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CASE REPORT

Editorial

Acute Kidney Injury in Intensive Care Unit

Basant Kr. Sharma*

Acute kidney injury (AKI) in ICU is still associated with very high mortality in spite of various modalities of treatment. These include intermittent hemodialysis (IHD); continuous renal replacement therapies (CRRTs); and hybrid therapies, also known as prolonged intermittent renal replacement therapies (PIRRTs), such as sustained low-efficiency dialysis (SLED) and extended-duration dialysis (EDD).

Although there is use of various modalities the mortality in the patients with AKI who require dialysis has remained high ranging from 40 percent to >60 percent[1,2,3]. A modest degree of renal insufficiency due to ATN may also increase in-hospital mortality[4]. There isn't significant difference in outcome with the modality chosen. The modality is chosen according to the clinical situation, expertise available, patient's hemodynamic status and cost. Various definitions of AKI are used from the earlier RIFLE[5], then AKIN[6] to now to KDIGO[7].

RIFLE CRITERIA — The RIFLE criteria consists of three graded levels of kidney dysfunction (Risk, Injury, and Failure), based upon either the magnitude of increase in serum creatinine or urine output, and two outcome measures (Loss and End-stage renal disease [ESRD]). The RIFLE strata are as follows :

- Risk– 1.5-fold increase in the serum creatinine, or glomerular filtration rate (GFR) decrease by 25 percent, or urine output <0.5 mL/kg per hour for six hours.
- Injury– Twofold increase in the serum creatinine, or GFR decrease by 50 percent, or urine output <0.5 mL/kg per hour for 12 hours
- Failure– Threefold increase in the serum creatinine, or GFR decrease by 75 percent, **or** urine output of <0.3 mL/kg per hour for 24 hours, **or** anuria for 12 hours
- Loss – Complete loss of kidney function (eg, need for renal replacement therapy) for more than four weeks
- ESRD – Complete loss of kidney function (eg, need for renal replacement therapy) for more than three months

The change in serum creatinine was specified as occurring over not more than seven days.

AKIN CRITERIA — A modification of the RIFLE criteria was developed by the Acute Kidney Injury Network (AKIN), providing both diagnostic criteria and a staging system for acute kidney injury. The AKIN diagnostic criteria for AKI specify an abrupt (within 48 hours), absolute increase in the serum creatinine concentration of ≥0.3 mg/dL (26.4micromol/L) from baseline; a percentage increase in the serum creatinine concentration of ≥50 percent; or oliguria of <0.5 mL/kg per hour for more than six hours.

Kidney Disease: Improving Global Outcomes (KDIGO) criteria viz.

- Stage 1 – Increase in serum creatinine to 1.5 to 1.9 times baseline, or increase in serum creatinine by ≥0.3 mg/dL (≥26.5 micromol/L), or reduction in urine output to <0.5 mL/kg per hour for 6 to 12 hours.
- Stage 2 – Increase in serum creatinine to 2.0 to 2.9 times baseline, **or** reduction in urine output to <0.5 mL/kg per hour for ≥12 hours.

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■ Stage 3 (an increase in serum creatinine to three times baseline, or increase in serum creatinine to ≥4.0 mg/dL [≥353.6 micromol/L], or reduction in urine output to <0.3 mL/kg per hour for ≥24 hours, or anuria for≥12 hours).

The KDIGO criteria only utilize changes in serum creatinine and urine output, not changes in glomerular filtration rate (GFR) for staging.

In a recent study RIFLE (84.2%) and KDIGO (87.5%) identified more patients with AKI than AKIN (72.8%) (P< 0.001). AKI defined by AKIN and KDIGO was associated with in-hospital mortality {AKIN: adjusted odds ratio [OR] 2.3[95% confidence interval (CI) 1.3–4], P = 0.006; KDIGO: adjusted OR 2.7[95% CI 1.2–6.2], P = 0.021} while AKI defined by RIFLE was not [adjusted OR 2.0 (95% CI 1–4), P = 0.063]. The AUROC curve for in-hospital mortality was similar between the three classifications (RIFLE 0.652, P < 0.001; AKIN 0.686, P < 0.001; KDIGO 0.658, P < 0.001). the authors concluded that RIFLE and KDIGO diagnosed more patients with AKI than AKIN, but the prediction ability for in-hospital mortality was similar between the three systems[8].

The exact incidence and prevalence of AKI worldwide is still not known. This is primarily due to use of various criteria for defining AKI.

However it has been found that the incidence of AKI in ICU is increasing. A recent cross-sectional study of 97 intensive care units (ICUs) from 33 countries with data from 1802 patients during their first week of ICU admission showed a much higher AKI burden. 57.3 percent of enrolled patients fulfilled the KDIGO criteria for AKI (95% CI 55.0-59.6)[9].

It is important to note when the renal replacement therapy is initiated, and what modality is used for which category of patients. The urgent indications for initiation of RRT includes Hyperkalemia, Uremia (Pericardial rub, Encephalopathy), refractory fluid overload, metabolic acidosis (pH <7.1), or ingestion of certain drugs and poisons.

Various studies have come out with conflicting results regarding the relation between initiation of dialysis and mortality. However dialysis should be initiated in patients who are showing worsening of hyperkalemia, fluid overload or metabolic acidosis. As studies have shown the relationship of mortality with worsening fluid overload and other parameters.

Modality of RRT:

No modality has been shown to be superior to the other in various studies.

The modality of dialysis should be chosen according to the availability, expertise and the cost of therapy.

Peritoneal Dialysis.

Peritoneal dialysis has been used for the longest time for the treatment of AKI. There have been very few head to head comparison with other modalities. In one study in Vietnam there was increased mortality in patients treated with peritoneal dialysis in comparison to those treated with CVVH, (47 versus 15 percent, odds ratio [OR] 5.1, 95% CI 1.6-16)[10]. However in this study the peritoneal dialysis fluid contained acetate rather than lactate. Meta-analysis of other studies however has not shown any difference in mortality in patients treated with peritoneal dialysis as compared to other modalities of treatment.

Intermittent Hemodialysis (IHD) versus CRRT.

Studies have shown no significant difference between IHD and CRRT when adjusted for disease severity. Although the clearance of middle and large molecules is better with CRRT using convective therapy (hemofilteration) , this has no bearing on the outcome, mortality, recovery of renal function.

Prolonged intermittent renal replacement therapy (PIRRT).

The hemodynamic as well as metabolic effects of PIRRT are similar to CRRT. The mortality also is same in patients treated with either modality. However no of days spent in ICU, number of days on mechanical ventilation, and units of blood transfused are less in patients treated with PIRRT thus reducing the cost of therapy[11].

Mortality with AKI however, tends to differ with the dosing of dialysis. A retrospective study involving 844 ICU patients with AKI, treated with IHD. The patients who received a Kt/V >1 dose of dialysis showed improved survival, especially in patients with intermediate severity of disease[12].

In another study of 160 patients treated with daily versus alternate day dialysis, mortality was found to be less in the daily group (28 percent versus 46 percent),

fewer episodes of intradialytic hypotension, and earlier recovery from AKI[13].

In contrast no difference in survival or recovery of kidney function was observed with more intensive treatment in the Hanover Dialysis Outcome (HAND-OUT) study comparing extended-duration dialysis (EDD), provided for approximately eight hours per day, with a more intensive regimen where additional eight-hour treatment sessions were provided to maintain the blood urea nitrogen (BUN) <42 mg/dL[14].

The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for AKI recommend delivering a Kt/V of 3.9 per week for patients undergoing intermittent therapy[7].

The present study doesn't elaborate on the exact criteria for initiation of dialysis, was the dialysis daily or intermittent and what was the dosing of dialysis. As these have a bearing on the outcome of these patients.

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Original Article

Clinical Profile of Acute Kidney Injury in Intensive Care Unit : A Single Center Data of A Developing Nation

M. Sharma[*], R. Baruah[**], R. Goel[***], M. Pegu[****], A. K. Barman[*****], S. K. Baruah[******]

Abstract

Background: Acute kidney injury (AKI) is a common clinical problem with significant clinical and economic consequences. Recent advances in defining AKI, understanding its pathophysiology, and improving the diagnostic accuracy will impact disease management and clinical outcomes. The aim of the study was to evaluate the incidence and clinical profile of acute kidney injury in our intensive care setting. **Methods :** The study was conducted in Gauhati Medical College and Hospital, Guwahati, from 1st July 2014 to 30th June2015. 90 patients were enrolled for the study. Definition of AKI was according to AKIN criteria. Patients were followed up till their stay in ICU to determine the short term outcome. **Results :** The incidence of AKI in ICU in the present study was 10.65%. Most common type of AKI was renal (55.5%). sepsis (50%) was found to be the commonest cause of AKI followed by prerenal azotemia (43.33%). Hypertension and Type 2 Diabetes Mellitus were the major associated comorbidity. AKI mortality (51%) was statistically significant ($p<0.01$) as compared to overall ICU mortality. Mortality rate was higher in elderly, in patients with comorbidities, in AKIN stage 3, patients requiring RRT and mechanical ventilation. **Conclusion :** The results of the present study indicated that incidence of AKI in ICU is quite high. Sepsis was the most common cause. Compared to overall ICU as well as non AKI ICU mortality, AKI was associated with significant higher mortality. However prospective studies with larger number of samples are necessary to arrive at a definitive conclusion.

