. Sahoo*, B. Sahu**

ABSTRACT

AIM: *To find out clinical presentation, sonographic appearance and response to antihelmithic therapy in cases of Hepatobiliary Ascariasis which were detected in NTPC Hospital, Kaniha.* ***Material and Methods*** *– This study was a conducted over a period of 7 months from October 2011 till March 2012. All the case of Hepatobiliary ascariasis i.e. Round worms detected in common bile duct, gall bladder, Hepatic ducts or liver by ultrasonography where the subjects of this study. Their clinical presentation USG appearances were studied in detail all patients were given antihelminthic therapy- Albendazole 400 mg daily for 3 days/Mebendazole 100 mg bd for 3 days. Whenever required the antihelmithic course was repeated.* ***Results*** *– During this period we had done 613 cases of abdominal ultrasonography. Out of this, in 34 cases Hepatobiliary ascariasis were detected. It was more common in females than males, M:F ratio being 1: 2.4. We got only 3 cases less than 10 years of age, rest 21 were above 10 years. Most common clinical presentation was pain abdomen in 29(85%) of cases. Other clinical presentations were obstructive jaundice, acute cholecystitis in 2 (5%) Cases each, vomiting in 3 (8%), features of APD in 3 (8%), Anorexia in 2 (5%) , fever, splenomegaly, nausea, mass in epigastrium in 1 (2.5%) case each. All the patients were treated with antihelminthic therapy and other treatment as required as per the clinical condition of the patient. Repeat USG was advised in all cases. The cases in which symptoms or motility of worms persisted; they were given repeat course of antihelminthic therapy. Out of 34 cases, 31 cases responded to antihelminthic therapy in our hospital and 2 cases were referred for ERCP / Surgical intervention to higher centre. These two cases were also treated conservatively and improved.* ***Key words****-Ascariasis, Hepatobiliary, Round worm*

INTRODUCTION

Ascariasis affects 25% of world's population. Although cosmopolitan in nature it is more common in developing nations of Asia, Africa and South America. Hepatobiliary and pancreatic ascariasis is a well known and common complication of intestinal ascariasis.

Females are affected more than males, female to male ration being around 3:1. It can cause acute cholecystitis, biliary colic, cholangitis, obstructive jaundice, acute pancreatitis and liver abscess. In India it is more prevalent in Kashmir where it is as common as gall stone disease. In Odisha it is under reported. Ultrasonography is a rapid, safe and reliable method for diagnosis of Hepatobiliary ascariasis. ERCP is reserved mainly for therapeutic purposes. Although majority of cases respond to conservative therapy, less than 25% need endoscopic or surgical intervention [1, 2]. We have undertaken this study over a period of 7 months from October 2011 till March 2012. We wanted to study the clinical presentations, sonographic appearances and response to antihelmithic therapy in those cases in which ultrasonography of abdomen detected Hepatobiliary ascariasis in NTPC hospital, Kaniha.

* Senior specialist (Medicine), ** Senior specialist (Radiodiagnosis), NTPC Hospital, Kaniha, Angul, Odisha.

TABLE-1 : AGE & SEX DISTRIBUTION

Age	0 – 10	11 – 20	21 – 30	31 – 40	41 – 50	51 – 60	> 60	Total
M	01	03	04	0	02	0	0	10
F	02	02	03	10	3	03	o1	24
Total	03	05	07	10	05	03	01	34

TABLE-2: CLINICAL PRESENTATION

Sl. No	Clinical presentation	No of cases	%	
1	Pain abdomen simulating Biliary colic	29	85	
2	Obstructive Jaundice	2	5	
3	Acute cholecystitis	2	5	
4	Vomiting	3	8	
5	Features of APD	3	8	
6	Fever	1	2.5	
7	Splenomegaly	1	2.5	
8	Nausea	1	2.5	
9	Anorexia	2	5	
10	Biliary colic	1	2.5	
11	Mass in epigastrium	1	2.5	

TABLE-3 : USG FINDINGS

Sl. No	USG FINDINGS	No of cases	%	
1	RW in CBD	17	50	
2	RW in GB	13	38	
3	Distended GB	5	15	
4	Acalculus cholecystitis	3	8	
5	Multiple RW in GB & CBD	5	15	

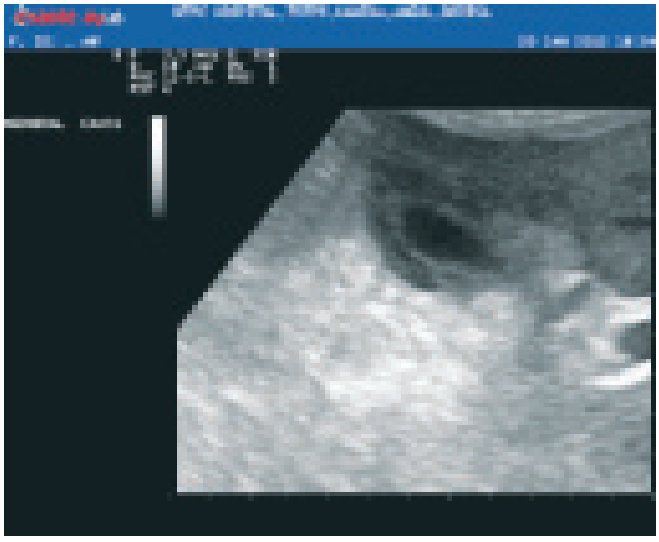

Figure-1 :
Round worm coiled inside gall bladder

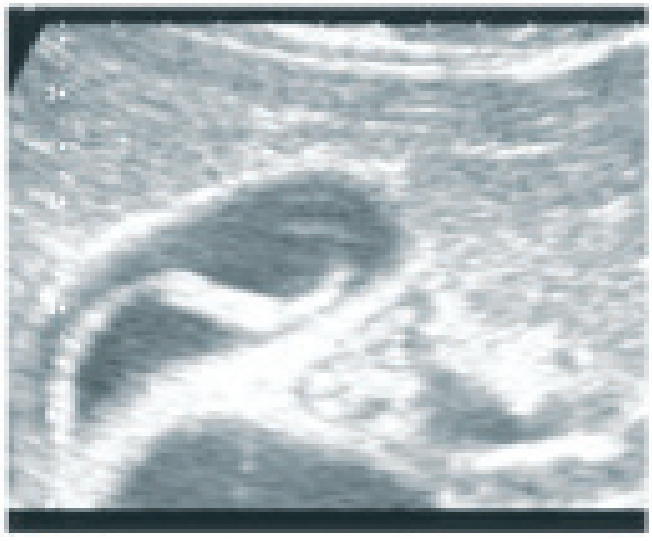

Figure-3 :
Round worm inside GB[11] Cited from N.B. Topal et all

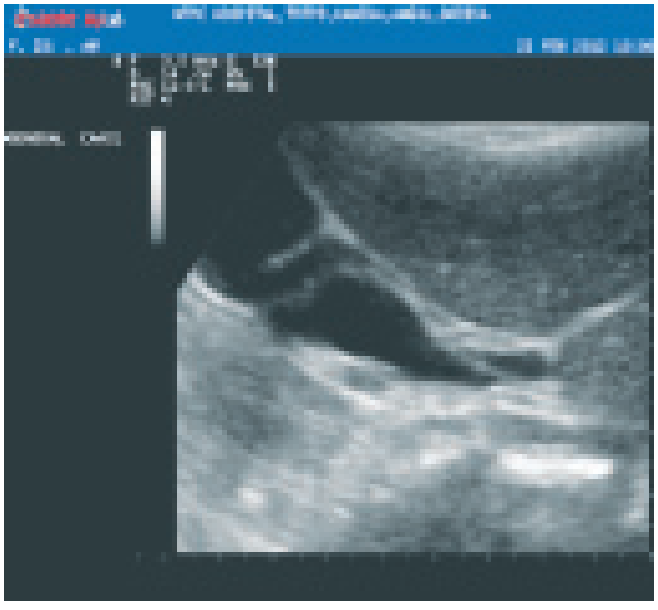

Figure-2 :
Multiple round worms (3 numbers) in gall bladder & cystic duct. Two seen in transverse section of GB,out of them one extends into the upper margin of GB & into cystic duct. Another seen in lower margin of GB extending in to cystic duct

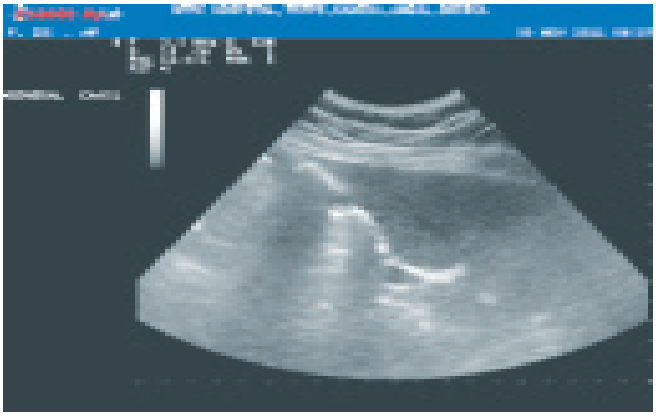

Figure-4 :
Round worm in CBD

MATERIAL AND METHODS

All the patients in whom Ascaris lumbricoides was detected in Gall Bladder, common bile duct, Hepatic duct or liver were the subjects of this study. We used 4.5 to 6.5 mega Hz curvilinear and 3.5 mega Hz sector probe for this purpose. Esaote USG machine model mylab – 40 was used. As described by Khuro et al (3) following appearances were used to detect Hepatobiliary ascariasis by USG. They are - linear or curvilinear

structure, single or multiple, with or without acoustic shadowing with movement not related to respiration. Other features were bull's eye sign, inner tube/ double tube sign i.e. visualization of elementary canal inside the round worm, impacted worm sign, spagatti appearance, dilatation of CBD, distended Gall Bladder, sludge in Gall bladder etc. Clinical presentation of all the cases and our ultrasonographic findings were studied in detail. Most patients were treated on OPD basis. But those with features of acute abdomen like acute cholecystitis were admitted as inpatient. All the patients were given antihelmithic therapy for 3 days i.e. Albendazole 400 mg OD X 3 days Mebendazole 100 mg BD for 3 days. When any patient didn't respond or showed partial improvement then antihelmithic therapy was repeated. Those cases which didn't respond to above therapy were referred for ERCP / surgical intervention.

RESULTS

During study period of 8 months total number of abdominal ultrasonography done were 613. Out of them Hepatobiliary ascariasis was detected in 34 (5%) cases. Among them 24 were females and 10 cases were males. M:E ratio was 1:2.4. Only 3 (8%) patient were bellow the age of 10. 16 (47%) cases were females in age group of 21 to 50.Three cases of children below 10 years were detected.

Commonest clinical presentation was pain abdomen. It was observed in 29 (85%) cases. Pain abdomen was present mostly in right hypochondrium, epigastrium and right loin. Sometimes diffuse pain abdomen was present. Features of acute cholecystitis with pain right hypochondrium, Tenderness, vomiting, guarding and rigidity was present in 2 (5%) cases. Obstructive Jaundice with cholestasis, pruritus, urticaria, raised serum bilirubin was seen in two (5%) cases. Other symptoms were vomiting in 3 (8%), features of APD were present in 3(8%) . Fever, nausea, anorexia, splenomegaly and epigastric mass in one case.

On ultrasonography round worms were detected in CBD in 17 (50%) cases, Gall bladder in 13(38%) cases. Distended gall bladder was detected in 5(14%), acalculus cholecystitis in 3 (8%) cases. Multiple round worms were visualized in 5 (14%) cases. Dilated Hepatobiliary tract was seen in two cases of obstructive jaundice. Thickened G.B wall with sludge was present in 3 cases. In most cases round worms were visualized as linear/ curvilinear structures which were moving in GB/CBD. All patient were given antihelmithic therapy – Albendazole 400 mg OD for 3 days or Mebendazole 100 mg BD X 3 days. Other symptomatic therapy like IV fluid, antibiotics, antispasmodics were given as and when required. Those patients in whom symptoms or motility of the worms persisted after 3 days of therapy, another 3 days of antihelmithic drug was given. Out of 34 patients 31 patients recovered completely with this therapy. One patient with obstructive jaundice had been given 2 courses of antihelmithic therapy. She couldn't come for repeat USG after 7 days. Two patients in whom symptoms didn't disappear were sent to higher centre for ERCP / Surgical intervention. But both these cases were treated conservatively and recovered. No case mortality was seen in our series.

DISCUSSION

Khuro et al[1, 2, 3] have studied 500 cases of symptomatic Hepatobiliary ascariasis by USG and duodenoscopy. They found biliary colic in 56% of cases, acute cholangitis in 24% cases. Acute cholecystitis 13% cases, acute pancreatitis in 6% cases and liver abscess in 1% cases. They have out lined several ultrasonographic features of Hepatobiliary ascariasis which are utilized in our study for the purpose of diagnosis. USG cannot visualize more common duodenal ascariasis. CT scan is helpful in finding R.W in Gall bladder neck, CBD and ampullary area of duodenum MRCP can detect worm in duodenum and those across the papilla, main pancreatic duct. It confirms USG findings. Khuro and Jarger from Kashmir have studied 109 cases of symptomatic Biliary and pancreatic disease with early ERCP with active symptoms. A total of 40 (36.7%) were proven to have Biliary/pancreatic disease related to ascariasis.

Round worms enter ampula of vater and Biliary tree frequently and most of the times return intestine

spontaneously within 72 hours of inducing biliary or pancreatic symptoms. When they are impacted in ampullary orifice, there occurs severe abdominal pain, in cystic duct there occurs a calculus cholecystitis, in CBD/ hepatic duct, they cause cholangitis & cholestatic jaundice. As per sanjay K. Satpathy et al[5]. In Hepatobiliary Ascariasis worm may be living in 66% of cases, dead 13% of cases and both living and dead in 2% of cases. Dead worms in long run are associated with cholelithiasis. According to them, 80% of case of HBA improve by conservative therapy, ERCP extraction and surgical intervention are required in complicated cases. There is discrepancy between number of cases having roundworm in CBD (17 nos.) and obstructive jaundice (2 nos.) in our series. The explanation is as follows: According to G.H. Mahour et al.[12] outer diameter of ascaris lumbricoides is 2-4 mm in adult male and 3-6 mm in adult female. Outer diameter of CBD is 4-12 mm (avg. 7.39mm), Inner diameter of CBD is 2.4-7.64 mm (avg.-5mm). As per Wari et al.[13] when there is heavy intestinal infestation one or two round worm may enter in CBD producing features of uncomplicated biliary ascariasis and they return back without producing obstructive jaundice and cholecystitis. They presented 198 cases of biliary ascariasis in which jaundice, colangiris, cholecystitis were found in 12%, 14%, 7% cases respectively. As per them, if round worm remains in CBD for a long time around 10 days they produce complications like obstructive jaundice, colangitis, stricture, calculi, cholecystitis, pancreatitis etc.

Liver abscess due to ascariasis is very rare as these worms can't negotiate easily into liver. However few cases of liver abscess due to ascariasis have been reported. Indrani Chakraborty et al [7] reported a case of liver abscess due to ascariasis in which they got fertilized decorticated eggs of Ascaris lumbricoides in the FNAC sample of liver abscess.

Though Hepatobiliary ascariasis is uncommon in children because of narrow ampula of vater and Biliary tree in them, Bahu et al[8] reported seven cases of Hepatobiliary and pancreatic ascariasis in children bellow the age of 11. All were diagnosed by USG. Clinical presentations in their series were vomiting, Pain abdomen, abdominal distension, pallor, Hepatomegaly. They reported pancreatitis in 5 cases, necrohaemorrhagic pancreatitis in two cases, and passage of round worm in vomitus in two cases with one mortality.

In our series clinical presentation and USG findings are similar as discussed by different authors. Out of 34 cases 33 (97%) cases responded to conservative therapy as most of the cases came immediately after their symptoms appeared and prompt antihelminthic therapy along with other symptomatic treatment was given immediately.

CONCLUSION

Hepatobiliary ascariasis is a common entity in developing countries. Ultrasonography is a simple, safe, cost effective, highly sensitive, outpatient procedure for diagnosis of this disorder. Out of all cases of abdominal USG, 5% cases were detected to be Hepatobiliary ascariasis. Pain abdomen, acute cholecystitis, obstructive jaundice, features of APD, vomiting are commonest clinical manifestations of HBA. Motile, round or curvilinear structures with inner or double tube sign in gall bladder or CBD are the commonest ultrasonographic findings. It is uncommon in children as it is difficult for adult worms to negotiate into ampula of vater. Most of the patients improve by conservative treatment along with oral antihelminthic therapy (Albendazole/Mebendazole). ERCP extraction or surgical interventions are reserved for complicated cases not responding to conservative therapy

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Original Article

EVALUATION OF THYROID FUNCTION IN PATIENTS OF CHRONIC KIDNEY DISEASE

Sahu A K*, Tripathy S K, Padhi P K*****

ABSTRACT

In chronic kidney disease patients endocriopathies are not so uncommon. There were controversies regarding the thyroid dysfunction in CKD patients. So this study was conducted to find out any thyroid dysfunction in CKD patients and correlate it with etiopathogenesis and severity of renal failure. It was found that though all the thyroid hormonal indices decrease in CKD but statistically significant decrease is seen only in Total T3 levels. So it can be told that there occurs defective thyroid hormonogenesis and decreased peripheral conversion of T4 → T3. ***Keywords :*** *Chronic kidney disease, Thyroid function, Hypothyroidism.*

INTRODUCTION

CKD is defined as the presence, for at least 3 months, of evidence of kidney damage with an abnormal GFR or alternatively, by a GFR < 60 ml/min /1.73m2 BSA.[1]

Kidney as an important endocrine organ regulates different body functions by secretion of renin, erythropoietin, active metabolite of Vit.D and Prostaglandin[2]. Though uremia in some instances causes clearly recognizable endocrinopathies, more commonly the endocrine dysfunction consists of only laboratory abnormalities. Chronic kidney diseases alters the thyroid status at biochemical levels, sometimes leading to overt clinical syndromes. The thyroid status in chronic renal failure has been studied extensively by many workers. Most of them have demonstrated biochemical evidence of hypothyroidism, few have detected hyperthyroidism ; even goiter and exophthalmos have been observed by some[3,4]. Although uremia shares some of the clinical features of myxoedema, overt clinical disturbances of thyroid function ordinarily does not occur [5,6].