KEY WORDS: *Acute Kidney Injury, Intensive Care Unit, Sepsis*

INTRODUCTION :

Acute kidney injury (AKI) characterized by rapid decline in glomerular filtration rate, reflects a broad spectrum of clinical presentations and may result in permanent and complete loss of renal function[1]. A uniform and precise operational definition of AKI (formerly- Acute renal failure)) has remained somewhat elusive[2]. However, a recent proposal by Acute kidney injury network[3] appears to have gained clinical acceptance.

The incidence of AKI during hospital admission ranges from 3 to 25% depending on criteria applied, and up to 30% of admission to intensive care unit[4]. It carries a mortality rate from 15 to 60%.[5]. Though many literatures are available worldwide on Acute Kidney Injury in Intensive care unit, however there is lack of data from developing nations particularly from India. Therefore the study was taken up with the following objectives.1) To determine incidence of Acute kidney injury in Intensive care unit patients.2) To determine aetiology of Acute kidney injury.3) To determine the short term outcome (during ICU stay).

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METHODS :

It was a single centre, prospective study, conducted in Gauhati Medical College and Hospital, Guwahati, from 1st July 2014 to 30th June 2015. A total of 845 patients were admitted in ICU during this period. 90 patients, who developed signs and symptoms of acute kidney injury in our ICU, were taken for analysis. Definition of Acute Kidney Injury was according to AKIN criteria[3]. Patients were followed up till their stay in ICU to determine the short term outcome. AKI was made on basis of history, signs and symptoms, supported by blood investigations, and radiological data. All patients with age more than 12 year who developed AKI during ICU admission were included for study. Patients with age less than 12 year, with pre-existing chronic kidney disease, renal transplant

recipients and patients with past history of AKI were excluded. Statistical analysis was done by MS excel 07 and INSTAT software. p value less than 0.05 was considered significant. The study protocol was reviewed and approved by institutional ethics committee.

RESULTS :

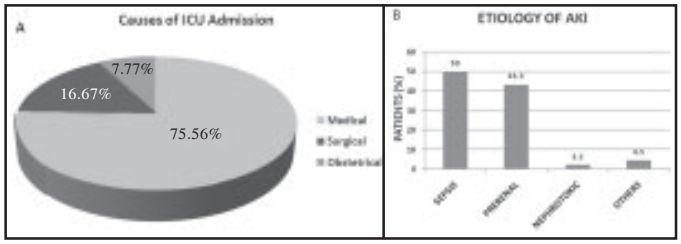
In our study, 90 (10.65%) patients developed AKI after admission, out of 845 cases admitted to ICU during the study period. Out of 90 cases, 61 (67.8%) were male while 29 (32.2%) were female (Male: female ratio = 2.1:1). The mean age of the patients was 51.04±17.2 years (18 - 89 years). The number of patients with age more than 60 year was highest closely followed by patients who were in the age group between 5-60 years (Table 1).

Table 1 : Age Distribution

Age(yrs)	Number	Percentage
13-20	5	5.56
21-30	13	14.44
31-40	8	8.89
41-50	12	13.33
51-60	22	24.44
≥ 61	30	33.33

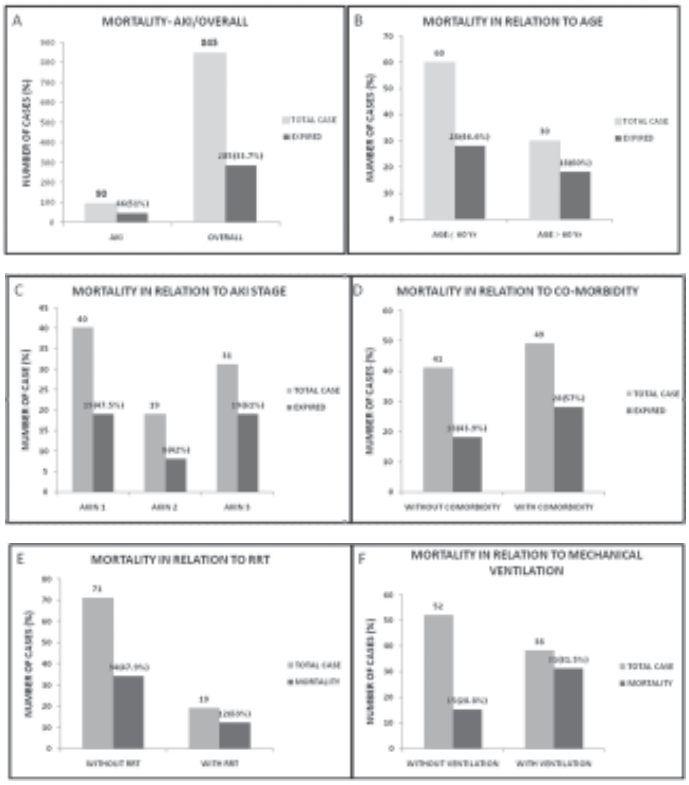
Out of 90 patients, 50 (55.55%) developed AKI due to renal causes. According to AKIN criteria, 40 (44.44%) patients were in stage 1, 19(21.11%) in stage 2 and 31(34.44%) were in stage 3. Sepsis (50%) was found to be the commonest cause of AKI followed by prerenal azotemia (43.33%). 68(75.5%) patients were admitted due to medical causes while 15 (16.7%) patients had surgical cause (Figure 1). 49 (54.4%) patients had co morbidities at the time of admission in ICU.

Figure 1: A. Different causes of ICU admission. B. Various etiology of AKI in ICU patients



Hypertension (30.6%) was the major co-morbidity followed by Type 2 Diabetes Mellitus. Out of 90 cases developing AKI, 19 (21%) patients received renal replacement therapy (Haemodialysis - 9, Peritoneal dialysis - 10) and 38 (42%) patients were under mechanical ventilation.

Out of 90 cases with AKI, 46 (51%) patients expired during ICU stay. Mortality in patients with AKI was significantly high (p<0.01) as compared to overall ICU mortality (33.72%, 285/ 845) as well as mortality due to non AKI causes (31.7%, 239/755). In the subgroup analysis, high mortality was found in patients with age above 60 year (60%), who presented with various co-morbidities (57%), with AKIN stage 3 AKI (61%), who received haemodialysis (63%), and those patients who were under mechanical ventilation (81.5%)[Figure 2]. Though this high mortality was statistically significant only with patients who were under mechanical ventilation (p<0.001).



DISCUSSION :

In our study, the incidence of AKI in ICU was 10.65%. The result of the present study was comparable to Dinna N et al[6] who reported an incidence of 10.8%. However, other studies[7-9] reported slightly higher incidence of about 30 to 35%. Bagshaw et al[10] observed lower incidence of 5.2% which differ from the other studies because it was an estimated crude cumulative incidence. The difference in incidence in various studies may be due

to different protocols for ICU admissions and different definition of AKI being used as in our study, we included only those patients who developed AKI after admission in ICU without any pre-existing renal disease. In our study, higher incidence of AKI in elder population corresponded well with other similar studies[6,7,11]. However, Hamid et al[9], in their series, reported a mean age of 39.5 year with a range of 5 to 106 years. This is probably due to inclusion of paediatric population in their study.

In the present study AKIN criteria was used to classify patients with AKI. Our study correlates well with other similar study[11] as maximum number of patients (47.3%) were in AKIN Stage 1. Using RIFLE criteria, Dinna N et al[6], observed 19% were classified as risk (R), 35% as injury (I), and 46% as failure (F), which corresponds to stage 1, 2 and 3 of AKIN criteria respectively. In the present study, sepsis (50%) was found to be the commonest cause of AKI that correlates well with Laszlo et al[11] with 44.0% of patients, AKI was associated with septic shock. However result was different in another study[6] that found, the most commonly cited cause for AKI was a pre renal (38.0%), followed by sepsis (25.6%). The difference in guidelines for admissions in ICUs may be the cause of difference in aetiology. In a subgroup analysis in our study, the percentage of female affected by AKI due to sepsis was much higher than male patients ($p < 0.01$). High incidence of sepsis in female patients admitted in ICU due to obstetrical cause is one of the reasons for above result.

In our study, it was observed that 49 (54%) patients with AKI had one or more underlying co-morbidities. Hypertension (30.6%) was the major co-morbidity followed by Type 2 Diabetes Mellitus (10%), Chronic liver disease (8%), COPD (8%), Malignancy (6%), combined Hypertension and Type 2 DM (4%) and combined Hypertension and CAD (4%). This compares well with Hamid et al[9], who noted 58.1% patients had one or more underling diseases including pre-existing chronic disease (neoplasm, hypertension, diabetes mellitus, obstructive and restrictive lung diseases, cardiovascular diseases, connective tissue disorders and neurologic disorders).

In our study, out of 90 cases, 46 (51%) patients expired. Reported mortality in ICU patients with AKI varies considerably between studies depending on AKI definition and the patient population studied[6,10,11]. In our study, mortality in Patients with AKI was significantly higher ($p<0.05$) than overall ICU mortality. Hamid et al[9] also observed a much higher mortality (72.6%) in AKI patients during ICU stay.

In our study, age more than 60 year, associated co-morbidity, advanced AKI as AKIN stage 3, need of renal replacement therapy and mechanical ventilation were identified as some of the few important risk factors responsible for increased mortality during ICU stay though mechanical ventilation was the only factor associated with significant increase in mortality ($p<0.001$). Similar finding was reported in other studies[10,11] who described higher mortality in elderly age group. Laszlo et al[11], also observed that AKI Stage 3 and mechanical ventilation were an independent risk factor for ICU mortality. Many studies[10,12,13] reported a mortality rate of approximately 50% to 70% in patients with severe AKI requiring RRT. This correlates well with our study where the mortality rate in this group of cases was 63%. Need of mechanical ventilation is always associated with significant increase in mortality in ICU patients, with or without AKI[11].

CONCLUSION :

The results of the present study indicated that incidence of AKI in ICU is more in elderly male patients and patients with co-morbidities. Majority of the cases belong to stage 1 of AKIN criteria. Sepsis was found to be the most common cause of acute kidney injury, followed by prerenal azotemia. Compared to overall ICU as well as non AKI mortality, AKI was associated with significant higher mortality. Advanced age, associated co-morbidities, AKIN stage 3, need for renal replacement therapy and mechanical ventilation were identified as some of the important risk factors for increased mortality in patients who developed AKI in ICU. However prospective studies with larger number of samples may benefit, by better identifying modifiable risk factors to prevent the development of AKI.

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Original Article

Prevalence of type 2 Diabetes mellitus in Dibrugarh town, Assam

R. P. Medhi*, B. B. Sutar**

Abstract

Aims and Objective: To find out the prevalence of type 2 diabetes mellitus in Dibrugarh town area.

Materials and method : Dibrugarh town is selected to study the prevalence of diabetes mellitus. We carried the survey work on the basis of stratified and systemic sampling. The randomly selected wards were now taken up for our study to find out the prevalence of Diabetes in Dibrugarh town. All the members above the age of 12yrs of house were our samples for study. **Results :** Out of total no. 2411 subjects, 338 Diabetes subjects were found and analyzed. **Conclusion:** (1) Majority of population have good knowledge about diabetes and were on regular medication. (2) Diabetes incidence increase with age, as majority of population were within the age of 41 to 70 years. Maternal family history of Diabetes has great impact on Diabetic population. (3) The overall prevalence of diabetes was found to be 9.71% in present study.

INTRODUCTION :

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases.[1] In 2013, according to International Diabetes Federation, an estimated 381 million people had diabetes.[2] Its prevalence is increasing rapidly, and by 2030, this number is estimated to almost double.[3] Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030.[3] The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented.[3]

Almost one Chinese adult in ten has diabetes. A 2010 study estimated that more than 92 million Chinese adults have the disease, with another 150 million showing early symptoms.[4] The incidence of the disease is increasing rapidly; a 2009 study found a 30% increase in 7 years.[5]

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India has more diabetics than any other country in the world, according to the International Diabetes Foundation,[6] although more recent data suggest that China has even more.[4] The disease affects more than 62 million Indians, which is more than 7.1% of India's Adult Population.[7] An estimate shows that nearly 1 million Indians die due to Diabetes every year.[6] The average age on onset is 42.5 years.[6] The high incidence is attributed to a combination of genetic susceptibility plus adoption of a high-calorie, low-activity lifestyle by India's growing middle class.[8] Additionally, a study by the American Diabetes Association reports that India will see the greatest increase in people diagnosed with diabetes by 2030.[9]

According to a report published by International Diabetes Federation (IDF; 5th Edition), the number of people with diabetes (20-79 years) in urban setting of India are about 27 million in 2011 which is projected to reach about 56 million in 2030[10].

The Indian Council of Medical Research (ICMR) has completed the phase I of task force project entitled, "ICMR-India Diabetes (INDIAB) Study-Phase-I" with the aim to determine the national prevalence of type 2 DM and pre-diabetes in India, by estimating the state-wise prevalence of the same. Also it aims to compare the prevalence of type-2 diabetes and pre-diabetes in urban and rural areas across India.[10]

In the first phase of the study, the rural and urban settings in three states and one union territory namely Tamil Nadu, Jharkhand, Maharashtra and Chandigarh have been included. The adjusted prevalence of diabetes (both known and newly diagnosed) in Tamil Nadu was 10.4 %, Jharkhand-5.3%, Chandigarh-13.6% and Maharashtra-8.4%. The prevalence of pre-diabetes was 8.3%, 8.1%, 14.6% and 12.8 % respectively. [10]

India is currently experiencing an epidemic of diabetes mellitus. In order to understand the true extent of the problem and its impact on diabetes care, there is a need to review the epidemiology of diabetes from different regions of India. Epidemiology of diabetes in India has an extensive history. The earliest national study reported an overall prevalence of 2.1 % in urban areas and 1.5% in rural areas. From the available region wise population based studies it is clear that in the last two decades, there has been a marked increase in the prevalence of diabetes among both urban as well as the rural Indians, with southern India having the sharpest increase. Subsequent studies confirmed this high prevalence of diabetes in urban south India. Today, the prevalence of diabetes in the urban metros of India is approaching the figures reported in the affluent migrant Indians. Although in rural India the prevalence of diabetes is much lower than in the urban population, even here the prevalence of diabetes is rapidly rising, though clearly more studies are needed. Nevertheless, there is enough information to derive significant conclusions and projections that will not only help define the burden of diabetes in India but also throw some light on the causes of the diabetes epidemic. Environmental and lifestyle changes resulting from industrialization and migration to urban environment from rural settings may be responsible to a large extent, for this epidemic of Type 2 diabetes in Indians. In addition, given the large number of people with Type 2 diabetes in our country, the morbidity due complications associated with it would still be very high. Thus, effective preventive programmes need to be urgently implemented to stem the tide.

A present study to assess the prevalence of known diagnosed cases of Diabetes milletus irrespective of duration, sex, or treatment pattern among the population in randomly selected areas of Dibrugarh town, Assam was undertaken in year of 2014.

Aims and Objective:

1. To find out the prevalence of type 2 diabetes mellitus in Dibrugarh town area.

MATERIALS AND METHOD :

Dibrugarh town is selected to study the prevalence of diabetes mellitus. Dibrugarh is a big town situated in the eastern part of Assam, India, with population of 1,39,565 (male 72,384 and female 67,181 as per census 2011). We carried the survey work on the basis of stratified and systemic sampling. The town covers an area of 15.5 Sq.K.M. and divided into 22 Municipal wards numbering from 1 to 22. We excluded 3 wards (no. 8, 15, 22) as some other survey works on Diabetes mellitus were carried out just few days ahead of our planned period of work. After excluding 3 municipal wards, we are left with 19 wards. These 19 wards were now stratified into 3 classes.

Upper class= ward no. 14, 19, 20, 21.

Middle class= ward no. 1, 2, 4, 5, 6, 7, 12.

Lower class= ward no.3, 9, 10, 11, 13, 16, 17, 18.

The above classification is made indicating major number of population of particular class residing in that ward. This was done after discussion with representative of Municipal board and our own general idea over the population pattern of particular ward.

From each group (Upper, middle, lower), we selected 2 wards by random sampling using Barlow's table. We selected total 6 wards out of 19 wards. Accordingly the following wards were marked out randomly

Upper class= ward no. 20, 21.

Middle class= ward no. 2, 4.

Lower class= ward no. 9, 16.

The randomly selected wards were now taken up for our study to find out the prevalence of Diabetes in Dibrugarh town.

In our selected wards, we choose every 5th house in a street. All the members above the age of 12yrs of house were our samples for study.