Ramirez et al (1973) studied chronic renal failure cases undergoing haemodialysis and showed that besides biochemical evidence of hypothyroidism, goiter was seen in a number of cases[7]. *Lim et al (1977)* found biochemical as well as clinical evidence of hypothyroidism in their cases of uremia [8]. In contrary to the above studies, clinical euthyroidism was universally found among the uremic patients of *Spector et al (1976)* though some biochemical abnormalities were observed.[6] Various workers have attributed different cause of the trivial clinical abnormalities, frequent biochemical hypothyroidism and the occurrence of goiter in substantial number of uremic patients. However *Victoria et al (1987*) in their study of thyroid abnormalities before, during haemodialysis and after renal transplant comprehended the abnormalities at three different levels. *Firstly* there is a blunted TSH response to TRH suggesting pituitary dysfunction, *secondly* there occurs intrathyroidal defects in hormonogenesis, hormonal secretion or both and *lastly* impaired conversion of T4 to T3 in extra thyroidal tissues, resulting in selective and marked reduction in serum Total T3 concentration [9].

With these implications and controversies in opinion the work- *"Evaluation of thyroid function in patients of chronic kidney diseases with different etiopathogeneses"* has been undertaken to make an attempt to correlate various abnormalities of thyroid function in CKD patients with different etiopathogeneses

*Senior Resident,**Associate Professor,***Professor,
Dept. of Medicine, SCB Medical College, Cuttack, Odisha.

and to find out correlation between the severity of renal failure and the alteration of the thyroidal indices.

AIM :

To measure the total T3 , total T4 , free T3, free T4, TSH, Thyroid binding globulin (TBG) levels in CKD patients & correlate them with severity of renal failure and with its different etiopathogeneses .

MATERIAL AND METHODS

This study was undertaken at S.C.B. Medical College & Hospital, Cuttack, Odisha between 2010-2011. 50 cases of Chronic Kidney Diseases were taken, diagnosed and staged by following the criteria given by- National kidney foundation: K/DOQI guidelines .They were divided into two groups- GROUP-A- Those on conservative management (n=35) & GROUP-B- Those on hemodialysis (n=15). Group A patients were further classified into various stages based on their GFR which was calculated using Cockroft-Gault Equation. Group B cases were taken as stage 5 as per the recommendation. Another group of 20 healthy persons was taken as GROUP C (n=20). Those patients having past history of thyroid dysfunction i.e. either hypo- or hyperthyroidism and those on thyroid supplement therapy or on antithyroid drugs were excluded from the study.

The cases taken were examined clinically and they were subjected to various routine and specific laboratory investigations including thyroid function tests.

RESULTS

Out of 50 CKD cases taken 37 cases (74%) are males and 13 cases (26%) are females. Males predominate with a M : F ratio of 2.9 :1 . Diabetes mellitus was found to be the commonest cause of CKD (40%). Hypertension, SLE and obstructive uropathy account for 10% each, chronic GN for 4%. No definite cause of CKD could be found in 12 cases (24%) (TABLE-1). Out of 50 cases of CKD, 50% cases (25) were in stage 5, 28% cases in stage 4 , 20% in stage 3 and 2% in stage 2 .

All the 50 cases were having pallor (100%). Next in frequency of physical signs was Hypertension (84%) followed by coarse skin (54%), pedal edema (40%) and facial puffiness (20%). Thyromegaly was not found even in a single case.

CKD cases of GROUP A had Total T3, Free T4,Free T3 lower than the healthy group, but only Total T3 is significantly low (p=0.004). Though TSH of GROUP A CKD patients is higher than GROUP C (control) but it is not statistically significant (p=0.068).(TABLE-2)

The mean values of Total T3, Free T4,Free T3 are lower in GROUP B than the healthy group, but only Total T3 is significantly low (p=0.0071).Though TSH of GROUP B CKD patients is higher than GROUP C but it is not statistically significant(p=0.354)(TABLE-3). When the thyroid function test values of all the CKD cases of both groups (GROUP A & B) were compared with the controls (GROUP C) it was found that though mean values of Total T3, Free T4,Free T3 are lower than the control group, only Total T3 is significantly low (p=0.0011)(TABLE-4).

The thyroid function tests were correlated with different stages of CKD .It was found that as renal function worsens in terms of stages of CKD from stage 2 to stage 5,the mean values of Total T4,Total T3,Free T4,Free T3,TBG go on decreasing from stage 2 to stage 5 and the mean TSH goes on increasing. But when these values are compared with healthy controls (GROUP C), only the fall in Total T3 was found statistically significant (p<0.01)(TABLE-5).

Out of 50 CKD cases, 20 were diabetic.When the thyroid function test values of the *diabetic CKD* cases were compared with those with *non diabetic*

TABLE-1

ETIOLOGIES	NO. OF CASES	PERCENTAGE
DIABETES MELLITUS	20	40
HYPERTENSION	5	10
SLE	5	10
OBSTRUCTIVE UROPATHY	5	10
CHRONIC GLOMERULONEPHRITIS	2	4
POLYCYSTIC KIDNEY DISEASE	1	2
UNKNOWN ETIOLOGY	12	24
TOTAL	50	100

TABLE-2

	Total T4	Total T3	Free T4	Free T3	TSH	TBG
GROUP A (n=35) CONSERVATIVE	7.772 ±2.547	1.193 ±0.423	1.146 ± 0.423	2.898 ±1.074	7.38 ± 11.66	19 ±1.029
GROUP C (n=20)CONTROL	7.325 ± 1.42	1.54 ± 0.39	1.256 ±0.268	3.05 ± 0.39	2.487 ± 1.5	19 ± 0.917
P VALUE	0.474	0.004	0.299	0.5475	0.0684	>0.99

TABLE-3

	Total T4	Total T3	Free T4	Free T3	TSH	TBG
GROUP B HEMODIALYSIS (n=15)	7.62 ± 1.475	1.196 ± 0.292	1.245 ± 0.23	3.101 ± 0.425	3.505 ± 1.133	19 ± 1.069
GROUP C CONTROL (n=20)	7.325 ± 1.42	1.54 ± 0.391	1.256 ±0.268	3.05 ± 0.393	2.487 ± 1.50	19 ± 0.917
p VALUE	0.5537	0.0071	0.8993	0.716	0.354	0.889

TABLE-4

	Total T4	**Total T3**	**Free T4**	**Free T3**	**TSH**	**TBG**
ALL CKD PATIENTS(A+B) (n=50)	7.726 ±2.65	1.194 ±0.386	1.176 ±0.376	2.959 ±0.928	6.218 ±9.986	19 ± 1.03
CONTROL (n=20)	7.325 ± 1.42	1.54 ± 0.391	1.256 ±0.268	3.05 ± 0.393	2.487 ± 1.50	19 ± 0.917
p **VALUE**	**0.4655**	**0.0011**	**0.3896**	**0.6742**	**0.0994**	**>0.99**

TABLE-5

THYROID FUNCTION TESTS	STAGE-2 (n=1)	STAGE-3 (n=10)	STAGE-4 (n=14)	STAGE-5 on conservative mgmt (n=10)
TOTAL T4 (mcg/dl)	9.4	9.32 ±1.486	7.0885 ±2.739	7.048 ±2.701
TOTAL T3 (ng/ml)	2.34	1.361 ±0.221*	1.1085 ±0.362*	1.029 ±0.46*
FREE T4 (ng/dl)	1.46	1.367 ±0.282	1.037± 0.415	1.065 ±0.515
FREE T3 (pg/ml)	3.66	3.47 ±0.855	2.515± 0.962	2.807 ±1.287
TSH (micro U/ml)	1.25	3.889 ±5.795	11.34± 16.37	5.9 ± 6.94
TBG (mcg/dl)	20	19.4 ±1.074	19.07± 1.141	18.5 ± 0.707

TABLE-6

	Total T4	Total T3	Free T4	Free T3	TSH	TBG
DIABETIC (n=20)	6.939 ±2.188	1.096 ±0.3510	1.127 ±0.3703	2.756 ±0.6209	6.765 ±9.892	18.95 ±1.05
NON DIABETIC (n=30)	8.251 ±2.194	1.2593 ±0.3992	1.208 ±0.3828	3.0947 ±1.0749	5.836 ±10.05	19.03 ±1.033
p VALUE	0.0434	0.144	0.4614	0.2095	0.7487	0.791

FIGURE-1- COMPARISON OF THYROID FUNCTION TESTS : ALL CKD CASES (A+B) vs HEALTHY PERSONS(C)

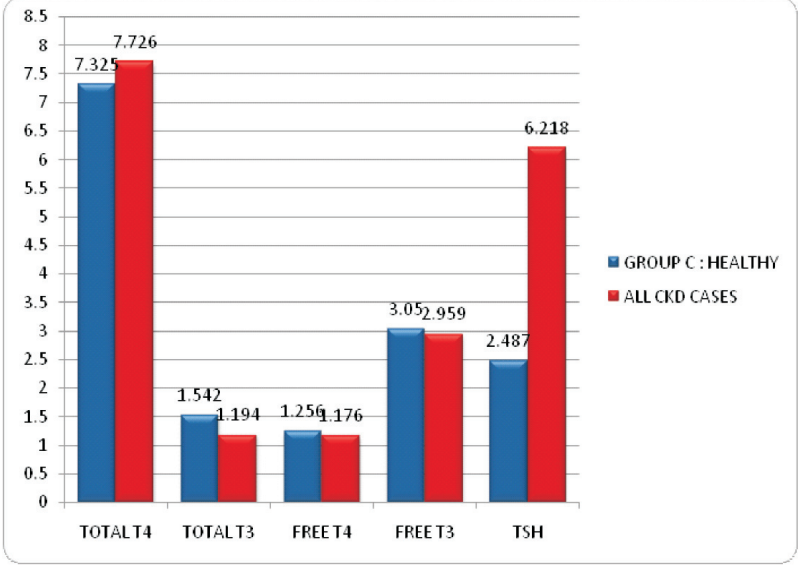
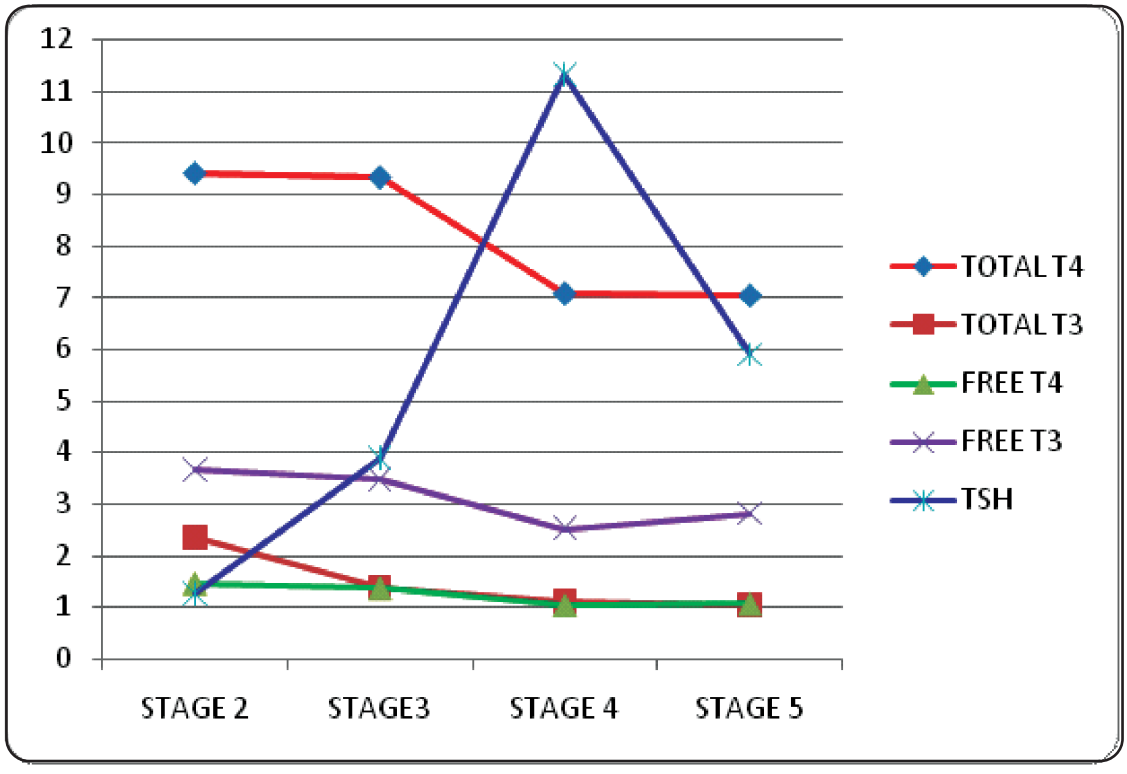


FIGURE-2
CORRELATION OF THYROID FUNCTION TESTS BETWEEN ALL THE STAGES OF CKD



CKD cases(n=30) it was found that the mean values of Total T4, Total T3, Free T4, Free T3 were lower in diabetic group than non diabetic group and the TSH level is higher in diabetic group. But these differences are not statistically significant except for Total T4 (p=0.0434). (TABLE-6)

The thyroid function test values of the CKD cases with history of Hypertension were compared with those without history of Hypertension. It was found that there is no significant difference between the mean values of Total T4, Total T3, Free T4,Free T3, TSH, TBG (p>0.05) between these two groups.

Among the 5 CKD cases with SLE Total T4, Free T4 were low in 1 (20%)case each, Free T3 was low in 2 (40%) cases and TSH was higher in 1 (20%) case than the normal range. But none of them had low Total T3 .

DISCUSSION

Most common presenting symptoms were anorexia, lethargy, oliguria, nausea, vomiting and hiccups. Common physical signs were anemia , hypertension, coarse skin, pedal edema, facial puffiness. There was no goiter in any of the CKD patients. Proteinuria and broad granular casts were the commonest urinary abnormalities. Serum sodium were in low normal range. Most common ultrasonographic finding were bilateral contracted kidney and loss of corticomedullary differentiation. Diabetes mellitus was the commonest cause of CKD followed by hypertension, SLE and obstructive uropathy. Though some of the signs and symptoms were common to both CKD and hypothyroidism but classical features of hypothyroidism were lacking.

In all CKD cases the Total T3, Free T4,Free T3 levels decrease and TSH rises whereas TBG and Total T4 remains in normal range. But only the decrease in Total T3 is statistically significant. As the stage of CKD worsens, there is decrease the absolute values of all thyroid hormones and rise in TSH.So these

changes may be due to intrathyroidal defects in hormonogenesis, hormonal secretion or both and impaired peripheral conversion of T4 to T3 .

The same trend of changes is seen in the CKD cases of all etiologies. The diabetic CKD cases(40% of all cases) show lower thyroid hormones and higher TSH.But this difference is not significant. So it can be told that in CKD, the thyroid hormone abnormality is not because of the etiology rather it is due to the renal function derangement.

In our series TBG was normal in almost all cases and there is low FreeT4 in spite of normal Total T4. Hence the decrease in thyroid indices cannot be attributed to decreased TBG as it was thought earlier.

CONCLUSION

To conclude from the above study, it is presumed that there occurs a state of biochemical hypothyroidism in patients of CKD, the extent of which correlates with the severity of renal failure. The causes of thyroidal dysfunction may be intrathyroidal defect in hormonogenesis, hormonal secretion or both and a defect in peripheral conversion of T4 to T3. A significantly low Total T3 despite a near normal Total T4 indicates more towards the defect in peripheral conversion. As similar results are obtained in dialysis and non-dialysis group, it appears that there is no effect of dialysis on this thyroid dysfunction. Inspite of the biochemical hypothyroid state, the metabolic status remains normal and there occurs no overt clinical hypothyroidism.

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Original Article

CLINICAL PROFILE OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A TERTIARY CARE HOSPITAL IN ODISHA

S. Bhuyan*, N. Dhal, A. Debbarma*, S. Tirkey***

ABSTRACT

Aim: *To study the clinical profile of SLE in a tertiary care hospital in Odisha.* ***Material & Methods :*** *We studied 80 consecutive patients with SLE diagnosed according to ACR criteria 1997, with age more than 18 years (18 - 52 years).* ***Results :*** *The disease is more prevalent in females, Female:Male= 24: 1. It is more marked in the age group of 26 - 35 years. Majority of patients displayed oral ulcers (70%), arthritis (66%), malar rash (60%), nephritis (37.5%), photosensitivity (30%), vasculitis (13.75%), serositis (7.5%), NPSLE (6.2%) and myocarditis (2.5%).* ***Conclusion :*** *SLE is a disease of young females presenting commonly with fever, oral ulcer, arthritis and skin rash. Kidney is the major organ involved followed by vasculitis.* ***Keywords :*** *Systemic lupus erythematosus, clinical profile, lupus nephritis.*

INDTRODUCTION :

Systemic lupus erythematosus (SLE) is a multi-factorial chronic autoimmune disorder characterized by dysfunction of T and B lymphocytes and affects various vital organ systems. B cell hyperactivity resulting in overproduction of autoantibodies against cytoplasmic, nuclear, and surface antigens and immune complex formation[1,2]. The majority of autoantibodies found in SLE are targeted at intracellular nucleoprotein particles. 98% of patients have antinuclear antibodies and antidouble-stranded DNA antibodies are found in 50-80% of patients[3]. These autoantibodies are frequently targeted against intracellular antigens of the cell nucleus (double and single stranded DNA (dsDNA and ssDNA, respectively), histones, and extractable nuclear antigens (ENAs). Most of these autoantibodies are not specific for SLE and might be produced non-specifically as a result of polyclonal B cell activation[4,5].

The etiology of the disease is still unclear, although environmental, host, genetic and hormonal factors have been proposed to play major roles in pathogenesis of SLE[6]. 70 to 90% of SLE patients are female[7]. There are limited studies on Indian SLE patients. Although the prevalence of SLE in India is rare (3/100,000)[8], the survival rates of these patients (70% at 5 years, 50% at 10 years) are very low compared to Western cohorts[9,10]. Systemic Lupus Erythematosus (SLE) at its onset may involve one or more organ systems and over a time additional manifestations may appear after a variable period. The systems involved in SLE are musculoskeletal, cutaneous, renal, nervous system, hematological, vascular, pulmonary, gastrointestinal, and ocular. Hematological manifestations (abnormalities of the formed elements of the blood, of the clotting and fibrinolytic factors and related systems) of SLE are diverse and often they are the presenting manifestations of the disease[11-13].

MATERIAL & METHODS:

80 consecutive patients diagnosed to have SLE (according to revised ACR criteria 1997), more than 18 years of age admitted to different wards of Department of Medicine, S.C.B. Medical College & Hosptial, Cuttack over a period of one year from September 2012 to September 2013 were included.

Detection of ANA was done by indirect immunofluorescence using a commercial kit (EUROIMMUN medizinche labordignostica AG, D23560 lubek (deuchland, seekamb). Dilution of serum used was 1:100.

* Post-Graduate Student, ** Asst. Professor, Dept. of Medicine, SCB Medical College, Cuttack, Odisha.

Antibodies to dsDNA was detected by indirect immunofluorescence using a commercial kit (EUROIMMUN MEDIZINSCHE LABOR-DIAGNOSTICA, AG D 23560 LUBEK, DEUTSCHLAND SEEKAMB)

Antibodies to different anti nuclear antigen were detected by using immuno blot strips (EUROIMMUN MEDIZINSCHE LABOR-DIAGNOSTICA, AG D 23560 LUBEK, DEUTSCHLAND SEEKAMB) coated with 14 different antigens: nRNP, Sm, SSA, SSB, RO-52, SCL-70, PM-SCL, JO-1, CENPB, PCNA, dsDNA, nucleosome, histone, ribo-P-protein, AMA-M2. Besides routine haematological and biochemical parameters were evaluated.

RESULTS:

A total of 80 patients were enrolled in the current study. The disease is more prevalent in females (n=77; 96%) compared to males (n=3; 4%). 51.25% of patients were in the 26-35 age group. Older age group patients (36-45 and >45 years) had prolonged disease duration compared to younger patients. (Table-1)

TABLE -1

Age	Male (n=3)	Female (n=77)	Total (%) (n=80)	Duration of Disease ± S.D. Years
15-25	1	15	20%	2.79 ± 2.00
26-35	2	39	51.25%	2.25 ± 1.20
36-45	0	13	16.25%	5.22 ± 1.78
> 45	0	10	12.50%	5.00 ± 3.60

TABLE -2

Clinical Profile	SLE (n = 80)	Healthy Control (n = 50)
Sex (Male/Female)	3/77	0/50
Age in years (Mean±S.D.)	27.81±8.16	25.536±4.604
Duration of disease months (Mean±SD) ACR Criteria	2.906±1.96	—
Photosensitivity rash	24 (30%)	—
Malarrash	48 (60%)	—
Discoldrash	8 (10%)	—
Oral Ulcer	56 (70%)	—
Arthritis	53 (66%)	—
NPSLE	5 (6.2%)	—
Myocarditis	2 (2.5%)	—
Serositis	6 (7.5%)	—
Nephritis	30 (37.5%)	—
Vasculitis	11 (13.75%)	—

Majority of patients displayed oral ulcer (70%), arthritis (66%), malar rash (60%). 37.5% patients had nephritis, follwed by photosensitivity rash (30%), vasculitis (13.75%)discoid rash (10%), serositis (7.5%), NPSLE (6.2%) and myocarditis (2.5%). (Table -2).

TABLE-3

COMPARATIVE DEMOGRAPHIC PROFILE OF SLE

	Out Study 80 pts Odisha	Kartikayan et al[16] 82 pts. 2008,T.Nadu	Malavya et al[15] 101 pts. 1985, N. India	Binoya et al[14] 75 pts 2003,Madras	Renu Saigal et al[17] 60 pts 2008,W. India
Age	26-35	21-30	24-26	21-26	21-30
Sex	24:1	15.4:1	8:1	19:1	11:1
Duration of Diesease	33 Months	NA	17 Months	NA	24 Months

TABLE-4

COMPARATIVE CLINICAL PROFILE OF SLE

Clinical Feature	Out Study 80 pts Odisha (%)	Kartikayan et al[16] 82 pts. 2008,T.Nadu (%)	Malavya et al[15] 101 pts. 1985,N.India(%)	Binoya et al[14] 75 pts 2003,Madras(%)	Renu Saigal et al[17] 60 pts 2008,W. India (%)
Oral Ulcer	56	15	64	64	61.7
Arthritis	53	52	66	89.3	86.7
Malarrash	48	26	38	40	33.3
Nephritis	30	NA	73	33.3	56.7
Photo. Sensivity	24	19	67	32	75
Vasculitis	11	45	32	2.7	21.7
Discoid rash	08	NA	05	5.3	1.7
Serositis	06	NA	NA	2.7	NA
NPSLE	05	NA	15	13.3	13.3

DISCUSSION :

In the demographic profile recorded there were 3 males and 77 females as indicated in Table-1. The age group most affected was 26-35. It is well known that females in reproductive age group are suceptible to SLE[18]. In a comparative study from different regions of India (Table -3) the female predominance is evident as well as the affection of younger age group. Our study had more female patients i.e. (24:1) which indicates that females are comparatively more affected or it may be a skewed data in view of hospital based analysis. Surprisingly, the median duration of disease was 3 years before they presented to tertiary care hospital indicating lack of awareness of the problem leading to late referral.

On analysis of the clinical profile from different

parts of country (Table-4). It is evident that the musculosketal symptoms are important presentation of lupus. The variability of some of the features may be related to the stage of detection of disease. Interestingly, Malavya et al 1985[15] reported 73%. cases having nephritis compared to 30-50% in other centres. Since the report of Malavya et al[15] came from a tertiary care centre in North India, these patients have probably developed nephritis at the time of presentation.

Asian population have high succeptibility to nephritis and renal failure remains one of the commonest causes of death in SLE[18]. The exact reason for this susceptibility is not known.

Neuropsychiatric lupus is relatively uncommon in Indian population compared to the Western cohorts. Genetic susceptibility may be involoved in the variation of clinical manifestation seen in defferent populations.

To summerise SLE is a disease of young females presenting commonly with fever, arthritis, oral ulcer and skin rash. Kidney is the major organ invoved followed by vasculitis. A high index of suspicion is necessary for making an early diagnosis.

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Pictorial CME

SISTER MARY JOSEPH'S NODULE

M.R. Behera*, B.L. Parija, J. Narayan***, S. Tripathy***, P. Panda***, M. Mandal*****

A 58 years old male presented with progressive swelling of abdomen over last two months; Loss of appetite, loss of weight, intermittent vomiting and generalised weekness over last 3 months. No h/o alcoholism, smoking, diabetes mellitus or hypertention. General examination revealed moderate degree of pallor. Systemic examination revealed: Normal oral cavity, abdominal examination revealed palpable, non tender, firm nodules on either side of umblicus (Fig.1) and evidence of free fluid in abdomen. Other systemic examinations were within normal limit. Laboratory examinations revealed: Hb 6.2gm%, microcytic hypochromic anaemia, DC, TLC, FBS/2hr PGBS, urea, creatinine, LFT, were within normal limit, Na^+ 122 meq/lit, K^+ 2.9 meq/lit, S-protein 5.9 mg/dL, S. Albumin 2.9 mg/dl, S.Glubulin 3 mg/dl, and stool test was positive for occult blood. Chest x-ray was normal. USG abdomen & pelvis revealed gastric wall thickening near pylorus & moderate ascites. FNAC of the paraumblical nodule revealed metastatic adenocarcinoma (Fig.2), upper GI endoscopy revealed growth involving antrum & pylorus of stomach (Fig.3). Endoscopic biopsy report revealed adenocarcinoma of stomach (Fig.4). Ascitic fluid examination revealed sugar 40mg/dl, protein 3g/dl, ADA was normal, Total cell count 460/microlitre, Lymphocytee 40%, Histiocytes 40%, Mesothelial Cells 10% and atypical cells 10%. Hence a diagnosis of Adenocarcinoma of stomach, malignant ascites with sister Mary Joseph's nodule was made and patient was referred to Cancer Hospital for further management.

Sister Mary Joseph (1856-1939) was Superintendent Nurse at St. Mary's Hospital in Rochester, US (at present the Mayo Clinic). First observed that patients with intraabdominal and/or pelvic malignancy occasionally have an umblical nodule indicating umblical metastasis. Consequently in 1949, the English Surgeon Hamilton Bailey, acknowledged her observation in his famous text book "Demonstrations of Physical signs in clinical surgery" and coined the term "Sister Mary Josephs nodule" for umblical metastasis. Now, it has been accepted widely as a marker of intrabdominal malignancy presumed to have spread by either peritoneal (most commonly) or by the venous or lymphatic route. It is estimated that 1-3% of abdominal/pelvic tumours metastasize to the umblicus. The histologic nature of metastatic umblical tumors usually reveals adenocarcinoma but there have also been reports of umblical metastasis from sarcoma, mesothelioma & melanoma. In 14-33% cases, umblical metastasis lead to diagnosis of previously occult neoplasm, where as in 40% cases with a known neoplasm the nodule is an early sign of relapse. In men, Gastrointestinal tract is the most common primary site where as in females gynaecological neoplasms particularly ovarian cancer is the most common primary site. Stomach malignancy as a primary source of umblical nodule, has been observed in only 23% cases. Unfortunately, this sign is a reflection of a poor prognosis due to wide spread internal malignancy and most patients have a life expectancy of less than one year. As it is a rare sign a high index of suspicision and a good clinical examination is required to get such findings which will enable us to approach cases of occult/internal malignancies. This again emphasises the value of good clinical examination in day to day clinical evaluation.

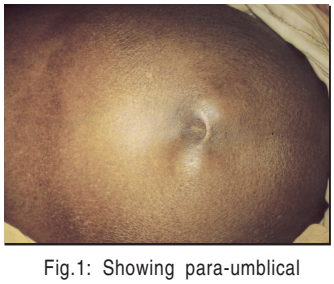

Fig.1: Showing para-umblical nodules

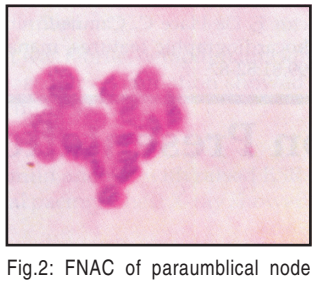

Fig.2: FNAC of paraumblical node showing metastatic denocarcinoma

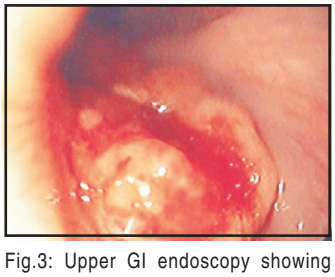

Fig.3: Upper GI endoscopy showing growth in stomach

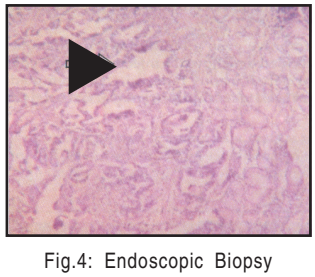

Fig.4: Endoscopic Biopsy showing gastric adenocarcinoma

* Asst. Prof, ** Asso. Prof., *** PG Student, Dept. of Medicine, SCB Medical College, Cuttack.

Review Article

POLYCYSTIC OVARY SYNDROME AND OBESE DIABETICS

S. Das*, D. Bhattacharyya, S. Misra*****

ABSTRACT

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women in the developed world and also in rapidly being diagnosed in the developing countries like India.[1] With changes in lifestyle, food habit, incidence of obesity and consequent rise of its complications are also increasing. Insulin resistance (IR) is an obvious outcome of obesity. The triad of obesity, IR and glucose intolerance play a crucial role in pathogenesis of PCOS.[2] All these make the individual prone to develop frank type 2 Diabetes mellitus. Various treatment strategies are being evaluated for management of PCOS as well as Obesity. Insulin sensitizers like metformin are most promising drugs regarding treatment of PCOS and prevention of diabetes. ***Key Words****: PCOS, Obesity, Insulin Resistance, Type 2 Diabetes mellitus, Insulin Sensitizers.*

Obesity

Obesity is a state of excess adipose tissue mass.[3] Although not a direct measure of adiposity, the most widely used method to gauge obesity is the body mass index (BMI), which is equal to weight/height^2 (in kg/m^2). Using data from the Metropolitan Life Tables, the midpoint of BMI for all heights and frames among both men and women range from 19–26 kg/m^2.[3] At a similar BMI, women have more body fat than men. Based on the data of substantial morbidity, a BMI of 30 is most commonly used as a threshold for obesity in both men and women. Large-scale epidemiological studies suggest that all-cause, metabolic, cancer, and cardiovascular morbidity begin to rise when BMIs are >25, suggesting that the cut-off for obesity should be lowered.[4] Most authorities use the term overweight (rather than obese) to describe individuals having BMI between 25 and 30. A BMI between 25 and 30 should be viewed as medically significant and worthy of therapeutic intervention, especially in the presence of risk factors that are influenced by adiposity such as hypertension and glucose intolerance.[5]

Obesity, Insulin Resistance and Type 2 Diabetes Mellitus

The distribution of adipose tissue in different anatomic depots also has substantial implications for morbidity. Specifically, intra-abdominal and abdominal subcutaneous fat have more significance than subcutaneous fat present in the buttocks and lower extremities. Many of the important complications of obesity, such as insulin resistance (IR), diabetes mellitus (DM), hypertension, hyperlipidemia and hyperandrogenism in women, are linked more strongly to intraabdominal and/or upper body fat raher than to overall adiposity.[5] The mechanism underlying this association is unknown but may relate to the fact that intraabdominal adipocytes are more lipolytically active than those from other depots. Release of free fatty acids (FFA) into the portal circulation has adverse metabolic actions, especially on the liver. Whether adipokines and cytokines secreted by visceral adipocytes play an additional role in systemic

* Prof. & HOD, ** Post Graduate Student, Dept. of Medicine, SCB Medical College & Hospital, Cuttack. *** Asso. Prof., Dept. of O&G, SCB Medical College & Hospital, Cuttack, Odisha.

complications of obesity is an area of active investigation. In the past, adipocytes were generally been regarded as a storage depot for fat, but current knowledge reveals that the visceral adipocytes are endocrine cells that release numerous molecules in a regulated fashion.[6] These include

i. the energy balance–regulating hormone leptin, cytokines such as tumor necrosis factor (TNF) and interleukin (IL)-6.

ii. complement factors such as factor D (also known as *adipsin*),

iii. prothrombotic agents such as plasminogen activator inhibitor I (PAI)

iv. a component of the blood pressure regulating system, angiotensinogen.

Adiponectin, an abundant adipose-derived protein, the levels of which are reduced in obesity, enhances insulin sensitivity and lipid oxidation and it has vascular protective effects, whereas resistin and RBP4, whose levels are increased in obesity, may induce insulin resistance. These factors play a role in the physiology of lipid homeostasis, insulin sensitivity, blood pressure control, coagulation, and vascular health, and are likely to contribute to obesity-related pathologies.[7]

Polycystic Ovary Syndrome(PCOS)

PCOS is one of the commonest female endocrinopathies and is the commonest cause of anovulatory infertility affecting 1-5 % of women in the reproductive age group.[8] It is considered to be a syndrome that manifests with heterogeneous clinical features. The most common feature of PCOS are irregular menstrual cycles (oligomenorrhoea or amenorrhoea), signs of androgen excess (hirsutism, acne, alopecia), and often obesity. However, only 5-10% of women with PCOS express all the typical clinical features of the syndrome .[9]

At present, the diagnosis of PCOS is usually based on the criteria derived from 1990 NIH-NICHHD (national Institutes of Child Health and Human Development) conference.[10] The criteria includes ovulatory dysfunction, clinical evidence of hyperandrogenism and/or hyperandrogenaemia and exclusion of related disorders such as congenital adrenal hyperplasia, hyperprolactinemia or Cushing's syndrome.[11]

The sonographic criteria for PCOS requires the presence of 12 or more follicles in either ovary measuring 2 to 9 mm in diameter and or increased ovarian volume more than 10 ml. A single ovary confirming these criteria is sufficient to affix the diagnosis of PCOS. The revised criteria for the diagnosis of PCOS is depicted in Table 1.[10]

The morphological appearance of polycystic ovaries is inherited as an autosomal dominant trait, even if no signal gene has been identified as casual.

Obesity and PCOS

Obesity is a feature in between 35 to 60 % of woman with PCOS and associated with a greater severity of clinical manifestations than non-obese women with PCOS.[12] Obesity has long been associated with menstrual abnormalities in women, particularly in those with upper body obesity. A Common finding is increased androgen production, decreased sex hormone binding globulin (SHBG) and increased peripheral conversion of androgen to estrogen. Most obese women with oligomenorrhea have PCOS. It is associated with anovulation and ovarian hyperandrogenism; forty percent of women with PCOS are obese. Most nonobese women with PCOS are also insulin-resistant, suggesting that IR, hyperinsulinemia, or the combination of the two are causative or contribute to the ovarian pathophysiology in PCOS in both obese and lean individuals. In obese women with PCOS, weight loss or treatment with insulin-sensitizing drugs often restores normal menses.[13]

Figure 1. Relation between Serine Phosphorylation, Hirsutism and Diabetes.

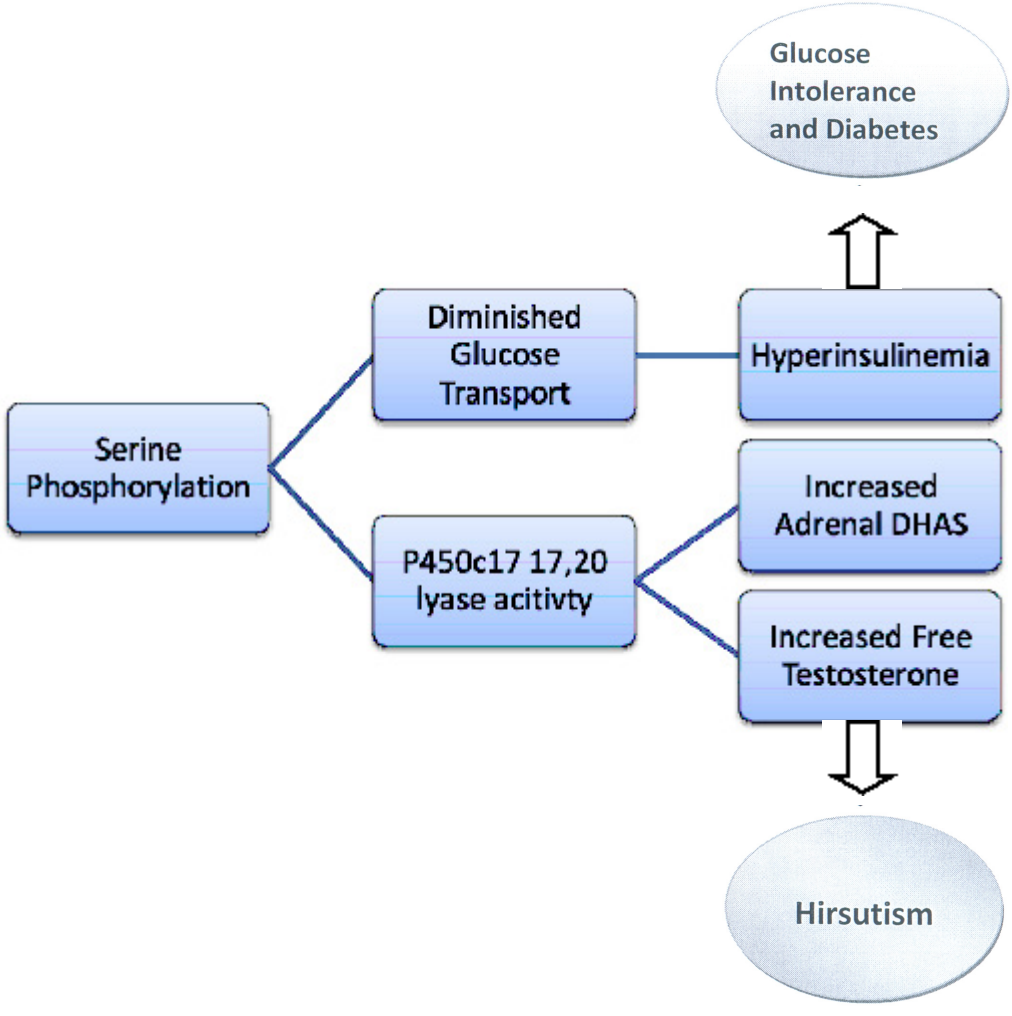

Table 1. Diagnostic criteria of PCOS[10]

1999 Criteria(both 1 and 2)	Revised 2003 Criteria (2 out of 3)
1.Chronic anovulation 2. Clinical and/or biochemical signs of hyperandrogenism, and exclusion of other aetiologies	1. Oligo- and/or anovulation 2. Clinical and/or biochemical signs of hyperandrogenism 3. Polycystic ovaries and exclusion of other aetiologies

Table 2. Evaluation of IR before and after treatment with metformin[22]

Parameters	Before Treatment	After Treatment	t value	Significance
FBG	92.16(8.99)	85.16(8.86)	4.97	p<0.01
Insulin	14.48(7.90)	8.65(2.14)	2.14	p<0.01
HOMA	3.34(2.04)	1.82(0.51)	4.56	p<0.01
QUICKI	0.32(0.23)	0.35(0.01)	-8.15	p<0.01

Mean values FBG in mg/dl and insulin in microU/ml(SD). HOMA, homeostatic model assessment; QUICKI, quantitative insulin sensitivity check index.