Survey Work : We worked from 1st February 2014 to 14th February 2014. During this period we covered 1084 houses that housed total number of 4,589 people and checked a total population of 2,411 people from the total 6 wards. Before starting the survey, we divided volunteers into 6 groups. We had given necessary training to the volunteers regarding the methods about the work to be performed in details.

RESULTS AND OBSERVATIONS :

Out of total no. 2411 subjects, 338 Diabetes subjects were found and analyzed.

Table 1: showing age and sex distribution of diabetic population (N=338)

Age in years	Male	Female	Total	Percentage
12-20	-	-	-	-
21-30	8	12	20	5.91
31-40	11	29	40	11.83
41-50	39	45	84	24.85
51-60	36	52	88	26.03
61-70	25	27	52	15.38
>71	36	18	54	15.97

Data presented in table 1 shows that diabetic incidence increases with age. In our study the numbers of diabetic were more as age level crossed 50 yrs. We also observed more females than male having diabetes. In our study male-female ratio of diabetes was 1:1.18. Though as per census report of 2011, the male population of Dibrugarh town is higher than that of female population.

Earlier as we observed that female number exceeds that of male in various aspects relating to Diabetes. Diabetes mellitus and body mass index were also analyzed.

Table 2: shows that sex distribution of Diabetes mellitus as per body mass index (BMI)

BMI	Male	Female	Total	Percentage
<18.5 Underweight	8	6	14	4.14
18.5-24.9 Normal	72	108	180	53.25
25-29.9 Overweight	57	48	105	31.05
>30 Obese	12	27	39	11.53

In table 2, We recorded large number 180 (53.25%) of diabetic were within normal body mass index. Nearly one third were overweight. Among the group obese female diabetic were more than male numbers.

In our study we also found females had waist circumference more than 90 cm in 33.13% where as male at that level were 18.93%.

In our study, we observed strong family history of Diabetes among the Diabetic population. In our study 42.8% diabetic patients had maternal family history, 36.09% paternal history, 11.53 brother's and sister's history. Maternal relationships appeared to be higher than other relationships.

In our study we observed that 47.33% population had good knowledge on diabetes whereas 17.75% people had poor knowledge on diabetes.

Table 3: showing Physical activity and stress of the Diabetes population (N=338)

	Yes (Percentage)	No (Percentage)
Physical activity	84(24.85)	254(75.14)
Stress	234(69.23)	104(30.76)

Table 3 shows that absence of physical activity was found in 254 (75.14%) diabetic subjects and presence of physical activity was found in 84 (24.85%) diabetic subjects. In our study we found that out of 338 diabetic patients 234 (69.23%) has stress whereas 104 (30.76%) diabetic patients were without stress. Patient having more mental stress suffered more in number as compared to those without or less stress.

In our study, it was observed that people from upper class suffer more in Diabetes mellitus (57.39%) than the combined number of middle and lower class (42.61%). There is a strong association of Diabetes with socioeconomic condition.

We observed that large no. of diabetic subjects had good knowledge on diabetes. We also observed that major percentage (66.27%) was on regular medication compared to irregular medication (33.72%).

Table 4: showing data self monitoring blood sugar by diabetes population using Glucometer and /or laboratory

Blood glucose monitoring	Regular (%)	Occasionally (%)
Glucometer : SMBG	99(29.28)	239(70.71)
Laboratory	71(21)	267(78.99)

In our study, we observed that Glucometer used for blood sugar monitoring was done by 99 (29.28%) diabetic patients whereas laboratory was used by 71 (21%) diabetic patients. is 29.28% whether laboratory used is 21%. Results showed that the percentage of regular checking of blood sugar is less than the occasionally checking of blood sugar. Finding also showed that consultation with doctor about Diabetic status regularly was very low (17.15%) and most of diabetics occasionally checked their glycemic status >83%.

In our study we covered 1084 household covering a total numbers of 2411 people above the age of 12 years. The overall prevalence of diabetes in our study was 9.7%.

DISCUSSION :

The prevalence of Diabetes has been increasing in India. We have carried out a survey to find out the prevalence of diabetes in Dibrugarh Town of Assam. The

overall prevalence of diabetes was found to be 9.7% in the present study. Similar prevalence of diabetes 8.3% has been reported from Guwahati, Assam in year 1999. A very high prevalence of 16.3% was reported in Thiruvanathpuram in Kerala state in the year 1999. A cross-sectional population survey was done in Kashmir valley in 2000 and the prevalence of 'known diabetes' among adult aged >40 yrs was found to be 1.9%.

Age and Sex distribution:

It has been established that incidence of Diabetes increases with age. In our study there was sudden rise of diabetes as age group raised from 41 years above. Age is an important risk factor for diabetes. In Reshma S. Patil et al. 2013[11], the prevalence of diabetes mellitus found in this study was 4.6%; prevalence was found higher in elderly group i.e. above 50 year of age. Thus rising trend of diabetes was seen as age increases which correlates with our study. Rao C R et al, Shah S K et al, Arora V, Ramchandran A et al, Ravikumar P et al reported significant association between increasing age and diabetes[12,13,14,15,16]. Most of the studies from various regions of India reported increasing prevalence in younger age group. The present study did not show any light on occurrence of diabetes mellitus in younger age.

In our study we observed greater number of diabetes among females than males. Acemoglu H et al, Anand K et al, bener A et al, reported higher prevalence in females compared to males[17, 18, 19] and Ramchandran et al, Shrestha U K et al found higher prevalence in males than females[15,20].

As per Chennai urban rural epidemiological study (CURES), this study was conducted on a representative population of Chennai; the prevalence of diabetes seems to be more or less the same in both genders. This study also reported a temporal shift in the age at diagnosis to a younger group. A study from Delhi also reported that a higher prevalence of insulin resistance in post pubertal children which was associated with excess body fat and abdominal adiposity. This is of great concern because if the epidemic shifts to children it could have serious consequence on the health of nation.

The increase in Diabetes is not going to be restricted to the urban areas, but is expected to be seen equally in the rural areas also. This could be due to population growth, ageing, urbanization, and increasing prevalence of obesity and physical activity.

Type 2 Diabetes and other factors:

It is observed that from research studies that there is strong genetic elements in the development of type 2 diabetes and a genetic susceptibility probably predisposes individuals with changes in their lifestyle, to develop diabetes. Certain ethnic groups such as native Americans and Hispanics have a higher genetic predisposition for the development of diabetes. The same is true with Asian Indians like us. An individual's risk of developing diabetes is doubled, if one number of their family already has the disease. The risk gets quadrupled if there are two family members with diabetes.

In our study, we observed strong association of family history, maternal history of diabetes was higher than other relationships. Family history of type 2 diabetes mellitus is one of the major contributing factor in causing diabetes in next generation or it can act as one of the important preventing factor for those who have positive family history and by this we can avoid the development of diabetes in early age. Similar findings were noted by Bener A et al his study. Rao C R et al, Shah S K et al, Arora V, Ramchandran A et al, Ravikumar P et al, they have reported a significant association with family history. In study of Vishwanathan et al[21], a large proportion of diabetes subjects in India have a family history of diabetes in first and second degree relatives. There is a greater paternal influence in transmission of NIDDM.

In our study, we have observed that the study population had good knowledge regarding diabetes (47.33%), one third of the population had average and very few had poor knowledge on diabetes. In Dibrugarh town the literacy rate in male is 92% and in female it is 86% as per census 2011. Kharpe et al[22] 2011, 18% had poor knowledge about the diabetes and more than half believed that it is communicable disease. In Kharpe et al study, 32% had poor knowledge on etiology of diabetes as half of them were aware of hereditary nature of disease while other risk factor was known to only 30-40% of patients and 30% had excellent knowledge on signs and symptoms of diabetes. Only 48% thinks that diabetes is manageable and just one fifth of them were aware of life-long treatment and regular revision of drugs. The difference in finding among different studies may be due to difference in literacy status, gross income of country and patients. In our study we observed that awareness regarding diabetic

complications was known to 89.64% of our subjects. Nearly 66.27% were taking medication for DM regularly, 33.72% occasionally or not taking any measures at all.

The present study showed that in those without physical activity, diabetes was 75.14% and with physical activity it was decreased to 24.85%. Our study showed that diabetes mellitus was more prevalent in sedentary workers or those who perform mild activity. Rao C R et al found maximum persons engaged in moderate activity. While Singh R B et al showed significant association between sedentary activity and diabetes[23]. Globally physical inactivity accounts for 14% of diabetes mellitus and it also acts as a major risk factor for obesity which again has significant relation with diabetes mellitus.