Table 3. Glycemic Changes and Anthropo,etric Changes after Metformin therapy[22]

Variables	Before Treatment	After Treatment	p value
BMI(kg/sq. m)	25.45±3.7	23.95±3.2	<0.05
Waist hip ratio	0.75±0.18	0.63±0.14	p<0.01
FBG(mg/dl)	92.16±8.8	85.48±8.2	p<0.01
2-h PGBS(mg/dl)	116.56±19.6	104.8±11.4	p<0.01

Table 4 . Hormone Profile in patients with PCOS before and after metformin therapy[22]

Hormone levels		Before treatment		After treatment	
		No	%	No	%
Serum Testosterone	High (>1.19)	13	52	1	4
(mg/ml)	Normal (0.65-1.19)	12	48	24	96
	Low(<0.65)	0	0	0	0
Serum Insulin (microU/ml)	High (>27)	3	12	0	0
	Normal (6-27)	22	88	25	100
	Low (<6)	0	0	0	0

Table 5. Pelvic Ultrasonogram change after treatment of PCOS[22]

	Before treatment		After treatment	
Ovarian Morphology ,typical of polycystic change	No	%	No	%
	14	56	2	8

PCOS, Obesity, Insulin Resistance and Type 2 Diabetes Mellitus- the Axis

Increased IR is a cardinal feature of obesity and overweight. It play a pathognomonic role in women with PCOS. It has been shown correlation with raised serum testosterone, androstenedione and insulin in women with PCOS. IR is consistently accompanied by hyperinsulinmia. Insulin is able to stimulate steroid genesis both in granulosa and thecal cells by increasing 17alpha hydroxylase and 17-20 lyase activity. [14]

SHBG is a glycoprotein produced in the liver and acts as a carrier for different sex hormones with high binding affinity for testosterone and dihydrotestoterone (DHT) and a lower affinity for oestradiol. SHBG are stimulated by factors such as oestrogens, cortisol, iodothyronines and Growth hormone, and decreased by androgens, insulin, prolactin and Insulin like growth factor (IGF-1). Insulin is thought to lower serum SHBG levels by inducing reduced hepatic SHBG synthesis.[15]

PCOS is characterized by chronic anovulation. An underlying disorder in androgen biosynthesis or metabolism may be the central event. An important stage of androgen synthesis is activity of P450c17 enzyme which is located in ovarian theca-interstitial cell and adrenals. Hyperacitivity of P450c17 enzyme leads to hyperandrogenism. With regards to glucose homeostasis, IR induces phosphyralation of serine residue instead of tyrosine residue of insulin receptor on the target cells leading to compensatory hyperinsulinaemia. In PCOS, serine phosphorylation of beta chain of insulin receptor causes enhanced activity of P450c17 enzyme system and consequent rise in androgen. Therefore while IR supresses insulin activity on target cells and reduces glucose utilization in subjects with type 2 DM, it enhances pathogenic mechanism of PCOS. (Figure No 1).[16]

There are theoretical possibilities of dietary composition playing a role in the development of the obesity in PCOS since there are data suggesting that women eating vegetable-rich and fibre-rich diet may have lower serum androgen concentrations compared to those following typical western diets. Moreover, a very high lipid intake has been described to be associated with PCOS and significant negative correlation has been found between lipid intake and SHBG values.[17]

The studies examining IR in obese and non-obese women with PCOS have shown that obese PCOS women had significantly lower insulin sensitivity than non-obese women.[18]

Both fasting and glucose-stimulated insulin concentrations are in fact significantly higher in obese and non-obese women with PCOS.

Acanthosis nigricans (AN) is a reliable marker of IR and often occurs in patients with insulin receptor defects.

The percentage of obese women with PCOS is high and this subgroup of PCOS affected women is characterized by increased prevalence of glucose intolerance ranging from 20-40 %. In contrast, IGT in non-obese women with PCOS has been found only occasionally.

Women with PCOS are at high risk of dyslipidemia because they are obese and have elevated androgen level. Obese women with PCOS have lower level of high –density lipoprotein and higher level of triglyceride, apolipoprotein B and free fatty acids. Women with PCOS have higg LDL-III subfractions which make them prone to develop atherosclerosis early. In 2004 Taponem et al observed that women with hirsutism and regular cycles do not have dyslipidemia compared to control women whereas those with both hirsutism and oligomenorhoea have lowerHDL-C and higher triglyceride suggesting a correlation between menstrual irregularity and dyslipidemia. [18]

The endothelium regulates blood flow and blood pressure through the production of powerful vasoactive substance such as NO, endothelin-1 and thromboxane A2. Endothelial dysfunction can lead to defective vasolidation and disturbance of the balance of vasoactive substances favouring vasoconstriction and development of hypertension. The vascular endothelium is a key regulator of haemostasis and fibrinolysis, controlling the activities of the intrinsic pathway, the fibrinolytic and protein-C anticoagulant pathways as well as influencing platelet activation and adhesion. Endothelial dysfunction can account for the increased levels of PAI-1 observed in patients with the 'insulin resistance syndrome. [19]

It was demonstrated that menstrual abnormalities are more frequent in obese than non-obese PCOS women.

Weight loss may improve menstrual abnormalities and both ovulation and fertility rate. Moreover, it was confirmed that hirsutism and acanthosis nigricans were significantly improved in most patients following weight loss. Reduction of hyperandrogenaemia appears to be the key factor responsible for these effects.

Loss of body weight more than 5% causes an improvement in menstrual pattern, endocrine profile and fertility in obese women (BMI>25) with PCOS.

Obese women with PCOS are significantly more insulin resistant and have higher insulin levels than weight matched controls or non-obese affected women. The primary role of IR and hyperandrogenism and related clinical features can be improved by reducing insulin levels. Obese women with PCOS have a higher risk for cardiovascular disease, endothelial dysfunction and IGT or Type-2 DM than non-obese women with PCOS. Therefore, we emphasize weight loss as a first line approach in the treatment of obese PCOS women, which significantly improves clinical features hormonal and metabolic abnormalities of these patients.[20]

Treatment strategies regarding management of PCOS are chiefly Weight reduction by diet, exercise, Insulin Sensitizers like Metformin, Laparoscopic Electrocautery of ovaries. [21]

In 2004, in study on Effect of Metformin in Asian Indian women with PCOS", it was shown that significant change in the levels of androgen, insulin, fasting and post prandial blood sugar, BMI and even in ovarian morphology occur after treatment with metformin, as shown in table no 2, 3, 4, 5.[22]

Conclusion:-

PCOS is a not only isolated disease of ovary but a metabolic disease spectrum comprising of obesity, dyslipidemia, atherosclerosis, IGT, type 2 DM, infertility and menstrual abnormality. Therefore treatment of PCOS is to be done by multidisciplinary approach. Treatment involves not only correction of specific clinical consequences of PCOS, DM and obesity, but also reduction of adverse effect on overall health by creating a preventive health care attitude towards women with PCOS.

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Current Concept

LEVACECARNINE : A NOVEL APPROACH IN THE MANAGEMENT OF GERIATRIC DEMENTIA

G. Kumar[*], P.K. Rathor[**], K.P. Pattnaik[***], D.N. Moharana[****]

Introduction

The word "Dementia" has been derived from the latin word "*Demens*" meaning without mind. Chronic brain failure (to parallel Heart failure, Renal failure, Liver failure, etc) is an alternative first suggested by Bernard Issacs & Francis Caird more than 30 years ago. More recently it has been suggested that alternative umbrella terms of "Cognitive Impairment" or "Neurocognitive Impairment" are clear and less stigmatizing and may be preferred when dealing with patients and families[1].

Dementia is a syndrome(not a diagnosis)describing a characteristic pattern of multiple cognitive deficits, usually including memory impairment, associated with a progressive decline in the ability to carry out activities of daily living (ADL) and often associated with personality and behavioural changes[5].

General criteria for dementia include the DSM – IV (Diagnostic and Statistical Manual of Mental disorders -4th edition) criteria and ICD-10 (International Classification of Diseases) criteria, each features the requirements of both Cognitive Impairment(in more than one domain of cognition) and functional impairment[11].

Dementia is one of the major causes of dependency among older people worldwide and has physical, psychological, social and economical impact on caregivers, families and society[2].

Global burden of Dementia

Worldwide 35.6 million people have dementia and there are 7.5million new cases added every year[16]. Alzheimer's disease (AD) is the most common cause of dementia and may contribute to 60 -70% of cases followed by Vascular dementia[2].

Management of Dementia : Present Scenario

Both pharmacologic and nonpharmacologic treatments are effective. Management goals in early dementia centre on improving or stabilizing cognitive ability and mood, maintaining and re-establishing independence, promoting autonomy, and effective planning for future. As the condition progresses, emphasis shifts to facilitating mental and physical stimulation, managing behavioural disturbances, and providing practical care for patients and respite for their families.

At present, the available drugs of proven efficacy include Acetylcholinesterase inhibitors (AChEIs), donepezil, galantamine and rivastigmine, and the N-methyl-D-aspartate(NMDA) receptor antagonist, memantine[3].

The AChEIs work by blocking the enzyme acetylcholinesterase and so inhibit the breakdown of the neurotransmitter acetylcholine. Numerous placebo – controlled clinical trials have shown consistent, if modest benefits on cognitive and global measures in a majority of patients with mild to moderate AD and most studies show improvement (or less deterioration) in activities of daily living, behaviour, caretaker burden, and use of resources. Memantamine by antagonizing NMDA receptor blocks pathologically elevated glutamate and consequent calcium overload while still allowing physiologic receptor activation. It is usually used in combination with AChEIs[3].

Despite their clinical efficacy and safety in Alzheimer's disease, the cost effectiveness of AChEIs has been questioned and in the United Kingdom, the NICE (National Institute for Health and Clinical Excellence) appraisal process controversially

[*]Post Graduate student, Dept. Of Pharmacology, [**]Asst. Prof., Dept. Of Medicine, [***]Asso. Prof. Dept. Of Pharmacology, ****Prof. & HOD, Dept. Of Geriatric Medicine, S.C.B. Medical College & Hospital, Cuttack, Odisha.

recommended their use only in moderate dementia[15]. Hence the search for an ideal drug still continues.

Levacecarnine (L- Acetyl Carnitine)

Introduction :

Carnitine is an essential nutrient for the transport of long chain fatty acids into the mitochondrial matrix. Carnitine (â-hydroxy ã- butyro betaine) was originally isolated from meat extracts in 1905 and its exact chemical structure determined in 1932[6].

Carnitine is present in cells and tissues as free carnitine and as acetyl- derivatives of which Levacecarnine is one.

Levacecarnine (Acetyl-L-Carnitne) is formed in the mitochondria by Carnitine- Acetyl transferase, which combines L-Carnitine with an acetyl group from CoA. Levacecarnine is then transported across the inner mitochondrial membrane by Carnitne Acetyl Translocase, where it diffuses out of the mitochondria into the cytoplasm and serves as a source of Acetyl groups for cytosolic proteins. Acetyl group provides for generation of Acetylcholine[7].

Levacecarnine has been described as: Agonist of mitochondrial function, neuronal growth factor and antioxidant in CNS neurons[14].

LEVACECARNINE : Reverses Mitochondrial decay with Age

Mitochondria are the cellular organelles that provide ATP for metabolism and help to mantain calcium homeostasis within the cell.

Damage that compromises these key functions may adversely affect survival of the organism. Mitochondria decay with age due to oxidation of lipids, proteins, RNA and DNA. The decay of mitochondria with age impairs cellular metabolism and leads to cellular decline of mitochondrial membrane potential, Respiratory control ratios and cellular oxygen consumption[12].

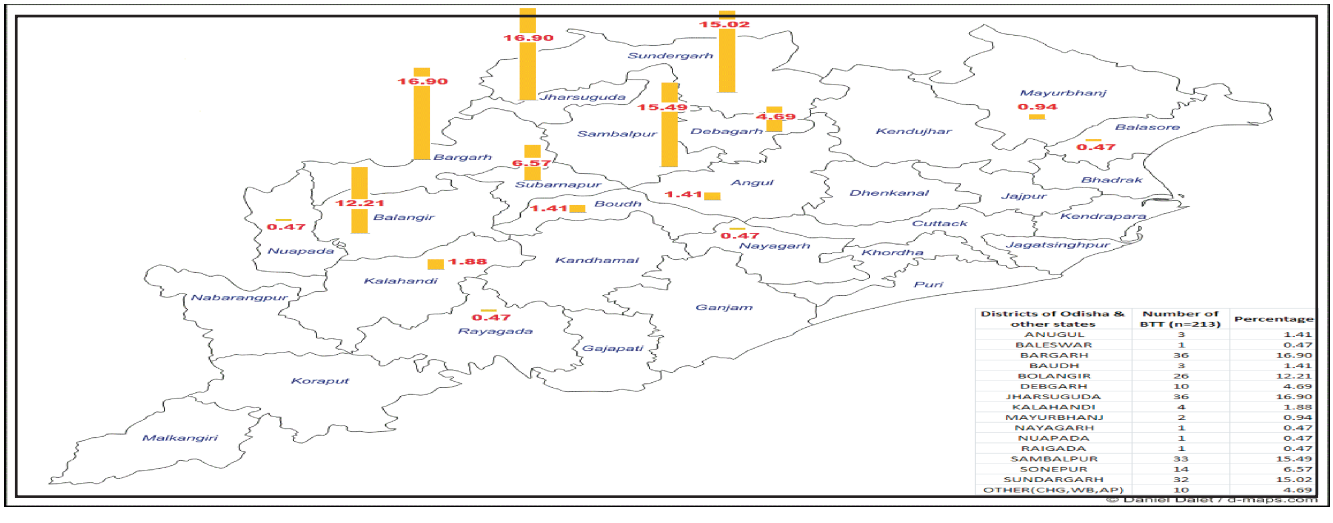
Levacecarnine restores the activity and substrate binding affinity of a key mitochondrial enzyme, Carnitine acetyl transferase. It protects neuronal cells from neurotoxin and oxidant induced toxicity and damage[6].

LEVACECARNINE : Role in Dementia

Levacecarnine has been described to be having several properties beneficial in dementia.

- A presynaptic mechanism is proposed for the effect of Levacecarnine on cholinergic transmission i.e. Levacecarnine induces an increase in Ach release, as measured by microdialysis in the Caudate – Putamen and Hippocampus. - Levacecarnine may promote membrane stabilization via its ability to increase adenosine levels. - The hydrophobic acetyl moiety of Levacecarnine improves the ability of this drug to cross the blood brain barrier and be taken up by neuronal tissues.

Levacecarnine supplementation prevents or slows age- related memory impairment by means of increased Neurotransmitter production and maintains synaptic contacts and levels of certain hormonal receptors[7].



Districts of Odisha & other states	Number of BTT (n=213)	Percentage
ANUGUL	3	1.41
BALESWAR	1	0.47
BARGARH	36	16.90
BAUDH	3	1.41
BOLANGIR	26	12.21
DEBGARH	10	4.69
JHARSUGUDA	36	16.90
KALAHANDI	4	1.88
MAYURBHANJ	2	0.94
NAYAGARH	1	0.47
NUAPADA	1	0.47
RAIGADA	1	0.47
SAMBALPUR	33	15.49
SONEPUR	14	6.57
SUNDARGARH	32	15.02
OTHER(CHG,WB,AP)	10	4.69

A meta-analysis of 16 double-blind randomized controlled trials established the beneficial effects of Levacecarnine in patients of Dementia.

· Improvement in Cognitive scales:

There was a statistically significant treatment effect on MMSE at 24 weeks

· Improvement in Cognitive skills:

3 trials found improvements in subscales testing cognitive skills including Verbal fluency, Rey's test and Digit span.

· Positive changes in Global Impression:

When considering Clinical Global Impression (CGI) scale, 6 studies found differences in one or more subgroups when comparing Levacecarnine with placebo. Statistically significant treatment effects in favour of Levacecarnine were found at 12 and 24 weeks.

A 1 year, double blind, placebo controlled, randomized parallel group study in patients with probable Alzheimer's disease reported that patients aged 65years or younger may benefit more from treatment with Levacecarnine (3g/day) than older patients[14].

An open study done in patients of Alzheimer's disease resistant to AChEIs found that the response rate increased from 38% to 50% when Levacecarnine was added on to the regimen[10].

LEVACECARNINE in post-stroke dementia

The hydrophobic acetyl – moiety of Levacecarnine improves the ability of this drug to cross the blood brain barrier and to be taken up by neuronal tissues. Levacecarnine has been shown to regenerate nerves; provide protection against glutamate and ammonia induced neurotoxicity in stroke patients. Benefits of Levacecarnine in Stroke has been postulated as: Reduction in Neurologic damage post ischemia, Neuroprotection from glutamate induced injury, Reduction of oxidative stress markers[7].

A study done in 20 patients with chronic cerebrovascular disease, who suffered an ischemic stroke atleast 6 months before the study established that Levacecarnine at the i.v. dosage of 1.5g acutely enhanced Cerebral blood flow in patients with chronic cerebral infarcts.