Regarding blood sugar estimation only 15.68% were doing it regularly and 37.27% were doing as and when advised by Doctor. Consultation with a Doctor for Diabetic status was done regularly by 17.15% and 82.84% was doing occasionally. Record keeping of blood sugar was done occasionally by 31.06% of patients and 68.93% patients were doing it regularly. In 2010, Muninarayan *et al*[24], shows only 9.7% diabetic subjects visited doctors for regular check up.

In regard to dietary habits, sweet intake was observed in 7.69% on regular basis in spite of known harmful effects and occasionally by 92.3%. There were no diabetics without taking sugar. In 2010, Muninarayan et al, shows 67.7% diabetic subjects were avoiding sugar in diet.

Alcohol on regular and occasional basis was consumed by about 31.36% of subjects. Excessive amounts of alcohol (three or more drink per day) on consistent basis contribute to hyperglycemia. In 2010, Muninarayan et al, shows 67.7% diabetic subjects stopped smoking and alcohol.

Anthropometric values and diabetes (Waist-hip ratios):

In our study, females had waist circumference more than 90cm in 33.13% of cases whereas males at that level were 18.93%. Waist circumference was reported to be associated with high blood sugar in higher percentage in Assamese community.

Central obesity is one of the important risk factor for type 2 Diabetes mellitus. Reshma S Patil et al, Oct 2013, R C Rao et al, Bener et al, Singh R B et al, found association between diabetes and abdominal obesity. Our study correlates with this study.

Several studies suggest that central distribution of fat is associated with high blood sugar and is a risk factor for diabetes regardless of age and BMI. In our study we found that large numbers (57.39%) of diabetic were within normal body weight. It was reported that increase waist hip ratio and obesity were more commonly associated with diabetes.

Diabetes and socio-economic status:

In our study we found that people from upper classes (57.39%) suffered more in number from diabetes than that of middle and lower classes of people (37.57%). The poor class of people detected to have negligible 5.02% diabetes. There is a strong association of diabetes with socio-economic status. The highest prevalence of type 2 DM in developing countries occurs in higher socioeconomic groups and this is true for the Indian population.

In our study, we observed that higher number of diabetes in upper class residing in particular locality. In the study of Vijaykumar et al[25], in 2008, Kerala, have looked for prevalence of diabetes across same socio-cultural. High socio-economic status has only a weak association. Evidence from Western studies suggests an inverse relation with SES, while evidence from India suggests a positive relation. In Western population, the more affluent adapt to a healthier lifestyle with increasing voluntary leisure time physical activity and greater consumption of healthy foods; in developing society, less physical activity and consumption of more calories accompanies one's ascent in the socio-economic spectrum. In our study population, low socioeconomic, who have a lifestyle characterized by more physical activity, though an inverse relationship was observed between physical activity and prevalence of Diabetes Mellitus. The reason for varying prevalence of type 2 DM across religion remain unclear and have to be explored further.

Early identification and prevention -Indian Diabetes Risk Score:

Early identification of high risk individuals would help in taking appropriate intervention in the form of dietary changes and increasing physical activity, thus helping to prevent or delay, the onset of diabetes. This means that identification of risk individual is extremely important if we want to prevent diabetes in India.

An Indian Diabetes risk score (IDRS) has been recently developed by Mohan *et al,* which uses four simple

variables namely age, family history, exercise frequency and intensity and waist circumference to arrive at a risk score. It has shown to be a highly cost effective way of testing for diabetes in a resource poor setting like India. IDRS score more than 60 supposed to high risks for Diabetes and cardiovascular disease.

Table no. 5 shows Indian Diabetes Risk score:

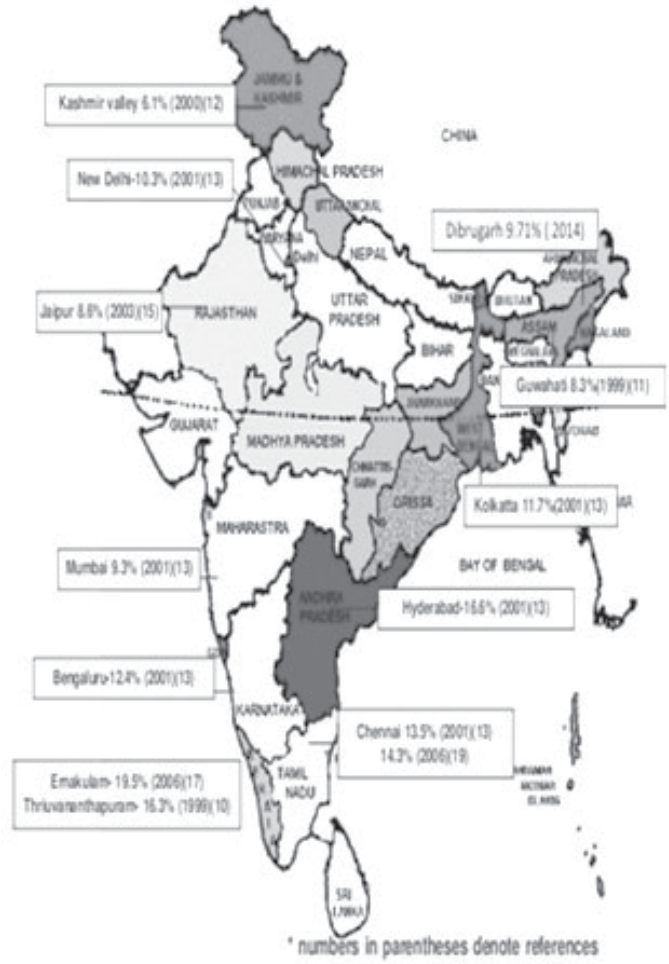
Particulars	Score
1. Age (yrs)	
<30	0
35-49	20
>50	30
2. Abdominal obesity	
Waist <90cm (M) / <80cm (F)	0
Waist >90-99cm (M) / >80-89cm (F)	10
Waist >100cm (M) / >90cm (F)	20
3. Type of Physical activity	
Vigourous exercise or strenuous (manual) labour at home /work	0
Mild to moderate exercise or mild to moderate physical activity at home /work	20
No exercise and sedentary activity at home /work	30
4. Family history	
No family history	0
Either parents	10
Both	20

The current state of Diabetes Mellitus in India:

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. Many influences affect the prevalence of disease throughout a country, and identification of those factors is necessary to facilitate change when facing health challenges. So what are the factors currently affecting diabetes in India that are making this problem so extreme?

The aetiology of diabetes in India is multifactorial and includes genetic factors coupled with environmental influences such as obesity associated with rising living standards, steady urban migration, and lifestyle changes. There are, however, patterns of diabetes incidence that are related to the geographical distribution of diabetes in India. Rough estimates show that the prevalence of diabetes in rural populations is one-quarter that of urban population for India and other Indian sub-continent countries such as Bangladesh, Nepal, Bhutan, and Sri Lanka[26].

Fig 1. Indian map showing prevalence of Diabetes in various states



Preliminary results from a large community study conducted by the Indian Council of Medical research (ICMR) revealed that a lower proportion of the population is affected in states of Northern India (Chandigarh 0.12 million, Jharkhand 0.96 million) as compared to Maharashtra (9.2 million) and Tamil Nadu (4.8 million)[27]. The National Urban Survey conducted across the metropolitan cities of India reported similar trend: 11.7 per cent in Kolkata (Eastern India), 6.1 per cent in Kashmir Valley (Northern India),[27] 11.6 per cent in New Delhi (Northern India), and 9.3 per cent in West India (Mumbai) compared with (13.5 per cent in Chennai (South India), 16.6 per cent in Hyderabad (south India), and 12.4 per cent Bangalore (South India).[28] A suggested explanation for this difference is that the north Indians are migrant Asian populations and south Indians are the host populations,[29] however this possible cause-and-effect has not been corroborated through further research. Similar ethnographic disparities have been observed in indigenous and non-indigenous populations in countries colonized by the Great Britain: indigenous people from New Zealand

and Australia have been shown to suffer from diabetes and cardio-metabolic disorders more than the non-indigenous people.[30,31.] Further studies are required in India to highlight cultural and ethnic trends and provide a more complete understanding of the differences in diabetes etiology between Indian and other ethnic groups within India.

Although the Indian urban population has access to reliable screening methods and anti-diabetic-medications, such health benefits are not often available to the rural patients. There is a disproportionate allocation of health resources between urban and rural areas, and in addition poverty in rural areas may be multi-faceted. Food insecurity, illiteracy, poor sanitation, and dominance of communicable diseases may all contribute, which suggests that both policy makers and local governments may be undermining and under-prioritizing the looming threat of diabetes. Such inadequacies contribute to an infrastructure that may result in poor diabetes screening and preventive services, non-adherence to diabetic management guidelines, lack of available counseling, and long distance travel to health services. Aged care facilities in rural areas report disparity in the diabetes management compared with their urban counterparts,[32] with these populations more likely to suffer from diabetic complications compared to their urban counterparts. More needs to be done to address the rural-urban inequality in diabetes intervention.