Hence, Levacecarnine is presumed to have a beneficial effect in preventing Vascular Dementia (VaD) in patients of CVA[8].

LEVACECARNINE: Safety Profile

Levacecarnine is a comparatively safe drug with minor adverse effects like nausea, vomitting, diarrhoea and abdominal cramps. Fishy body odour has been noted in some patients, possibly due to formation of metabolite Trimethylamine.

Patients with renal impairment should not be given high doses of this drug because of accumulation of metabolites trimethylamine and trimethylamine- N-oxide[4].

Conclusion

Although there appears to be an armamentarium of drugs for the treatment of dementia, but the therapeutic efficacy of any one is far from adequate. Hence, the search for an ideal agent still continues. Levacecarnine is a new drug which appears to benefit in Age related dementia, Alzheimer's disease and Vascular dementia and has been found to be well tolerated. Other approaches in Alzheimer's disease include drugs targeting the abnormally phosphorylated tau protein, neurotrophic agents, and drugs impacting on multiple neurotransmitters. There remain many unanswered questions.

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Case Report

RENAL TUBULAR ACIDOSIS - A CASE REPORT

S.N. Das*, S.K. Dutta, J.K. Dasmohapatra**, B. Bellam**, A. Acharya*****

ABSTRACT

In this case report a 19 year old girl presented with pain abdomen and vomiting. On general examination there was bowing of both legs and hands with short stature. She was diagnosed as Type 1 Renal tubular acidosis on the basis of alkaline urine, nephrocalcinosis, hypokalemic hyperchloremic metabolic acidosis with normal serum anion gap. ***Key words:*** *Renal tubular acidosis, normal anion gap, hypokalemic hyperchloremic metabolic acidosis, alkaline urine.*

INTRODUCTION:

Renal tubular acidosis is a systemic acidosis due to impaired ability of the renal tubules to acidify the urine and there will be little or no overall reduction in renal function. RTA is characterised by hyperchloremic metabolic acidosis with a normal anion gap.[1] There are four types of RTA. Type 1 and Type 2 may be acquired or primary where as the most common form type 4 RTA is acquired in association with moderate renal dysfunction and is characterised by hyperkalemia.[3] Type 3 RTA is mixed type of RTA that exhibits impaired acidification of urine in DCT and also impaired Hco_3^- reabsorption in PCT and osteopetrosis, cerebral calcification and mental retardation.[2]

CASE REPORT:

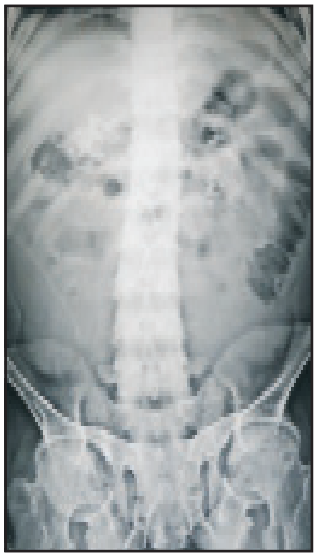
A 19 year old girl presented with generalised pain abdomen and vomiting for 5 days. She had breathlessness which was gradually increasing for 5 days. She was apparently normal at birth and up to the age of 12yrs. She was performing well at school and now was on +2nd year. Since the age of 13yrs she developed progressive kyphosis and bowing of B/L arms, forearms & legs. She is unable to walk since last 3 years, for which she never consulted anywhere. Her elder sister died at the age of 17 years with similar history and was diagnosed as a case of rickets according to her father. Patient has two brothers and both are healthy. She attended menarche at the age of 12 year. Cycles were irregular and she had oligomennorhoea. On general examination she had thin body built, short stature, kyphosis, bowing of B/L legs, arms and forearms but with normal intelligence. Pulse rate-78/min, BP-120/80 mmHg.

Investigations revealed Hb-11.4 gm%, ESR – 45mm/1st hr, TLC-19000/Cumm. N80, E2, L18, FBS-80 mg/dL, Blood urea – 94mg/dL, S Creatinine – 2.4 mg/dL, S.Na^+ – 137meq/L, S.K^+ – 3.2 meq/L, Urine RE & ME revealed Albumin- trace, pus cells – 10-15/hpf, RBC-nil, LFT: S. Bilirubin (T)-0.6mg/dL, (D)-0.3 mg/dL, SGOT-26 IU/L, SGPT-15 IU/L, ALP-273 IU/L.S. Protein-7.3g/dL, S.Albumin-4.1 g/dL, S.Calcium-7.8 mg/dL (8.1-10.4) ionised calcium 1.02mmol/L(>1.20), S.phosphorus-5mg/dL (2.5-4.8), S.parathyroid – 59.37 pg/ml(15-65), Vit.D3-14.17 ng/ml (20-30), S.Chloride - 109 meq/L(98-107).

Urine**:** pH-6.0, Ionised calcium- 3.03mg/dL (2mg/dL), Urine Phosphorous-9mg/dL (4-12mg/dL), Urine Chloride-50 meq/L, urine Na^+ 41 meq/L (41-220), urine K^+ 10 meq/L (25-125), urine $HCO3^-$15 meq/L.

* Associate Professor, ** Post Graduate Student, *** Senior Resident, Dept. of Medicine, SCB Medical College, Cuttack, Odisha.

X-ray showing multiple looser's zone (tibia, radio-ulna)



X-ray KUB showing nephrocalcinosis and nephrolithiasis

X-ray showing bowing of upper limb

X-ray showing bowing of lower limbs

ABG: pH-7.1, $HCO3^-$ 14, Anion gap-8

X ray of both tibia showed multiple looser's zone. X ray KUB showed multiple radio opaque showed in the both kidney sites (Nephrocalcinosis).

USG abdomen and pelvis showed B/L nephrocalcinosis with nephrolithiasis. On day 6th patient developed severe pain abdomen and vomiting that partly responded to antiemetics. Patient was treated with sodi-bi–carb inj for acidosis and drotaverine for pain abdomen and antibiotics. On day 8th patient became left against medical advice and the very next day re-admitted and died.

DISCUSSION:

Renal tubular acidosis (RTA) is acidification of blood out of proportion to reduction of renal glomerular filtration rate.[4]

Type 1 (distal) or classic RTA can present at any age. It is characterised by hypokalemic hyperchloremic metabolic acidosis with urine Ph >5.5. Distal nephron fail to acidify urine normally leading to excess bicarbonate in filtrate and unable to decrease urinary Ph below 5.5[4].

Type 1 RTA is due to either excess back

diffusion of hydrogen ions from lumen to blood or because of inadequate transport of hydrogen ions in the collecting ducts[5].

Chronic acidosis decreases tubular calcium reabsorption leading to renal hypercalciuria and secondary hyperparathyroidism. The hypercalciuria alkaline urine and hypocitraturia cause calcium phosphate stone and nephrocalcinosis[6]. Growth retardation occurs in children because of rickets and osteomalacia in adults.

Type 1 RTA can be familial with autosomal dominant, X linked and autosomal recessive. Hereditary causes of Type 1 RTA includes galactosemia, Ehlers danlos syndrome, fabry's disease, medullary sponge kidney, Wilson's disease and hereditary eliptocytosis. Secondary RTA type 1 is seen in sjogren's syndrome, hypergammaglobinemia, chronic active hepatitis or SLE.[7]

Familial Type 1 RTA have three variants, autosomal dominant and autosomal recessive with or without sensoryneural deafness. Dominant variant typically presents in adolescence and adulthood and recessive variant occurs in infancy or early childhood where growth retardation is common[7].

Autosomal dominant form of distal RTA has been found with mutation of SLC 4A1 gene encoding the cl^-/ $Hco3^-$exchanger AE1 (the electroneutral anion exchanger AE1)[8]. AE1 gene mutation leads to RTA and hereditary spherocytosis as the AE 1 gene expression occurs in two different cells (RBC and á inter calated cells of distal tubules[9]. The autosomal recessive Type 1 RTA occurs due to mutation in AE1 G701D gene.

In distal RTA Type 1b there is mutation of the gene ATP V1 B1 which is located in the chromosome no 2q13 and encodes B1 subunits of H^+ATPase expand apically on á intercalated cells and also in the cochlea and endolymph sac.[10] So there is RTA in association with hearing loss.

The diagnosis of type 1 RTA is suggested by a normal anion gap metabolic acidosis with simultaneous urine Ph >5.5, rickets or osteomalacia, calcium phosphate stones or nephrocalcinosis support the diagnosis. The NH_4Cl (ammonium chloride) loading test is diagnostic. If acidosis is not severe and urine Ph >5.5. Urinary tract infection must be excluded during the test as bacteria may posses urease which hydrolyses urea to ammonia producing alkaline urine.

Alkali suppliments are the standard therapy for distal RTA. Enough alkali should be given to titrate the daily metabolic acid load in the dose of 0.5 to 2 mmol/kg/day in 4 to 6 divided doses[6]. Shohl's solution and sodium bicarbonate are the common treatments.

Type 2 or proximal RTA is less common than type 1 RTA. This disorder usually presents as a generalised tubular defect together with glycosuria, aminoaciduria phosphaturia. Bicarbonate reabsorption the main defect.[5] The cardinal picture of type 2 RTA is hypokalemic hyperchloremic metabolic acidcis, urine Ph <5.5, bicarbonaturia despite subnormal plasma bicarbonate[1]. Rickets and osteomalacia may occur due to hypophosphatemia and low calcitriol level. Hypercalciuria occurs but stone formation is unusual because urine citrate level is normal[11]. Type 2 RTA may be inherited as an autosomal dominant, recessive or X linked disorder. It may be acquired with other diseases like Fanconi syndrome or secondary to drugs inhibiting carbonic anhydrase enzyme. The treatment of type 2 RTA large doses of alkali 5-15 mmol/kg/day with potassium supplementation and thiazide diuretics.

Type 3 RTA is extremely rare form of disease presents as combination of type 1 and type 2RTA. Now a days type 3 RTA is characterised by glomerular insufficiency leading to impaired NH_3 production[7]. There is normokalemic hyperchloremic metabolic acidosis.

Type 4 (Hyporeninemic hypoaldosteronism) Is the most common type of RTA. It is characterised by hyperkalemic hyperchloremic metabolic acidosis. It is an acquired disorder and moderate renal insufficiency is the rule. Causes are diabetic nephropathy, AIDS, hypertensive nephrosclerosis. Treatment is to reduce the serum potassium.

SUMMARY:

Renal tubular acidosis is a group of disorder observed in patients with normal anion gap metabolic acidosis. There are three major types of RTA. Type 1 RTA (distal), Type 2 RTA (proximal) or type 4 RTA. Type 1 is associated with inability to excrete the acid load and may present with hypokalemia. In type 2 there is a defect in bicarbonate absorption in proximal convoluted tubule. The most prominent abnormality in type 4 RTA is hyperkalemia caused by hypoaldosteronism.

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Case Report

COLOBOMA-MICROOPTHALMOUS SYNDROME ASSOCIATED WITH SENSORINEURAL HEARING LOSS, HEMATURIA, CLEFT LIP AND CLEFT PALATE COMPLICATED WITH SEVERE VIVAX MALARIA – A CASE REPORT

M.K. Mohapatra*, P.C.Karua, P.K.Bariha***, M.R.Patel****, A.K.Behera*****.**

ABSTRACT

Coloboma-microopthalmous syndrome associated with other ocular and systemic anomalies is a rare congenital anomaly. We report such a case when admitted for severe vivax malaria. ***Key words :*** *Coloboma, Microopthalmous, Sensorineural Deafness, Hematuria, Cleft lip, Cleft palate, Vivax Malaria.*

Introduction

Coloboma is a localized defect in a tissue caused by the incomplete closure of the ectodermal optic vesicle fissure. The normal embryonic fissure starts to close at centre and then proceeds posteriorly and anteriorly. It is completed usually by the 7th week of gestation. Failure of this process is believed to be responsible for coloboma [1]. It is frequently associated with other ocular and systemic defects [2,3,4]. This defect is very uncommon and most of the reports are from western countries [2,3,4,5] . Not a single case has been reported from India. Here we report a case of uveal coloboma and microopthalmous syndrome, diagnosed when admitted for severe vivax malaria.

Case Report

RRB, 16 years old male presented to Emergency Department of V.S.S. Medical College Hospital, Burla, Sambalpur, Odisha with history of fever for 3 days and loss of consciousness for 1 day. He developed fever, which was intermittent in nature and was associated with chill and rigor. Two days after fever he developed unconsciousness without any history of convulsion and vomiting. There was no history of taking any drug for fever.

Examination revealed a thin built body with average nutrition and weight of about 50 kg. He was febrile (temp - 101^0F), pulse -110/min, B.P. 120/80 mm of Hg, respiration rate – 24/min. There was no anemia or jaundice. There was scar mark of operated cleft lip on upper lip. Left eye was small.

On admission, peripheral blood smear was collected for Giemsa stain and ICT test was done from the same prick. Blood was also collected for routine hematological investigation, biochemical test and for QBC analysis for malaria.

The peripheral blood smear showed presence of P.vivax malaria with a count 6000/microlitre. QBC also showed only vivax and ICT test was positive for vivax but negative for falciparum malaria. Investigations showed: Hb – 8.0 gm/dl, total leukocyte count 11,800/ml , platelet cout-2.5 lakh/µl; differential leukocyte count, N-70%, L-28%, E-2%; blood urea-30.0mg/dl; S.creatinine 1.8 kg/dl; fasting blood glucose – 80.0 mg/dl; Alkaline phosphatase-60.4 IU/l; S.sodium-130.2 mEq/l; S. potassium 3.6 mEq/L. G-6 PD activity was normal. Urine examination showed presence of hematuria without any cast. CT scan of brain was normal. CSF analysis was within normal limits.

*Prof. Medicine, **Asso. Prof. Medicine, ***Asst. Prof. Medicine, ****PG Student, *****Senior Resident, Dept. of Medicine, VSS Medical College, Burla, Sambalpur, Odisha.

In view of presence of vivax malaria, patient was diagnosed as a case severe vivax malaria and was treated as severe falciparum malaria as per the recommendations of WHO with artesunate injections [6]. Patient had recovered from coma after 48 hrs and had complete recovery within 96 hrs. After recovery he was administered with primaquine 15mg/daily for 2 weeks for radical cure.

After recovery, history was again taken and he was reexamined for the congenital defects. The history revealed that he had loss of hearing, complete loss of vision on left eye from birth. Patient had normal mile stones of development, except for delayed development of language function and speech. This child was born with normal vaginal delivery and was 3rd in birth order. 1st child was a still born male child with congenital anomalies like cleft lip, palate. 2nd pregnancy resulted in twin with monozygotic females now aged 21 years old having no congenital abnormalities. Neither of the parents nor any member from paternal and maternal side has any congenital anomaly.

Re-examination revealed that there was operated bilateral cleft lip with scar marks on both sides of upper lip with prominence on left side. Cleft lip was associated with complete cleft palate and velopharyngeal insufficiency which was not operated. Right eye was having an inferior iris coloboma of size (4x5mm). Ocular movements were normal in right eye without any restriction or squint, with normal visual acuity. Ophthalmoscopy showed retinal coloboma of size 2 x3 mm, 2 disc space way from macula and there was a tortuous venous malformation around optic disc in right eye. Left eye was blind, dystrophic with micro-ophthalmia, micro cornea and small atrophic iris pupil complex. Audiometry showed sensorineural deafness on both sides. There was no genital abnormality. Secondary sexual characters were well developed. X-ray of limbs bones were normal and abdominal ultrasonography was normal. Karyotyping did not show any chromosomal abnormality.

In view of the congenital abnormalities, the diagnosis of Coloboma-microopthalmous syndrome associated with sensorineural deafness, hematuria, cleft lip and palate with severe vivax malaria was made.

Discussion

Coloboma-microopthalmous syndrome associated with sensorineural deafness, hematuria, cleft lip and palate is a rare autosomal dominant congenital anomaly [2]. It has been reported in one family, in literature. The present case has been admitted for severe malaria and the diagnosis of Coloboma-microopthalmous syndrome has been made subsequently when analyzed for the existing congenital anomalies.

Failure of complete closure of optic cleft results in coloboma of uveal tract with multiple and complex clinical presentations, which is due to wide

Fig.1 Left side micropthalmous and operated cleft lip.

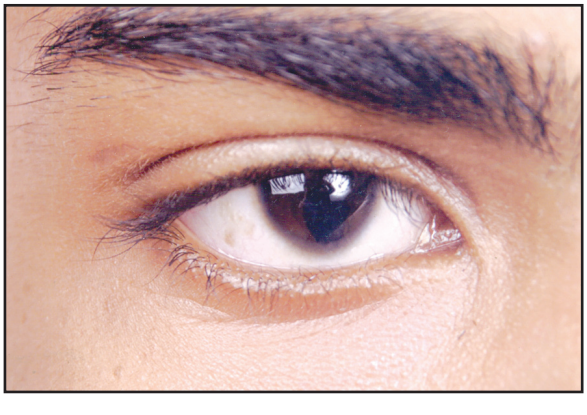

Fig.2 : Coloboma of iris of right eye

Fig.3 Cleft palate, bifid uvula and scar of operated cleft lip

variability phenototypic expression. Few case reports from some families were available from the western countries. Uveal coloboma may be associated with different systemic features like cleft lip-palate, oligophrenia, ocular-anal syndrome, oculo-splenic syndrome (with hypersplenism and leukoerythroblastic features), deafness, hyperplasia of mandible, growth retardation, mental retardation, cardiac abnormalities; anencephaly (results in still birth) [3,4,5]. Apart from systemic manifestations there may be other associated ocular manifestations, such as microcornea, microopthalmous, aniridia, nystagmus, heterochromasia of iris, persistence of primary vitreous, heterotopia of the macula, cataract, anterior chamber abnormalities and ptosis [2,3,4,5]. Due to this multiple and complex clinical manifestations, a proper clinical classification is not possible. Hence the syndrome has been named with important clinical features present. However, the primary defect is uveal coloboma [1].

Numerous inheritance patterns have been associated with this condition. It is well known to follow autosomal dominant inheritance but autosomal recessive inheritance, X-linked inheritance as well as sporadic cases have been described. The defect with oligoneprenia has been associated with trisomy D and E [1,2,3,4,5]. The present case had a history one brother being affected without affection of sisters that may suggest an x-linked inheritance. A follow up of the family is necessary for knowing the transmission.

The exact mechanism and genes responsible for the rare syndrome has not been fully evaluated. Irrespective of the inheritance pattern, there has been a high degree of phenotypic variability. It has been postulated that most chromosomal defects occurs before zygote formation. Hence the primary causation of coloboma may have their origin before fertilization and not during intra-uterine life [4]. However, a single gene defect had been postulated [3]. A single gene may exert its effect at a critical time or on a process involved in embryonic fusion. Among the mutated genes PAX2, PAX6, SHH play a central role [1]. Another multi system disorder is the CHARGE syndrome that derives its acronym from the non random grouping of a series of features: Coloboma micropthalmous, heart defects, choanal atresia, retarded growth, genital abnormalities and ear defects or deafness [1].

This patient was admitted for fever with unconsciousness and subsequently diagnosed to have vivax malaria and responded to the treatment completely[6]. It seems that there was no relation between the congenital defects with malaria. However, the former condition has been diagnosed accidentally when he was admitted and treated for severe vivax malaria. P.vivax has been considered as benign malaria since long. However, recent observation of vivax malaria showed that it can cause severe malaria in about 10% of cases in adults[7]. The exclusion of diagnosis of falciparum malaria with ICT test is as good as PCR diagnosis. Hence a negative of if ICT is the presence of vivax malaria excludes the falciparum co-infection[8]. Though p-vivax has severe manifestation its outcome is good[7,8].

In summary, this case describes a rare case of coloboma micropthalmous syndrome with vivax malaria.

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Case Report

ACUTE PANCREATITIS DUE TO ACUTE ORGANOPHOSPHATE POISONING: A CASE REPORT AND REVIEW

K.P. Tripathy*, P.K. Behera*, C. Das*, A Devi**

ABSRACT

The association between organophosphate(OP) poisoning and acute pancreatitis is still not widely recognised but there are case reports of acute pancreatitis induced by organophosphates from various parts of the world. A young boy of 15 years who developed acute pain abdomen 15 days after self poisoning with organophosphate pesticide containing chlorpyrifos was diagnosed to have acute pancreatitis and we report the case in view of uncommon but clinically significant association between OP poisoning and pancreatitis. ***KEY WORDS:*** *Acute pancreatitis, organophosphate, amylase, lipase.*

INTRODUCTION:

Deliberate self poisoning has reached epidemic proportions in parts of the developing world, where the toxicity of available poisons and sparse medical facility ensure a high fatality rate[1]. Many deaths are due to organophosphate pesticides and occur in young and economically active age group posing a great burden on the country.[2]

Organophosphate toxicity manifests as muscarinic or nicotinic effects mostly on cardiovascular, respiratory, gastrointestinal or central nervous system and respiratory failure is the most common cause of death [3,4]. But there have been a number of case reports of acute pancreatitis due to OP poisoning.[5] However commonly used medical text books do not describe acute pancreatitis as one of presenting features of OP poisoning [3,4] nor OP poisoning is listed as one of the causes of acute pancreatitis.

CASE REPORT:

A 15 yr boy, 10 th standard student from a rural area of Khurda district was admitted to our hospital within 6 hrs of consuming pesticide after a domestic quarrel. The poison container which the family members showed at the emergency room had the label of chlorpyrifos. There was typical pesticide smell from the soiled clothing and clinical presentation like frothing from mouth, bradycardia, diffuse moist rales in the chest, wide spread fasciculation and pin-point pupil corroborated with the family member's claim of Chlorpyrifos poisoning. He was managed in the casualty as a case of OP poisoning with atropine and pralidoxime and subsequently shifted to ICU. A low serum choline esterase report also confirmed the organophosphate poisoning .He improved steadily with our treatment and was discharged home on 10 th day of hospitalisation.

After 5 days of discharge from the hospital, he developed severe upper abdominal pain with radiation to back associated with frequent vomiting. There was no history of loose motion, fever ,hematemesis or melena. He was non alcoholic, non smoker and there was no significant medical or surgical illness in past. On examination he was conscious, pulse 110/min, Blood pressure 110/70 mm of Hg, Respiratory rate 20/min, Temp 100 ^{0} F with mild dehydration. There was mild pallor, no icterus, cyanosis or clubbing. Abdomen was diffusely tender with maximum tenderness over left hypochondrium and epigastrium without localised guarding or rigidity. Murphy's sign was negative and there was no significant tenderness over Macburney's point. There was no organomegaly or evidence of free fluid in abdomen. Examination of Chest and Cardiovascular system revealed bilateral vesicular breath sounds and normal heart sounds without any

*Asso. Professor, **Prof & HOD, Dept. of Medicine, Hi-Tech Medical College, Bhubaneswar, Odisha.

Table 1. Laboratory values on admission and after four days

	Unit	Reference Range	On Admission	On 4th Day
TWBC	/mm^3	4000-10,000	22,000	12,000
Neutrophils	%	40-65	92	71
TPC	Lac/mm^3	2-4.5	2.2	1.5
Haematocrit	%	40-50	42	31
Amylase	U/L	Up to 90	500	220
Lipase	U/L	13-60	420	115
Glucose	mg/dl	70-110	230	140
AST	U/L	5-40	82	50
ALT	U/L	5-40	90	40
Serum Urea	mg/dl	10-45	60	30
Serum Creatinine	mg/dl	0.6-1.1	1.4	0.8

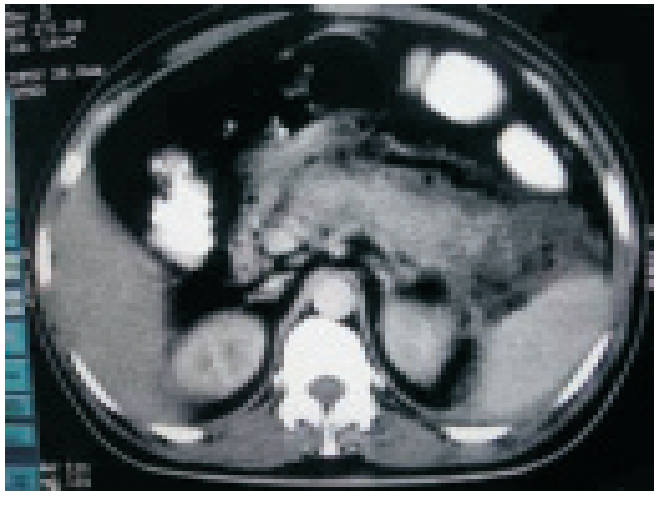

Fig1:-CT Scan of Abdomen showing Oedematous Pancreas

murmur. Nervous system examination revealed no abnormality.

On investigation Total white cell count (TLC) was elevated with neutrophil predominance, Serum amylase was elevated 5 fold and serum lipase nearly 6 fold. Aspartate aminotransferase (AST) was 82 U/L and Alanine aminotransferase (ALT) was 90 U/L.Total cholesterol was 205 mg/dl, Triglyceride -145 mg/dl, LDL-132 mg/dl. Others biochemical tests were within normal limits. Arterial blood gas showed pH of 7.45, HCO^3 -23mEq/L, PaO_2 85mm Hg, $PaCO_2$ 33 mmHg. Urine microscopy was normal. Chest radiograph showed blunting of left costophrenic angle and ECG was within normal limits. Serum choline esterase was normal.

Considering the severe abdominal pain, high level of serum amylase and lipase acute pancreatitis was suspected . Abdominal ultrasonograph showed a non homogenous edematous pancreas. There was no evidence of cholelithiasis or calculus in any viscera of abdomen or pelvis. CT scan of abdomen on the next day showed edematous pancreas with peri -pancreatic fluid collection.

He was managed conservatively for acute pancreatitis with total parenteral nutrition, and broad spectrum antibiotics. Pain abdomen and distension improved and bowel sounds appeared towards 3rd day. TLC and Biochemical tests done on 4th day showed a decreasing trend. He was discharged on 10th day of admission in apparently stable physical condition.

DISCUSSION:

In 1979, Dressel described the first case report of pancreatitis in a patient with OP poisoning [6] followed by another case report of OP poisoning with pancreatitis by Moore and James in 1981.In the same year Dagil and Shaikh studied 75 cases with definite history of malathion ingestion and hyperamylesemia was found in 47(63%) cases [7]. This hyperamylesemia is generally believed to be due to pancreatic injury. Experiments on dogs showed convincingly that pancreatitis could be produced by an intravenous infusion of secretin and diazinon .[8.] Significant increase in serum amylase and lipase was found at one, two and three hours. Light microscopy also revealed acinar cell vacuolization and progressive interstitial oedema. Pancreatic ductal hypertension as well as stimulation of pancreatic secretion secondary to cholinergic stimulation seems to be responsible for the development of pancreatitis. In agreement with these experimental results are the findings from electron microscopy showing greater acinar injury with vacuole formation and depletion of zymogen granules in pancreatic tissue that was exposed both to organophosphate and acetylcholine stimulation than those exposed to only one of these deleterious agents.[9]

The clinical picture of acute pancreatitis from OP poisoning is usually mild and the development of complications such as pancreatic necrosis is rare.[10]However pancreatitis can occur not only from ingestion but also secondary to cutaneous exposure to an organophosphate. On the other hand, painless pancreatitis is commonly under diagnosed in patients attempting suicide with organophosphates. Unlike most of the earlier case reports where pancreatitis developed during acute phase of organophosphate intoxication , our case developed pancreatitis in the third week of poisoning which is still a rare presentation.

CONCLUSION:

Though acute pancreatitis as a clinical manifestation of organophosphate poisoning is not given much importance in standard text books, it should be suspected in all critically ill patients with OP exposure. Also recognising that OP poisoning can be important differential diagnosis in a case presenting with acute pancreatitis without other obvious cause may be life saving.

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Case Report

BRONCHO ALVEOLAR CARCINOMA PRESENTING AS A CASE OF CAUDA EQUINA SYNDROME WITH SECONDARY METASTASIS IN LIVER & SPINE

M.R. Behera*, B.L. Parija, S. Mohanta***, J. Narayan****, P. Panda****, M. Mandal****, A. Acharya*****

ABSTRACT

Broncho Alveolar Carcinoma is a rare malignancy occurring in females & nonsmokers and having less incidence of metastasis. We report a patient who presented with multiple site and metastasis. ***Keywords****: Broncho Alveolar Carcinoma, Cauda Equina Syndrome, Metastasis.*

INTRODUCTION

Broncho Alveolar Carcinoma is a subset of pulmonary adenocarcinoma which is more common in nonsmokers and females. It is a non-invasive tumour where the neoplastic cell spread out a long pre-existing alveolar structure. It may manifest as solitary peripheral nodule or multifocal disease with rapid spread from one lobe to another. It manifests as mucinous or non-mucinous variant. Mucinous variant is multifocal and fatal, whereas non-mucinous variant arises from Type-II pneumocytes and EGFR mutation. We present a case of broncho-alveolar carcinoma, who was a male patient though non-smoker and presented without any respiratory complaint, but metastasis to abdomen and spine.

CASE REPORT

A 30 year old male admitted to Medicine Department of S.C.B. Medical College, Cuttack in March 2012 with chief complaints of loss of appetite and loss of weight for 10 months, low backache for 8 months, progressive weakness of left leg for 3 months followed by weakness of right leg for 2 months and retention of urine for 20 days.

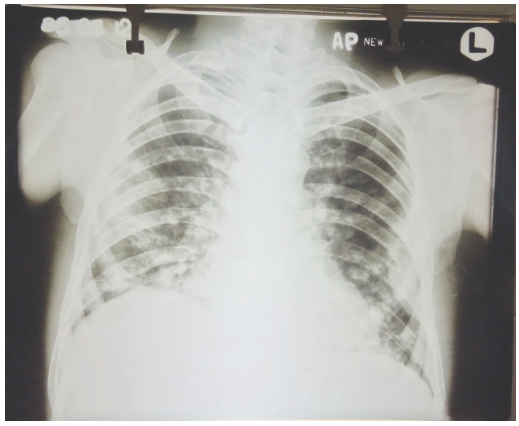
He had no history of Diabetes Mellitus, Hypertension, smoking or alcoholism. There was no history of addiction to tobacco related products.

* Asst. Professor, ** Asso. Professor, *** Sr. Resident, **** P.G Student, Department of Medicine, SCB Medical College, Cuttack, ***** Asst. Surgeon, CHC, Harichandanpur, Govt. of Odisha.

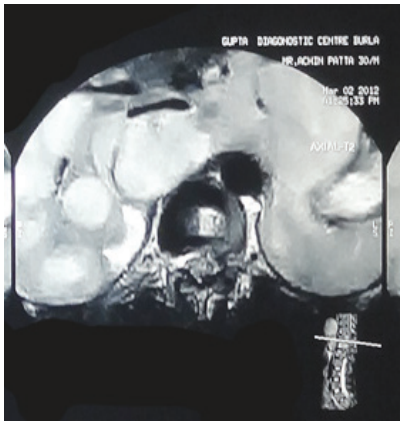
On examination, the patient was of average body built, moderate pallor, bilateral axillary and inguinal lymphadenopathy, no icterus, cyanosis or clubbing. On abdominal examination, Liver was enlarged 8 cm. firm in consistency, surface nodular, non-tender, spleen was enlarged 3 cm. firm, non-tender, no evidence of free fluid in abdomen, per rectal examination revealed no abnormality. Testicular sensation was intact and size was normal. On respiratory system examination, respiratory rate was 18 per minute, restriction of chest movement in lower part of right hemithorax, chest expansion was 4 cm., vocal fremitus was absent in right infra-axillary & infra-scapular area with stony dull percussion note over the same area with absent breath sound and there was diminished vocal resonance with presence of crepitations over left infraxillary and infrascapular area. On neurological examination, there was hypotonia in both lower limbs with generalized atrophy of bilateral lower limb and power in both limb was 2/5 with absence of knee and ankle jerks. Cremasteric reflex was absent and bilateral plantar was non-responsive. There was no other abnormal movements. All primary modalities of sensation were lost bilaterally below L_1. CVS Examination revealed no abnormality.

LABORATORY INVESTIGATION :

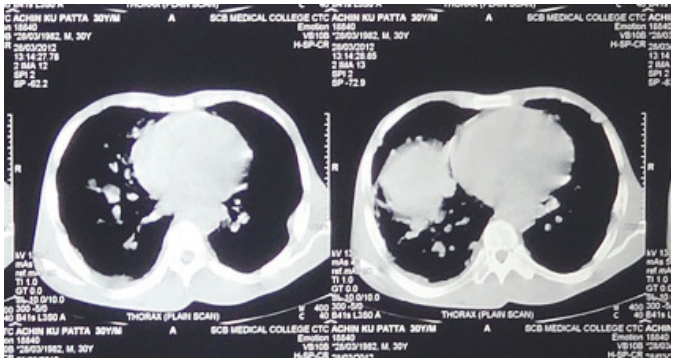
Investigations revealed Hb-8 gm%, TLC–7000/mm3, DC–N55 L44 E2, ESR–25mm, FBS–113 mg%, Serum Urea–25 mg%, Serum creatinine–1.3 mg%, Serum sodium – 138 meq/ltr., Serum Potassium - 4.8



Pic.1 : Chest X-ray PA view showing bilateral fluffy opacities over middle & lower lung zone



Pic.2 : CECT abdomen showing multiple rounded hyper intense lesions in liver



Pic.3 : CECT thorax showing multiple nodules in lung parenchyma (B/L)

Pic.4: MRI of spine showing peridural soft tissue swelling compression at D_{11}, D_{12}, L_1 level with compression collapse D_{11} vertebra, destruction of L_1 vertebra.

meq/ltr., Urine – Albumin – Trace, Pus Cell–4-6 / hpf, Stool for Occult Blood – Negative, HBsAg, HIV, HCV – Negative, LFT – Total–0.8 mg/dL, Direct–0.3 mg/dL, AST–72 u/L, ALT–24 u/L, ALP–687 u/L, Serum CEA –0.85 ng/dL (Normal), FNAC of Axillary Lymphnode - Reactive Hyperplasia, Chest X-Ray PA View: Fluffy Opacities in bilateral, middle and lower lung zone (Pic.1), USG Abdomen & Pelvis revealed gross hepatomegaly with multiple hyperechoic lesions, probably secondaries, CECT of Abdomen & Pelvis revealed: liver grossly enlarged with multiple large round hyper-intense nodules within, multiple large upper abdominal bulky periaortic and retrocaval nodes noted. Imp.- Features suggestive of diffuse malignant disease probably lymphoma (Pic.2). Ultrasound of Thyroid and Scortum was normal. Upper G.I. Endoscopy – Normal Endoscopy except external compression of fundus. CECT of Thorax – Multiple nodules of varying size in bilateral lung parenchyma with rib metastasis. (Left 10^{th} rib.), Vertebral metastasis, right pleural effusion, impression – broncho alveolar carcinoma (Pic.3). MRI of Spine: at D_3, D_{11}, D_{12}, L_1 level showed peridural soft tissue causing compression of spinal cord, conus and cauda equina. There was compression and collapse of T_{11} vertebral body & destruction of L_1 vertebral body (Pic.4). USG guided FNAC of Secondaries in Liver showed papillary adenocarcinoma. With clinical history, physical findings and available investigation, the case was finally diagnosed as a case of Broncho-alveolar carcinoma with secondaries to liver and spine,

presenting as cauda equina syndrome.

DISCUSSION :

Broncho alveolar carcinoma was formerly considered as a mystery tumour because of its varying radiology, clinical and histopathologic manifestation. Barsky et al.[1] have reported that broncho alveolar carcinoma appears to be increasing in incidence specially in young female. Barkley JE et al[2] have reported that patients of broncho alveolar carcinoma with history of cigarette smoking have decreased survival rate compared to non-smoker and also majority of patients in his study were asymptomatic at time of diagnosis, but median survival was short in asymptomatic patients. Regnard et al.[3] have described the patient of broncho alveolar carcinoma, who were initially presented with delayed resolution of pneumonia. Radiological features of broncho alveolar carcinoma include focal nodules or as pneumonia, for which they should be considered in differential diagnosis of solitary or multiple nodules. Though there are studies of broncho alveolar carcinoma by many workers, none have found so much of extensive metastasis in broncho alveolar carcinoma, that we have observed in our patient. There are studies in broncho alveolar carcinoma with recurrent disease presented with lymphangitis carcinomatosis.which was usually late and terminal stage of disease.

CONCLUSION :

The present case is an interesting patient as having an uncommon disease with additional evidence of hematogenous metastasis involving liver, and spine.