To reduce the disease burden that diabetes creates in India, appropriate government interventions and combined efforts from all the stakeholders of the society are required. Clinicians may be targeted to facilitate the implementation of screening and early detection programmes, diabetes prevention, self-management counseling, and therapeutic management of diabetes in accordance with the appropriate local guidelines form the backbone of controlling the predicted diabetes epidemic. Early screening and detection of pre-diabetes (especially in pregnant women, children and adults with BMI e"25) may yield positive health outcomes in society. Continuing education programmes for general practitioners may provide the "clinical inertia" required to initiate programme adherence, and may be a major step in achieving target glycaemic levels and the prevention of disease complications. Aggressive clinical measures in terms of early insulin initiation combined with optimal doses of oral hypoglycaemic agents and appropriate lifestyle modification could also have long-term positive effects in disease management.

Government policies may help in creating guidelines on diabetes management, funding community programmes for public awareness about the diabetes risk reduction, availability of medicines and diagnostic services to all sections of community.

CONCLUSION :

In this study a total of 2411 subjects were taken from 6 wards of Dibrugarh town to find out the prevalence of diabetes mellitus.

The following conclusions were drawn from the current study.

1. Majority of population have good knowledge about diabetes and were on regular medication.

2.Maternal family history of Diabetes has great impact on Diabetic population, as majority was maternal diabetic.

3.Diabetes incidence increases with age, as majority of population were within the age of 41 to 70 years.

4.The overall prevalence of diabetes was found to be 9.71% in present study.

5. A person from upper socio-economic class suffers more in Diabetes than lower and middle class people.

6. Normal Body Mass index was recorded in half of the population

It can be generalized from our finding of the study that developing awareness programmes on regular checking of glucose levels after the age of 50 years, educational packages on importance of increasing physical activity and lowering stress level will help the people to decrease the incidence in an' integrated manner.

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Original Article

Role of CBNAAT in Bronchoalveolar Lavage in Sputum Smear Negative Pulmonary Tuberculosis

B Hazarika[*], S Medhi[**], J Sarma[***]

Abstract

Background : CBNAAT/gene xpert in bronchoalveolar lavage specimens can be an useful diagnostic tool in the evaluation of sputum smear negative pulmonary tuberculosis, especially in a high burden country like India and thus facilitate an early diagnosis and treatment.This study aimed to assess the diagnostic accuracy of CBNAAT test in bronchoalveolar lavage (BAL) fluid by fibreoptic bronchoscopy, in sputum smear negative pulmonary tuberculosis and simultaneous detection of rifampicin resistance. **Methods:** We included 162 sputum smear negative pulmonary TB suspects and subjected them to fibreoptic bronchoscopy.BAL samples for AFB smear, AFB culture and CBNAAT test were obtained and AFB culture was taken as the gold standard. **Results:** Out of the total 162 cases, 88(54.32%) were diagnosed with pulmonary tuberculosis,63(38.89%) were non mycobacterial lung disease,11(6.79%) were observed to be NTM, taking culture as the gold standard. The sensitivity and specificity of AFB smear in BAL fluid was found to be 48.86% and 85.14% respectively. The PPV value was 79.63% and NPV was 58.33%.The sensitivity and specificity of CBNAAT/MTB gene xpert assay was 78.89% and 95.83% respectively; with a PPV of 95.95% and NPV of 78.41%.Out of the 74 CBNAAT positive cases, the number of rifampicin sensitive cases were 65 (65/74, 87.84%) and rifampicin resistant cases were 9 (9/74, 12.16%). **Conclusion:** Our study outlined that performing CBNAAT/gene xpert in BAL fluid in sputum smear negative pulmonary tuberculosis improves PTB case detection as well as Rifampicin resistance and augments diagnosis, clearly outperforming AFB smear.

KEY WORDS: *CBNAAT/gene xpert, bronchoalveolar lavage, fibreoptic bronchoscopy, pulmonary tuberculosis.*

INTRODUCTION :

Tuberculosis (TB) remains one of the world's deadliest communicable diseases. It is a major global health problem, responsible for ill health among millions of people each year. TB ranks as the second leading cause of death from an infectious disease worldwide, after human immunodeficiency virus (HIV)[1]. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease, 360,000 of whom are HIV positive[1]. Of the estimated 9 million people who developed TB in 2013, more than half (56%) were in the South-East Asia and Western Pacific Regions[1].India is the highest TB burden country accounting for one fifth of the global incidence[2].

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The decline in TB incidence has been slow, mortality remains unacceptably high and the emergence of drug-resistant TB has become a major public health concern. Detecting patients with active pulmonary tuberculosis (PTB) disease is an important component of TB control as early appropriate treatment renders these patients non-infectious and interrupts the chain of transmission of TB. Under the programme conditions, such as those endorsed by the World Health Organization (WHO) and implemented successfully in high burden countries including India's Revised National Tuberculosis Control Programme (RNTCP) of Government of India, the diagnosis of PTB is based on sputum smear examination[3]. However, in patients with a compatible clinical picture, sputum smears do not reveal acid-fast bacilli (AFB) in all patients, 'smear negative culture positive' state has been observed in 22% to 61% of the cases[4,5,6]. Sputum smear-negative pulmonary tuberculosis (SSN-PTB) still remains a common problem faced by the clinicians. This is particularly true in the case of children who are unable to produce an adequate sample of sputum, patients with immunosuppressed states such

as those with HIV infection and the acquired immunodeficiency syndrome(AIDS) in whom sputum smear negative PTB is quite common[7].

From the available published evidence, it has been observed that the number of bacilli in the sputum correlates well with sputum smear microscopy results when the smears are prepared properly and examined. Sputum microscopy is a highly specific test, a low-cost, appropriate technology but sputum smear microscopy alone, although inexpensive, misses many patients and detects only those with relatively advanced disease, having a bacillary load of atleast 10,000 bacilli per ml of sputum[8]. Culture for AFB in Lowenstein-Jensen medium is considered as the gold standard test for detection of pulmonary tuberculosis, but it is time consuming and takes about 6 to 8 weeks. Also it requires 100 AFB bacilli per ml of sputum to be culture positive[9]. Bacteriologic studies of sputum and gastric aspirates in the diagnosis of Pulmonary tuberculosis has shown positive results in 40 to 60% of cases using AFB smears[10].

Undetected cases of disease increase morbidity, mortality, and disease transmission. Thus, sputum smear-negative pulmonary tuberculosis (SSN-PTB) is a common problem faced by clinicians. Performing fibreoptic bronchoscopy (FOB), and subjecting the bronchoscopic secretions (bronchial washings, bronchoalveolar lavage), transbronchial lung biopsy (TBLB) material to conventional diagnostic methods of smear, mycobacterial culture and histopathology appears to be helpful in the diagnosis of sputum smear negative PTB.

The aim of this study was to assess the diagnostic accuracy of CBNAAT test in bronchoalveolar lavage(BAL) fluid by fibreoptic bronchoscopy, in detecting pulmonary tuberculosis in cases who are sputum smear negative or are unable to expectorate sputum, but having clinical and radiological features highly suggestive of pulmonary tuberculosis and simultaneous detection of Rifampicin resistance.

MATERIALS AND METHODS :

This study is an institutional based prospective study carried out on a total of 162 patients with suspected pulmonary tuberculosis, attending the Out Patient Department or admitted in the department of Pulmonary Medicine, Internal Medicine and its allied specialities, Gauhati Medical College and Hospital, during a period of one year from August 2014 to July 2015.

Selection of Cases:

The patients were randomly included in the study after considering the inclusion and exclusion criteria and written informed consent from the patients were taken.

Inclusion Criteria :

- Patients >12 years of age.
- Patients with cough e" 2 weeks, hemoptysis, fever, or history of contact with PTB cases.
- Patients with clinical and radiological features suggestive of pulmonary tuberculosis but sputum smear negative or not able to expectorate sputum.

Exclusion Criteria:

- Patients not willing to give consent.
- Smear positive cases, those with disseminated or extra pulmonary tuberculosis.
- Patients with contraindications of bronchoscopy like
  - Patients with hypoxia (SpO_2<92% at room air).
  - Patients with associated malignant arrhythmia.
  - Patients with unstable cardiac status.
  - Patients with bleeding diathesis.
  - Hemodynamically unstable patients.

After detailed history, clinical examination and investigations, all the cases were filled up in a predesigned and pretested proforma. Appropriate statistical methods were applied using SPSS 20 software.