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Case Report

DOXYCYCLINE INDUCED ESOPHAGEAL ULCER A STUDY OF THREE CASES

A. Kar*, K. N. Padhiary, N. K. Patel***, P. Debta*****

ABSTRACT

Drug induced esophageal disease is common. Doxycycline is one of the commonest drugs causing esophageal injury. The injury is usually self limiting but can occasionally cause serious life threatening complications. Here we report three cases of doxycycline capsule induced esophageal ulcers who presented with dysphagia, retrosternal chest pain, odynophagia and malena. Upper G.I. endoscopy confirmed the diagnosis. All of them recovered completely with standard treatment.
Key words: *Doxycycline; esophageal ulcer, DIOD (Drug induced esophageal disease)*

INTRODUCTION

Drug induced oesophageal disease (DIOD) was first reported in 1970[1]. Common drugs causing oesophagitis and esophageal ulcer are tetracycline, doxycycline, minocycline, potassium chloride, ferrous sulfate, quinidine, alendronic acid, Vit C, clindamycin and NSAIDS of which tetracycline, doxycycline, quinidine, potassium chloride accounting for 90% of reported cases[2]. Severity of injury ranges from mild inflammatory changes to severe ulceration, perforation or stricture formation[2]. Chemical content, drug formulation and patient factors are specific for DIOD[1]. The possibility of DIOD should be suspected in a patient who complains dysphagia, odynophagia and retrosternal chest pain[1]. The diagnosis is confirmed by Gastrointestinal endoscopy. Discontinuation of the offending drug, administration of proton-pump-inhibitor, prokinetics are the mainsteps of management. We report here three cases of doxycycline induced acute oesophageal ulcer.

Case I

A 40 years old lady presented to MOPD with history of one episode of black stool associated with retrosternal Burning pain, Dysphagia to solid and liquid food with retrosternal sticking sensation of food. Her past medical history was not of much relevance. She was on doxycycline capsules (100mg BD) for fever. On examination her vitals were stable. She was subjected to upper GI endoscopy which revealed 3-4 cm deep circumferential ulcer at lower 3cm of mid esophagus with exudates and erosions (Fig.1). A diagnosis of doxycycline induced acute esophageal ulcer was made. She was treated with PPI (Rabeprazole 20mg bid), Domperidone (10mg tid) and oral local anaesthetic gel (oxethazaine) and withdrawal of doxycycline. She recovered completely after 10 days of treatment.

Case – 2

A 42 yrs old male presented with retrosternal burning sensation and dysphagia to solid food at the level of mid sternum after taking 3 doses of doxycycline capsule (100mg) prescribed by local physician for acne vulgaris. He had no malena or hematemasis. Past medical history was of no relevance. There was superficial, vertical ulcer of 2cm length at the lower third of esophagus without any exudates or erosion revealed by endosopy. He recovered completely after

* Asst. Professor, ** Professor, *** Post Graduate Student, Department of Medicine, VSS Medical College, Burla, Odisha.

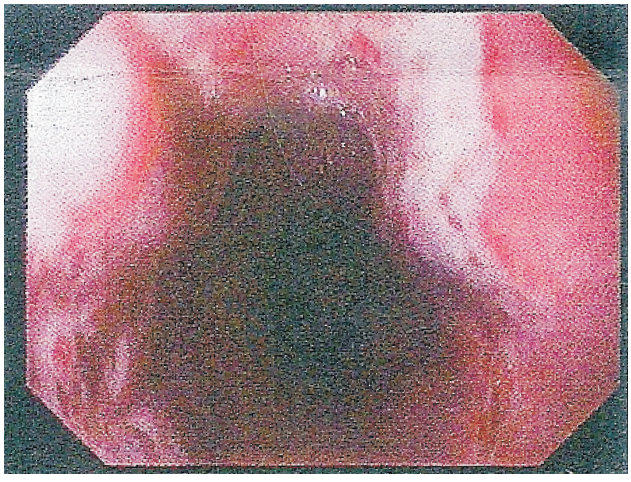

Fig.1 : Circumferential ulcer at mid-oesophagus with exudates & erosions.

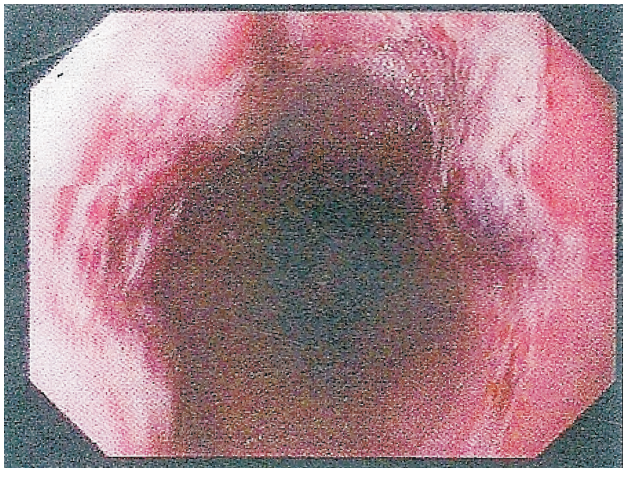

Fig.2 : Circumferential ulcer at mid-oesophagus

07 days of therapy with PPI (Rabeprazole 20mg od), domperidone (10mg tid) and sucralfate and oxethazaine solution and discontinuation of the doxycycline.

Case – 3

A 45 year old female presented with sticking sensation of food retrosternally with burning pain after taking first dose of doxycycline. Her upper GI endoscopy revealed mid esophageal, circumferential ulcer (fig.2). She was treated with PPI, Levosulpride (25mg tid) and lignocain viscus solution. She recovered after 10 – 12 days of therapy.

DISCUSSION

Drug induced oesophageal disease (DIOD) is a common condition and is under reported and largely preventable[1]. The incidence of 3.9 – 4 cases per 100000 population appears to be very low[3]. Doxycycline is commonly prescribed for pelvic inflammatory disease and acne. Hence DIOD is more common in female. Both drug and patient factors play a role in mucosal damage. Patients factors include preexisting esophageal disease like reflux esophagitis, scleroderma and esophageal motility disorder[1]. Elderly are more prone to develop DIOD due to their altered esophageal motility and decrease saliva production[4]. In our study all patients were of middle age group and had no preexisting esophageal disease.

Drug related factors include chemical nature of the drug, its solubility and contact time with mucosa. Pills coated with gelatinous material, like capsules can stick to esophageal mucosa especially when taken with little water[5]. Taken at bedtime the drug may remain in contact with the esophageal mucosa for a longer duration and can cause direct mucosal injury[1]. There is decrease salivation and swallowing during sleep and this may increase the transit time through esophagus[1].

The mechanism of esophageal mucosal injury induced by doxycycline may be explained by their acidic effect, gelatinous sticky capsules, increased mucosal concentration and intracellular toxicity[4]. Liquid formulations and tablet forms are less likely to cause esophageal injury compared to capsule form. Sustained release forms may cause esophageal injury as they tend to be large in size and hence difficult to swallow[1]. Doxycycline can produce a pH of less than three when dissolved in 10ml of water or saliva[6]. Esophageal damage mostly occur at the aortic arch level or above the lower esophageal sphincter which are the physiological narrowing[7]. Distal third of esophagus is involved only in 19% of the reported cases. It is also shown that doxycyclin in capsule form remains in esophagus for three times longer than the tablet form[8]. All of our patients were taking doxycline capsule with little water. It is recommended that such medicines

should be taken in sitting or standing position and with at least 100ml of water and to remain upright for at least 15 minutes after the ingestion of medicine[3].

The common symptoms of DIOD are dysphagia, odynophagia and retrosternal chest pain[1] and occasionally hematemasis and malena. Patient may complain of a foreign body sensation. In our study all the three patients had retrosternal chest pain, dysphagia and odyonophagia. Intractable hiccough have been described in some cases with lower esophageal ulcers[4].

Although history is sufficient to establish the diagnosis, endoscopy remains the diagnostic method of choice. The common endoscopic finding is one to several descrete clustered, shallow ulcer surrounded by normal mucosa[2]. Particles of the drug can also be found at the site of ulcer. Deeper ulcers are occasionally encountered. Pill–induced ulcers penetrating into the mediastinum and major vessels have occasionally led to mediastinitis and exsanguinating haemorrhages respectively[2]. In approximately 7% of the reported cases, deep circumferential ulcers result in fibrotic strictures that require dilatation[2].

DIOD is self limiting[1] and symptoms usually improve within 7 – 10 days but protracted course upto 6 weeks with severe symptoms have also been reported[4]. The first step in the treatment is to discontinue of the offending pill. It is also reasonable to provide emperic antireflux therapy to prevent exacerbation of the injury by acid reflux[2]. Topical protective agents and local anesthetic such as liquid sucral fate or viscous lignocain may be of benefit for ulcer healing and pain relief. The value of antacids, antisecretory and PPI remains questionable in patients without GERD[4]. Delayed esophageal stricture formation may require endoscopic dilatation. In our study all the three patients recovered after 7 – 10 days of therapy with PPI, local anaesthetic solution (Oxethazaine) and withdrawal of the drug.

CONCLUSION

DIOD is a common and largely preventable condition. Most of the drug induced esophageal injury are self limiting. A detailed history and high index of suspicion is the key to an accurate diagnosis. The offending medication should be discontinued and liquid preparations may be substituted if it is not possible to discontinue the medicine. Symptomatic treatment is all that is needed. Prevention is the best approach to the problem. Patients should be advised to take their medication with sufficient quantities of water in a upright position and avoid taking medication immediately before bedtime. Elderly and bed ridden patients who have difficulty in swallowing should be given liquid formulation.

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Case Report

MYCOBACTERIURIA - AS A CAUSE OF COMMUNITY ACQUIRED STERILE PYURIA IN MALE

T. Karuna*, S. Khadanga**

ABSTRACT

Genito-Urinary Tuberculosis is the 2nd most common cause of extra pulmonary tuberculosis[1]. Unlike pulmonary TB the classical symptoms of evening rise of temperature, night sweats, weight loss, lymphadenopathy are absent. Instead, local symptoms like frequency, dysuria, haematuria predominates. They present with sterile pyuria in acidic urine. Though 3 early morning urine AFB culture is gold standard still direct microscopy for urinary AFB will suffice.[2, 3] Since the symptoms confuse with common UTI and the investigations do not lead physician, so high index of suspicioun is required. ***Keywords:-*** *Tuberculosis (TB), Genito Urinary (GU), Urinary Tract Infection(UTI), Acid Fast Bacilli (AFB).*

INTRODUCTION

Tuberculosis is a common disease in our country. Despite RNTCP and DOTS, we are lagging far behind to control it. For past many years the incidence of extrapulmonary tuberculosis is increasing or it is diagnosed more frequently because of the awareness among the clinicians.[5] In order of frequency, the extrapulmonary sites most commonly involved in TB are the lymph nodes(35-40%), pleura(20%),, genitourinary tract(10-15%), bones and joints(10%), meninges(5%),GI tract-peritoneum(3.5%), and pericardium(2%).[6]

GU tuberculosis is the 2nd most common cause of extrapulmonary tuberculosis accounting for 10-15% cases. GU tuberculosis is usually a manifestation of the pulmonary acquisition of Mycobacteria. Direct vineral acquisition is more common in females and is very rare in males[5]. In males local symptoms predominate, and up to 75% of patients have chest radiographic abnormalities suggesting previous or concomitant pulmonary disease. Urinary frequency, dysuria, nocturia, hematuria, flank pain or abdominal pain are common presentations. However, patients may be asymptomatic and the disease is discovered only after severe destructive lesions of the kidneys have developed.

Among the males who present with symptoms of urinary tract infection-40 to 70 % cases do not yield any organism after 48 hour of aerobic inoculation. Sterile pyuria may be due to infective or non infective aetiology. Sterile pyuria may indicate infection with unusual agents such as *C. trachomatis, U. urealyticum,* or *Mycobacterium tuberculosis* or with fungi.[5] Alternatively, sterile pyuria may be documented in noninfectious urologic conditions such as calculi, anatomic abnormality, nephrocalcinosis , vesicoureteral reflux, interstitial nephritis or polycystic disease.

The documentation of culture-negative pyuria in acidic urine raises the suspicion of TB[5, 6]. Urinalysis gives abnormal results in 90% of cases, revealing pyuria and hematuria. Culture of 3 early morning urine specimens yield a definitive diagnosis in nearly 90% of cases and is considered gold standard. However 3 early morning direct microscopy for urinary AFB equates GU Tuberculosis though its sensitivity are less (40-

* Assistant Professor, Dept. of Microbiology, ** Assistant Professor, Dept. of Medicine, Hi-Tech Medical College, Bhubaneswar, Odisha.

70%).[2] IV Pyelography, abdominal CT or MRI may show obstruction, calcification and ureteral stricture suggestive of tuberculosis.

Since data from this part of world regarding the incidence of Mycobacteriuria among the sterile pyuria cases among males are lacking so we studied this aspect for documentation.

MATERIAL AND METHODS.

Inclusion Criteria

1. Symptoms of UTI- dysuria and / or frequency and / or urgency and / or suprapubic pain with or without fever. 2. Pus cell in urine > 5/H.P.F 3. Sterile urine culture after 48hr.of aerobic incubation

Exclusion Criteria

1. Prior history of instrumentation or catheterization and other co morbid conditions.

82 cases of community acquired male UTI with sterile pyuria were included in this study. All were subjected to 3 consecutive early morning AFB for direct microscopy. Whole of early morning urine was collected in wide mouthed sterile, leak proof, disposable, non wax plastic container and transported to the laboratory within 1hour. Sample was divided in 4 tubes and centrifuged at 2000 rpm for 30 minutes. One smear was made from each tube deposit and stained by Ziehl-Neelsen (ZN) method, the decolouriser being 20% acid and alcohol. At least 300 oil immersion fields were screened in each smear before reporting as negative. Negative cases were retested on two more occasions. Three negative tests were deemed as "Negative for AFB".

RESULT

Out of the 82 sterile pyuria cases, AFB was isolated in urine in 4 cases. All the 4 cases were between 15-50 yrs. (18, 42, 44, 48 yrs). Dysuria of varying intensity was found in all of them. Frequency was documented in 3 out of 4 cases. In one patient the frequency was 18 to 20 times in past 12 hour and he was miserable. 2 of the 4 patients were febrile. No patients presented with renal colic, flank pain or gross hematuria. On examination of pH all the urine samples were acidic. One of these patients showed microscopic

TABLE

Profile	**Patient1**	**Patient 2**	**Patient 3**	**Patient4**
Age	**18**	**42**	**44**	**48**
Symptoms	Fever Dysuria Frequency	Dysuria Frequency	Dysuria Frequency	Fever Dysuria Frequency
Hb TLC DC ESR Montoux	10.2 8400 N72, L25 40 12	10.8 7600 N70, L22, E5 46 8	12.0 11000 L48, N43, E6 58 8	11.2 6800 N64, L33 44 10
X-ray Chest	Normal	Normal	Rt. Upper Zone Calcification	Normal
X-ray KUB	Normal	Normal	Rt. Nephro Calcinosis	Normal
USG KUB	Normal	Normal	Rt. Nephro Calcinosis	Normal
Follow-up	Completed ATT	Completed ATT	Completed ATT	Completed ATT

hematuria. These patients were subjected to complete hemogram, ESR ,Skin PPD test, Sputum for AFB, X-ray chest , X-ray KUB, Ultrasonography KUB, None of the patient's sputum was positive for AFB. Only one patient showed upper zone calcification of RT lung. The same patient showed Rt. sided nephrocalcinosis.

All the 4 patients received-2 (HRZE) +4 (HR) as daily regimen. Only one patient agreed for urine PCR for AFB and the result was positive. All were subjected to urine AFB study at the end of 2nd month. All 4 cases were negative for urine AFB.

DISCUSSION

Genitourinary TB is not a rare cause of community acquired male UTI. It is more commonly a disease of young adults as described by Morrison et al[7]. Though 3 early morning urine AFB culture is gold standard diagnostic procedure we were unable to do so because of its unavailability in our lab which requires bio-safety level 3. Many studies equate passage of urinary AFB under direct microscope as GU tuberculosis. So we took this challenge to look for AFB in urine under microscope. Contrary to the previous assumption of contamination of urine by other *Mycobacteria*, this is very rare. The only species being recognized as contaminant is *Mycobacterium smegmatis. M.smegmatis* becomes a contaminant when the sample is transported late (>6 hour) in a wax container. So we tried to nullify both the factors.

2 Cases have been reported from Pune by Bapat V.B et al in 2006 which strengthens our belief.[8]

Case 1- A 35 years male with complaints of post dinner chills lasting 5-10 minutes. Twenty-four hour urine tested positive for AFB and PCR-tuberculosis. No clinical and imaging evidence of tuberculosis was found. Treatment was not instituted. He later developed backache and was detected to have Pott's spine 4 months after.

Case 2- Among the apparently healthy volunteers, one tested positive for AFB and PCR-tuberculosis. This person eventually developed cough and fever with AFB in sputum 2 months after urine tested positive.

CONCLUSSION

In the absence of AFB culture, early morning urine direct microscopy for AFB suffice to diagnose GU tuberculosis, though its sensitivity is less. GU tuberculosis should be suspected in young patients with sterile pyuria in acidic urine. Since the classical symptoms and investigations are not present so very high index of suspicion is required. It responds to treatment very good

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Case Report

DELAYED SPINAL CORD DEMYELINATION IN ORGANOPHOSPHORUS POISIONING.

J.K. Das Mohapatra*, B. Bellam*, S. Dutta*, S.N. Das, S. Behera***, S. Sethy******

ABSTRACT

Organophosphorus-compound intoxication is very common in Odisha. Three different types of paralysis are recognized based largely on the time of occurrence and their differing pathophysiology. We describe a patient who had a classic acute cholinergic crisis after exposure to organophosphates, with the subsequent development of organophosphate-induced delayed spinal cord demyelination in addition to peripheral neuropathy. ***Keywords :*** *Organophosphorus poisoning, Neuropathy, Myelopathy, Paralysis.*

INTRODUCTION

Organophosphorus-compound intoxication is very common in Orissa. Three different types of paralysis are recognized based largely on the time of occurrence and their differing pathophysiology.[1,2]

1. Type I paralysis or acute paralysis

2. Type II paralysis or Intermediate syndrome

3. Type III paralysis or Organophosphate- induced delayed polyneuropathy

Type I paralysis or acute paralysis is seen during the initial cholinergic phase. This is when large numbers of both muscarinic and nicotinic receptors are occupied by acetylcholine, leading to persistent depolarization at the neuromuscular junction.

Type II paralysis or Intermediate syndrome. This was first described in 1974 by Wadia et al. This syndrome develops 24-96 hours after the poisoning. The cardinal feature of the syndrome is muscle weakness affecting the proximal limb muscles and neck flexors. There is a relative sparing of the distal muscle group. One of the earliest manifestations in these patients is the inability to lift their head from the pillow (NECK FLOP).

* Post Graduate Student, **Associate Professor, ***Asst Professor, ****Senior Resident, Department of Medicine, SCB Medical College, Cuttack, Odisha.

Type III paralysis or organophosphate- induced delayed polyneuropathy (OPIDP) is a sensory-motor distal axonopathy that usually occurs after ingestion of large doses of an organophosphorus compound. The cardinal symptoms are distal weakness of the hands and feet. This is often preceded by calf pain, and in some cases, parasthesia of the distal part of the limbs.