Routine blood investigations were done. Sputum examination for AFB – 2 Samples (one spot and one early morning sample) carried out by Ziehl-Neelsen staining technique, gram stain and culture sensitivity was done. The patients underwent chest imaging like chest X-Ray (PA – view), CT- thorax, ECG and Flexible fibreoptic bronchoscopy. BAL fluid was subjected to AFB smear, CBNAAT, AFB – culture and BAL fluid gram stain and C/S, fungal smear. Endobronchial biopsy and TBLB was done in selected cases.

Procedure for flexible fibreoptic bronchoscopy

Consent was taken from the patients before undergoing bronchoscopy in addition to the consent taken for being included in the study population. Flexible fibreoptic bronchoscopy was used to obtain bronchoalveolar lavage(BAL) samples for AFB smear and CBNAAT test. The bronchoscope used during this study was a FUJINON FB 120 T model. It was performed

with the patient in supine position, through transnasal or transoral route (in special circumstances) with pre procedure assessment for BP, ECG and pulse oximetry. Oxygen saturation was monitored all throughout the procedure with an aim to maintain saturation at >92%. The patient was called nil per orally in the morning and nebulised with 4% lignocaine solution for about 15 to 20 minutes. During the bronchoscopy procedure, stepwise examination was done starting from the glottis, trachea, carina, then the normal side bronchial tree was examined first and then the abnormal side. Adequate BAL sample was taken from the radiologically suspected abnormal lobe. In case of diffuse involvement in chest X-ray or CT-scan, samples were taken from the right middle lobe.100 ml of sterile saline at room temperature was infused in five 20 ml aliquots through the bronchoscope wedged into a subsegmental bronchus. After each aliquot was infused, the fluid was recovered by using suction apparatus and collected in a specimen trap. The specimen was pooled in a sterile plastic container and processed for mycobacterial examination. After the procedure, patients were observed for potential complications and advised to be on empty stomach for another two more hours. They were made aware of slight bleeding or cough after the procedure.

The BAL samples were then sent for AFB smear, CBNAAT/genexpert assay and AFB culture. The reports of the patients were then followed up and entered in the pre-designed and pretested proforma. The data was calculated by appropriate statistical methods using SPSS 20.The diagnostic yield was defined and measured in terms of frequency and validity by calculating sensitivity, specificity, positive and negative predictive values.

AFB smear was done by Ziehl Neelsen staining procedure and AFB culture was done in Lowenstein Jensen media. For CBNAAT, sample with sample reagent was poured into sample tube. Then incubation for 15 minutes at room temperature done and pipette diluted sample poured into a self contained cartridge and assay was done. The CBNAAT/MTB (Gene xpert) assay uses 3 specific primers and 5 unique molecular probes to ensure a high degree of specificity. Assay targets the rpoB gene, which is critical for identifying mutations associated with rifampicin resistance. Results were obtained in 2 hours. The final diagnosis of pulmonary tuberculosis was made on the basis of BAL fluid AFB culture results which was taken as the gold standard.

RESULTS AND OBSERVATIONS :

A total of 162 patients, who fulfilled the inclusion and exclusion criteria were included in the study. There were a total of 105(64.81%) males and 57(35.19%) females. The mean age among males was 42.7 ± 13.94 years and the mean age among females was 41.60 ± 12.99 years. The most common presenting complaint among the patients was observed to be cough in 69.75%, of which 32.74% patients had dry cough and 67.26% had productive cough. The second most common complaint was hemoptysis (61.73%), followed by fever (45.06%) then loss of appetite (41.98%), weight loss (41.36%), shortness of breath (24.07%), weakness and malaise (19.75%) and lastly chest pain (17.28%). There were 15(9.26%) known cases of COPD among the study sample. Among all the cases, 56 (34.57%) were old cases of tuberculosis, i.e they had a previous history of ATT intake for atleast one month or more irrespective of completing treatment or not, while 106 (65.43%) cases were considered as new cases as they were never treated for tuberculosis (pulmonary/extra-pulmonary) or had taken treatment for less than one month.

Radiological features of the patients included cavity (12.96% on CXR; 12.96% on HRCT); consolidation (24.07% on CXR, 30.25% on HRCT), nodular opacities (2.47% on CXR; 14.20% on HRCT), pulmonary infiltrates (17.28% on CXR; 8.64% on HRCT); fibro-bronchiectatic changes (12.35% on CXR; 30.86% on HRCT);Ground glass opacity (3.08% on CXR; 14.20% on HRCT); miliary shadows (1.23% on CXR; 1.85% on HRCT); normal pattern (19.75% on CXR; 0% on HRCT); others(3.70% on CXR; 6.79% on HRCT).Normal pattern in CXR was found in 19.75% of the patients. On further evaluation on HRCT-thorax, these normal CXR were found to have bronchiectatic changes, small centrilobular nodules, miliary mottling, ground glassing which were not visible on the Chest X-rays. The other patterns mentioned above refers to emphysematous changes, bulla, air crescent sign, pleural effusion, and bronchocoele found in a minority of the patients.

Table 1: Clinical and demographic characteristics

Characteristics		N (%)
Gender		
males		105(64.81%)
females		57(35.19%)
Age		
males		42.7 ± 13.94 years
females		41.60 ± 12.99 years
Clinical features		
cough		113(69.75%)
hemoptysis		100(61.73%)
fever		73(45.06%)
loss of appetite		68 (41.98%)
weight loss		67(41.36%)
shortness of breath		39(24.07%)
weakness,malaise		32(19.75%)
chest pain		28(17.28%)
Radiological patterns	**CXR**	**CT-thorax**
consolidation	39(24.07%)	49(30.25%)
nodular opacities	4(2.47%)	23(14.20%)
pulmonary infiltrates	28(17.28%)	14(8.64%)
fibrobronchiectatic changes	20(12.35%)	50(30.86%)
ground glassing	5(3.08%)	23(14.20%)
miliary shadows	2(1.23%)	3(1.85%)
normal	32(19.75%)	0(0%)
others	6(3.70%)	11(6.79%)
New cases		106(65.43%)
Previously treated		56(65.43%)

Of the 162 suspected cases, 88 (54.32%) cases were diagnosed as PTB at the end of the study on the basis of AFB culture of BAL-fluid which was taken as the gold standard. Those cases who had no growth of mycobacteria in their BAL fluid i.e their culture was negative for mycobacteria were considered as non-mycobacterial lung disease group. There were 63(38.89%) cases in the non-mycobacterial lung disease group. The remaining number of cases i.e 11 (6.79%) patients had growth of NTM (non-tubercular mycobacteria) in their BAL fluid AFB-culture and were thus categorised as NTM at the end of the study.

The patients who were categorised as the non-mycobacterial lung disease group had other diagnoses like post TB sequelae (39.68%), pneumonia (31.75%), bronchogenic carcinoma (20.63%) and fungal infection (7.94%), confirmed by BAL fluid gram stain and culture sensitivity, fungal smear, endobronchial biopsy and TBLB.

BAL fluid for AFB smear was positive in 54 (61.36 %) cases in the total sample population. Out of which 43 (48.86 %) cases were true positive as their AFB culture was also found to be positive. Eleven (12.50 %) cases were falsely positive for AFB smear as their culture was negative for Mycobacterium tuberculosis but had growth of NTM. BAL fluid for CBNAAT/gene xpert was positive in 74(84.09%) cases out of 88 culture positive cases; among those 71(80.68%) were true positive and 3 (3.41%) cases were false positive, as AFB culture was negative in these 3 cases. In all these cases CBNAAT assay also detected rifampicin sensitive and resistant strains. Rifampicin was sensitive in 65(87.84%) cases and resistant in 9(12.16%) cases. Out of the 9 resistant cases, 6 (10.71%) cases were previously treated for tuberculosis and 3 (2.83%) were new cases.

Table 2 : ***Different diagnosis in the non-mycobacterial lung disease group.***

Diagnosis	N (%)
Post tubercular sequalae	25 (39.68%)
Pneumonia	20 (31.75%)
Bronchogenic carcinoma	13 (20.63%)
Fungal infection	5 (7.94%)

The sensitivity and specificity of AFB smear in BAL fluid was found to be 48.86% and 85.14% respectively. The PPV value was 79.63% and NPV was 58.33%. The sensitivity and specificity of CBNAAT/MTB gene xpert assay was 78.89% and 95.83% respectively; with a PPV of 95.95% and NPV of 78.41%. Out of the 74 CBNAAT positive cases, the number of rifampicin sensitive cases were 65(87.84%) and rifampicin resistant cases were 9 (12.16%) (Tab:3). Out of the 74 CBNAAT positive cases, the number of rifampicin sensitive cases were 65(87.84%) and rifampicin resistant cases were 9 (12.16%).