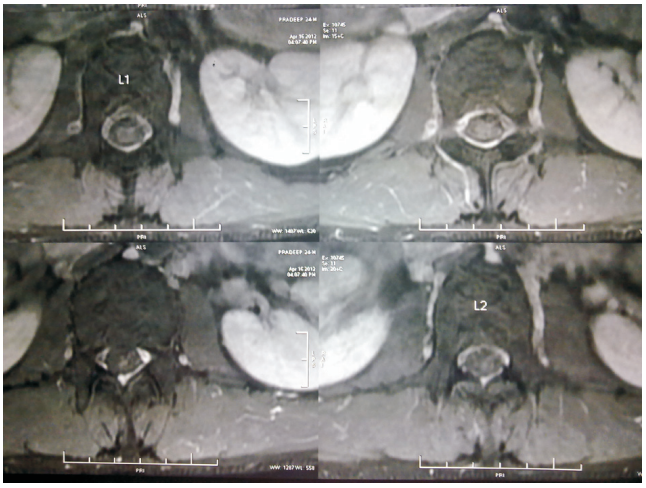
Less commonly Organophosphate-induces involvement of both peripheral and the central nervous systems.[3] The exact sequence of lesions in these systems remains controversial, and few reports have discussed central nervous system neuropathological changes in humans.

We describe a patient who had a classic acute cholinergic crisis after exposure to organophosphates, with the subsequent development of organophosphate-induced delayed spinal cord demyelination in addition to peripheral neuropathy. Magnetic resonance imaging (MRI) showed spinal cord demyelination that persisted long after the cholinergic effects had subsided.

CASE REPORT

A 24-year-old man attempted suicide by taking organophosphate insecticides — 50 gm of DANADAR. When he arrived at our emergency department, he was unconscious, with nonreactive, pinpoint-sized pupils; massive oral foaming; and bilateral crackles over the lung fields. We performed gastric lavage and

(picture showing weakness of lower limb after taking op poison)



(MRI Picture showing focal demyelination at L1–L2 level)

administered a large dose of atropine (100 – 200 mg /day and pralidoxime (6 gm/day) intravenously. The atropine was tapered gradually within 10 days. The patient's serum pseudocholinesterase level decreased to 390 iu (normal 5000 – 11000). On day 10 he reported calf pain with paresthesia.He was discharged after 3 days. Again He was readmitted to our hospital 17 days after the discharge for weakness of both lower limbs . On examination there was right foot drop with power around ankle 1/5, around knee 3/5, around hip 4/5 but the plantar reflex was bilaterally extensor, knee and ankle jerks were brisk . Examination of sensory, bladder and bowel function were normal. NCV study showed mild conduction block in bilateral median nerve, common peroneal nerve and post tibial nerve suggestive of demyelination neuropathy. MRI of thoracolumber spine showed patchy demyelination at the level of L1-L2 spinal cord.

DISCUSSION

Like delayed onset polyneropathy , delayed onset spinal cord demyelination also occurs in op poisioning probably due to inhibition of neuropathy target esterase.

CONCLUSION

We concluded that this patient's increased deep-tendon reflexes were caused by central axonopathy, leading to diffuse demyelination of the spinal column. One report4 describes pyramidal signs and central nervous system involvement, with partial functional recovery, after severe organophosphate-induced delayed neuropathy. Studies in chicks with organophosphate-induced delayed neuropathy5 have shown severe damage in the ventral and lateral tracts of the thoracic and lumbar spinal cord. The same neuropathological changes may have been associated with the prominent diffuse spinal cord demylination and atrophy especially in the thoracolumbar spinal cord that we observed in our patient.

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Case Report

DIAGNOSIS OF ACUTE LEUKAEMIA (AML) FROM INTRACEREBRAL HAEMORRHAGE AND BLAST CRISIS - A CASE REPORT

C. R. Khatua*, B. Pradhan, S. Tripathy***, R. Kadam****, C. Patra******

ABSTRACT

There are different types of initial presenting features of acute leukemia like hemorrhagic complications, disseminated intravascular coagulation (DIC), blast crisis and leucocytosis. Among the bleeding manifestations, intracerebral hemorrhage is having the worst prognosis. We present a patient with previously undiagnosed leukemia, presented with cerebrovascular accident due to fatal intracerebral hemorrhage in setting of acute blast crisis. ***Key words****: Fatal Intracerebral haemorrhage (FICH), acute promyelocytic leukaemia (APL), blast crisis*

Introduction

Hemorrhage in acute leukemia is caused by hemorrhagic diathesis, including disseminated intravascular coagulation (DIC), thrombocytopenia, sepsis, leukocytosis and treatment toxicity[1,2]. Among the hemorrhagic complications in acute leukemia, intracranial hemorrhage (ICH) is the most serious and most common[3,4], severely shortening the survival of patients with acute leukemia. Most fatal intracranial hemorrhages (FICH) occur during the early course of the disease (within 10 days of diagnosis), suggesting that early identification and management is crucial for preventing FICH [5],[6]. In one study it was found that 1.6% of patients with acute leukemia die from FICH without any opportunity for proper management[4,7]. Here we present a similar patient from our institution situated in western part of Odisha.

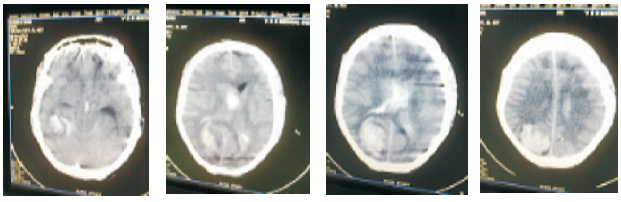
Case Report

A forty year male patient was brought to the emergency department with complaints of low grade fever, vomiting, bilateral decreased vision for 8 days and headache, convulsion and loss of consciousness on the day of admission. He was not a diabetic or hypertensive and there was no past history of cerebrovascular accident .On examination patient was unconscious, pulse rate–72/minute, blood pressure -160/90 mmHg, pupil bilateral middilated and nonreacting to light, plantar bilateral extensor, neck stiffness was absent. So the patient was admitted as a case of cerebrovascular accident and treated with injection mannitol, injection fosphenytoin, intravenous fluid, oxygen inhalation and catheterization. On routine examination, complete blood count showed Hb 10.8gm%, TLC – 1,50,000/cmm, TPC-30,000/cmm, comment on peripheral smear showed blast cells more than 50% with hypergranular promyelocytes .CT scan brain (A,B,C,D) showed intracerebral haemorrhage into left occipital lobe, right basal ganglia and thalamus with intraventricular extension. Since admission the patient's condition gradually detoriated and died after ten hours.

Discussion:

Intracerebral hemorrhage (ICH) contributes significantly to the morbidity and mortality of patients suffering from acute leukemia. While ICH is often identified in autopsy studies of leukemic patients, it is rare for ICH to be the presenting sign that ultimately leads to the diagnosis of leukemia**.** Hemorrhagic complications can come from the disease itself or can be a complication of chemotherapy. Chemotherapies for acute leukemia result in severe cytopenia of long duration, thus increasing the risk of FICH. So FICH

* Senior Resident, ** Asso. Professor, *** Asst. Professor, **** Post Graduate Student, Dept. of Medicine, VSS Medical College, Burla, Sambalpur, Odisha.



(A) (B) (C) (D)

(CT Scan of brain showing ICH with intraventricular extension)

can be divided into early or late categories, with late FICH usually occurring during chemotherapy-related cytopenia. Risk factor analysis revealed that female gender, APL, leukocytosis, ($>10 \times 10^9$/l)[8,9], thrombocytopenia and prolonged PT are the risk factors for FICH. Early hemorrhagic death in patients with APL has been reported to be influenced by higher blast cell count at diagnosis, lower plasma fibrinogen level and lower platelet counts.[5,6]. Hyperleukocytosis in acute leukemia is also associated with lymphadenopathy, hepatosplenomegaly, disseminated intravascular coagulation, and central nervous system complications. Bleeding involving the CNS is often catastrophic and is the main cause of death in induction for acute leukaemia[10,11,12,13]. Central nervous system (CNS) involvement with acute leukaemia commonly occurs in relapse; however, it is rarely seen at presentation. But in our case the patient presented with encephalopathy due to intracerebral hemorrhage. So the presentation emphasizes that in the presence of hyperleukocytosis, thrombocytopenia and blast crisis in the patient of intracerebral hemorrhage should raise the clinical suspicion of acute leukaemia. Different types of intracerebral hemorrhage occur in acute leukaemia like single hematoma, cluster multifocal hematoma, separated multifocal hematoma, sub arachnoid haemorrhage, sub-cortical hematoma and sub-dural hematoma[14].

Conclusion:

Encephalopathy due to intracerebral haemorrhage(ICH) may be the presenting feature of acute leukaemia. So the patient presenting with diminished sensorium in the setting of hyperleukocytosis should raise the suspicision of acute leukaemia. Although early mortality from FICH is inevitable in patients presenting with FICH, early detection and management of this condition will improve the survival of patients with acute leukemia

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Audited Account of the 31st Annual APICON, Odisha Branch, 2011 held at Cuttack submitted by Organising Secretary

G. PANDA & CO.,
CHARTERED ACCOUNTANTS
A.P. Market Complex
Link Road Square,Madhupatna, Cuttack-753010

Cuttack-(0671)
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2301348(R)

APICON ODISHA 2011
(CONFERENCE ACCOUNT)

BALANCE SHEET AS ON 31ST MARCH, 2012

LIABILITIES	AMOUNT(Rs.)	ASSETS	AMOUNT (Rs.)
GENERAL FUND :		**CURRENT ASSETS :**	
Excess of Income over		Balance with S.B.I.	
expenditure b/d.	2,80,808.00	SCB Medical College Campus	
CURRENT LIABILITIES		Branch-SB A/c.21631881832	2,83,808.00
Audit fee payable	3,000.00		
	2,83,808.00		**2,83,808.00**

AUDITOR'S REPORT

We have audited the above Balance Sheet of **M/s.APICON ODISHA 2011 (Conference Account) as on 31st March, 2012** along with annexed Income & Expenditure Account and Receipt & Payment Account for the period ending on even date.

Certified that these statements are in agreement with the books of accounts produced before us.

Cuttack
Date : 03.06.2012

For G. PANDA & CO.,
CHARTERED ACCOUNTANTS

(P. K. MOHAPATRA, FCA)
PARTNER
M.No.056058

G. PANDA & CO.
CHARTERED ACCOUNTANTS
A.P. Market Complex
Link Road Square, Madhupatna,Ctc-10

APICON ODISHA 2011
(CONFERENCE ACCOUNT)

INCOME & EXPENDITURE ACCOUNT FOR THE PERIOD ENDING 31ST MARCH, 2012

EXPENDITURE		AMOUNT(Rs.)	INCOME		AMOUNT (Rs.)
To	Decoration, sound		By	Delegation fee	1,81,000.00
"	and Banner etc.	1,53,900.00	"	Advertisement & stall charges	
"	Venue hiring charges	75,600.00		for Scientific Trade fare	13,80,400.00
"	Fooding expenses	5,74,241.00	"	Interest on S.B.A/c.	9,785.00
"	Souvenir Printing	70,000.00			
"	Accomodation & Travelling	1,37,375.00			
"	Purchase of memento	1,44,4567.00			
"	Photo & LCD Projection exp.	30,800.00			
"	Cultural Programme exp.	58,000.00			
"	Purchase of stationery	5,245.00			
"	Postage exp.	1,581.00			
"	Telephone charges	900.00			
"	Remuneration to staff	12,000.00			
"	Other incidental exp.	23,278.00			
"	Audit fee & exp.	3,000.00			
"	Excess of Income over exp.c/d.	2,80,808.00			
		15,71,185.00			**15,71,185.00**

*For **G.PANDA & CO.,**
CHARTERED ACCOUNTANTS

(P. K. MOHAPATRA, FCA)
PARTNER

Place : Cuttack
Date : 03.06.2012

G. PANDA & CO.
CHARTERED ACCOUNTANTS
A.P. Market Complex
Link Road Square, Madhupatna,Ctc-10

APICON ODISHA 2011
(CONFERENCE ACCOUNT)

RECEIPT & PAYMENT ACCOUNT FOR THE PERIOD ENDING 31ST MARCH, 2012

RECEIPT		AMOUNT(Rs.)	PAYMENT		AMOUNT (Rs.)
To	Opening balance	-	By	Decoration, sound and Banner etc.	1,53,900.00
"	Delegation fee	1,81,000.00	"	Venue hiring charges	75,600.00
"	Advertisement & Stall charges in Scientific Trade fare	13,80,400.00	"	Fooding expenses	5,74,241.00
"	Interest on S.B.A/c.	9,785.00	"	Souvenir Printing exp.	70,000.00
"	Loan (seed money)	20,000.00	"	Accomodation & Travelling	1,37,375.00
"	Loan from API	70,000.00	"	Purchase of memento	1,44,457.00
			"	Photo & LCD Projection exp.	30,800.00
			"	Cultural Programme exp.	58,000.00
			"	Purchase of stationery	5,245.00
			"	Postage exp.	1,581.00
			"	Telephone charges	900.00
			"	Remuneration to staff	12,000.00
			"	Other incidental exp.	23,278.00
			"	Refund of loan (Seed money)	20,000.00
			"	Refund of loan from API	70,000.00
			"	Closing Balance : Balance with S.B.I, SCB Medical College,Cuttack SB A/c.31631881832	2,83,808.00
		16,61,185.00			**16,61,185.00**

For **G.PANDA & CO.,**
CHARTERED ACCOUNTANTS

(P. K. MOHAPATRA, FCA)
PARTNER

Place : Cuttack
Date : 03.06.2012

JOURNAL OF THE ASSOCIATION OF PHYSICIANS OF INDIA ORISSA STATE BRANCH

Manuscript submission : Check List for Contributors

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4. Title page.

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   Number of pages, number of figures and number of tables.
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6. Article proper (double spaced on A/4 size paper).
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8. References (double spaced, separate sheets, Vancouver style).
9. Maximum number of references for Original articles - 20, Short articles-10,

   Case reports-6, Documentation-3, Correspondence-3.
10. Each table on separate sheet.
11. Figures/diagrams on separate sheet.
12. Photographs in envelope appropriately marked.
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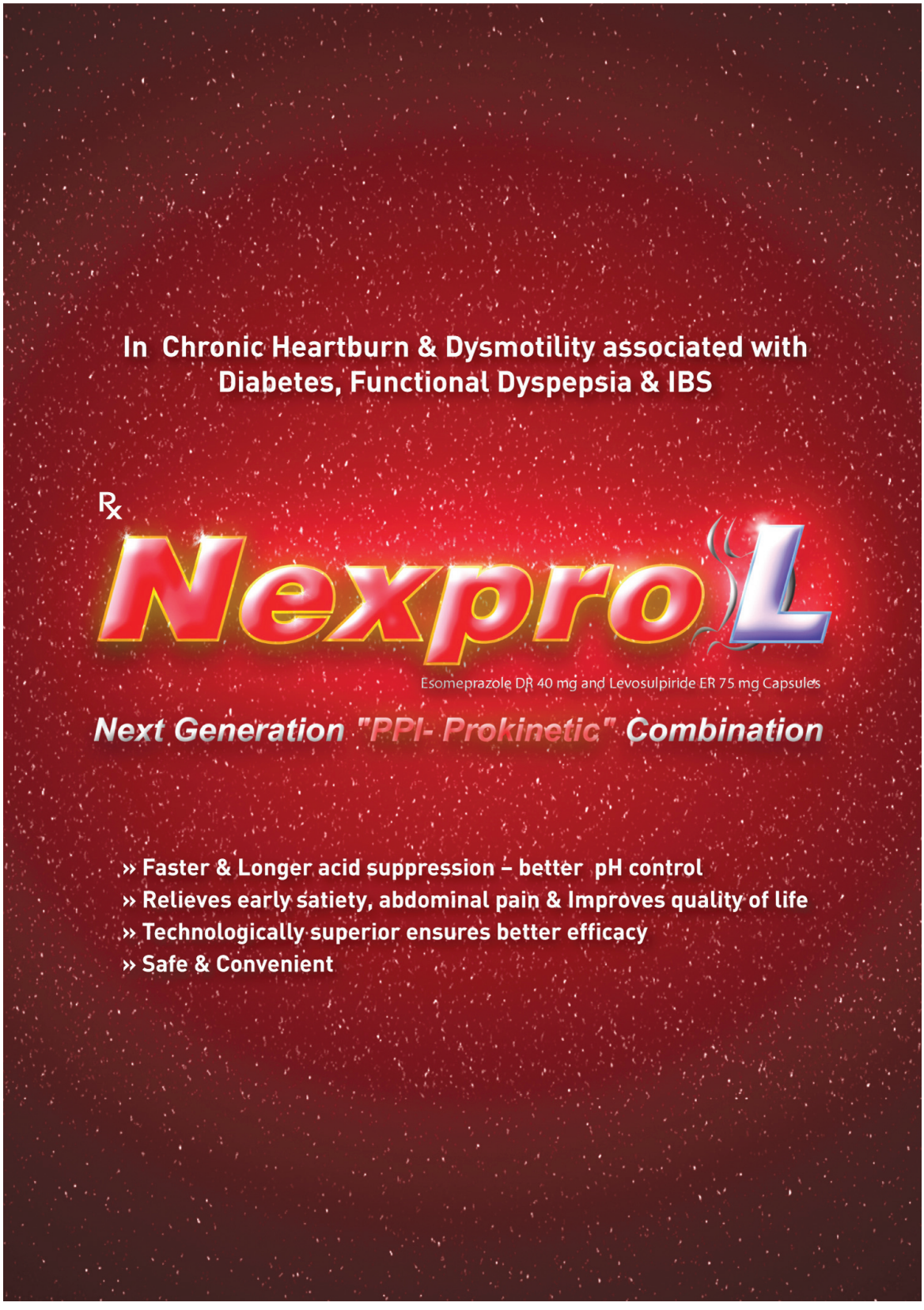
14. Covering letter signed by all authors confirming that they have read and approved the contents and also confirming that the manuscript is not submitted or published elsewhere.
15. Statement regarding Ethics Committee Approval and informed consent from subjects.*
16. Floppy diskettes are Compulsory Now*

* This is new addition to the check list, contributors to note.

- Hon Editor.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RAMISTAR-H
Ramipril 5mg + Hydrochlorothiazide 12.5mg
RAMISTAR-A
Ramipril 2.5mg + Amlodipine 5mg
PIN OM 40/20/10
Olmesartan 10/20/40 mg
PIN OM-H 40/20
PIN OM-A
Olmesartan 20mg+ Amlodipine 5mg
CLOPITAB
Clopidogrel 75mg,150mg
CLOPITAB-A
Clopidogrel 75mg + Aspirin 75,150mg
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