Table 3 : ***Diagnostic accuracy of BAL fluid AFB smear and CBNAAT/ gene xpert assay in sputum smear negative PTB.***

Test on BALF	Sensitivity	Specificity	PPV	NPV
AFB smear	48.86% C.I (38.05% to 59.75%)	85.14% C.I (74.96% to 92.34%)	79.63% C.I (66.47% to 89.37%)	58.33% C.I (48.45% to 67.75%)
CBNAAT/gene xpert	78.89% C.I (69.01% to 86.79%)	95.83% C.I (88.30% to 99.13%)	95.95% C.I (88.61% to 99.16%)	78.41% C.I (68.35% to 86.47%)

DISCUSSION :

Among the total 162 cases, 88(54.32%) cases were diagnosed as pulmonary tuberculosis at the end of the study, taking AFB culture of BAL fluid as the gold standard. Remaining 63(38.89%) cases had no growth of mycobacteria in their BAL fluid samples and were categorised in the non-mycobacterial lung disease group. And 11(6.79%) cases had growth of non-tubercular

mycobacteria in their BAL fluid and were thus categorised as NTM group.

Elizabeth M. Marlowe et al.(2011)[11] did a similar study on accuracy of genexpert,on sputum specimen and found that out of a total of 217 patients, 130 cases had PTB , 46 had no growth of mycobacteria in their sputum specimen and 41 patients had NTM .These findings correlated with our findings in BAL; however Elizabeth M. Marlowe et al. further subdivided the NTM group into various species of NTM, which was not done in our study.

Numerous studies have demonstrated the utility of Xpert MTB/RIF assay in diagnosis of pulmonary tuberculosis. Flexible fibreoptic bronchoscopy constitutes an interesting alternative for TB diagnosis in smear-negative or sputum-scarce patients. Given that WHO recommendations on the Xpert MTB/RIF assay only pertain to sputum samples[1], further investigation must be conducted regarding the use of this PCR on FOB samples.

In our study, the sensitivity and specificity of AFB smear in BAL fluid was observed to be 48.86% and specificity was 85.14%. The sensitivity of Xpert MTB/RIF in this study was 78.89% and specificity was 95.83%.

Grant theron et al.(2013)[12] did a study on the accuracy of gene xpert in bronchoalveolar lavage specimen in sputum smear negative patients and found the sensitivity of MTB/RIF to be 93% (25/27; 95% CI 77% to 98%) and significantly higher than smear microscopy performed on the same fluid, which had a sensitivity of 58% (15/26; 39% to 75%; p<0.001). The specificity of CBNAAT/MTB genexpert was 96% and smear microscopy was 99.3%. The sensitivity of gene xpert was higher than in AFB smear in this study as well as in our study but the specificity of our study was less than the above mentioned study. This maybe because of the variation in inclusion and exclusion criteria of both the study groups.

In a similar study done by Kanwal Fatima Khalil et al.(2015)[13] ; they found the sensitivity and specificity of AFB smear in BAL fluid to be 39.53% and 100 % respectively. The sensitivity of Xpert MTB/RIF was 91.86% and specificity was 71.42%.the sensitivity of AFB smear in BAL fluid was similar to ours but the specificity of AFB smear in this study was much higher than our study. This may be because of selection bias in this study which included only those patients who were very likely to have active tuberculosis.

CONCLUSION :

The present study concludes that the CBNAAT/gene xpert assay on bronchoalveolar lavage specimen provides an accurate diagnosis of pulmonary tuberculosis in patients with sputum smear negative results or those who cannot expectorate sputum. Conventional AFB culture takes 6 to 8 weeks for detection of tuberculosis and even more time to detect resistance pattern while CBNAAT/gene xpert can detect tuberculosis and rifampicin resistance within 2 hours. Therefore CBNAAT/gene xpert assay is a much more rapid diagnostic method to detect tuberculosis than conventional AFB culture method along with pattern of rifampicin resistance. CBNAAT/gene xpert is also cost effective compared to AFB culture. It was also observed that CBNAAT clearly outperformed AFB smear in sputum smear negative cases. Thus CBNAAT is a valuable tool for early diagnosis and treatment of sputum smear negative cases and can prevent disease progression as well as transmission to the community.

Abbreviation: CBNAAT (Cartridge-Based Nucleic Acid Amplication Test), PTB (Pulmonary tuberculosis), BAL(bronchoalveolar lavage), NTM (non-tuberculour mycobacteria), CXR (Chest X-ray).

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CONSENT FORM FOR CASE REPORTS

For a patient's consent to publication of information about them in a journal or thesis

Name of person described in article or shown in photograph :_____

Subject matter of photograph or article : _____

Title of article : _____

Medical practitioner or corresponding author : _____

I_____ [insert full name] give my consent for this information about MYSELF OR MY CHILD OR WARD/MY RELATIVE [insert full name]:_____, relating to the subject matter above ("the Information") to appear in a journal article, or to be used for the purpose of a thesis or presentation.

I understand the following :

1. The Information will be published without my name/child's name/relatives name attached and every attempt will be made to ensure anonymity. I understand, however, that complete anonymity cannot be guaranteed. It is possible that somebody somewhere - perhaps, for example, somebody who looked after me/my child/relative, if I was in hospital, or a relative - may identify me.
2. The Information may be published in a journal which is read worldwide or an online journal. Journals are aimed mainly at health care professionals but may be seen by many non-doctors, including journalists.
3. The Information may be placed on a website.
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Signature of requesting medical practitioner/health care worker:

_____Date:_____

Original Article

Cardiovascular Complications in Rheumatoid Arthritis

J D Phukan*, N R Daulat, S K Baruah*****

Abstract

Background : Rheumatoid arthritis may result in a variety of extra articular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis and hematologic abnormalities. The most common cause of death in patients with RA is cardiovascular disease. **Materials and methods:** The study sample comprised of 81 rheumatoid arthritis patients selected randomly from those who attended medicine department (OPD/Ward) and Rheumatology OPD of Gauhati Medical college and Hospital over period of 1 year, and fulfilled the 2010 ACR:EULAR Classification Criteria. All patients underwent ECG and 2 Dimensional Echocardiography for cardiac assessment. **Results and Observations:** Cardiac abnormalities were seen in 32 patients (39.5%) and it is found to be more common in males than in females. Left ventricular diastolic dysfunction was the most common and was seen in 20(24.69%) patients. Pericardial involvement was seen in 9 (11.11%) patients. Mitral valve regurgitation was seen in 6 (7.4%) patients, tricuspid regurgitation with pulmonary arterial hypertension was present in 4 (4.93%) patients, aortic valve regurgitation was found in 5 (6.17%), pulmonary valve regurgitation in 1 (1.23%). Ischemic heart disease was found in 2 patients (2.5%) and left ventricular systolic dysfunction in 1 patient (1.23%). Abnormal electrocardiographic findings were identified in 12 (14.81%) patients. **Conclusion:** From our study it can be concluded that cardiac abnormalities are quite common in RA patients and their occurrence increases with increase in age and duration of the disease. It is more common in males than in females. Cardiac abnormalities also increase with an increase in DAS28 score, increase in CRP level and presence of subcutaneous nodule. LVDD is the commonest abnormality found. Cardiac abnormalities are largely sub-clinical. Hence early detection of cardiac abnormalities can be very important in the correct assessment and management of the RA patients as cardiovascular disease is the most common cause of mortality in RA patients.

KEYWORDS: *rheumatoid arthritis (RA), cardiovascular, ECHO*

INTRODUCTION:

Rheumatoid arthritis may result in a variety of extra articular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis and hematologic abnormalities. The most common cause of death in patients with RA is cardiovascular disease. The incidence of coronary artery disease and carotid atherosclerosis is higher in RA patients than in the general population even when controlling for traditional cardiac risk factors, such as hypertension, obesity, hypercholesterolemia, diabetes and cigarette smoking. Furthermore, congestive heart failure (including both systolic and diastolic dysfunction) occurs at an approximately two fold higher rate in RA than in the general population. The presence of elevated serum inflammatory markers appears to confer an increased risk of cardiovascular disease in this population[1]. This study aims to document the incidence of cardiac involvement in patients suffering from rheumatoid arthritis and to correlate cardiac lesions with duration and severity of rheumatoid arthritis.

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AIM AND OBJECTIVE:

1. To evaluate the cardiac dysfunction in patients of rheumatoid arthritis with echocardiography and electrocardiography.
2. To correlate cardiac lesions with the duration and severity of rheumatoid arthritis.

MATERIALS AND METHODS:

The present study is a hospital based observational & descriptive which study was undertaken in the Department of Medicine, Gauhati Medical College & Hospital, Guwahati, Assam from 1st June 2014 - 1st June

2015. The study sample comprised of 81 rheumatoid arthritis patients selected randomly from those who attended medicine department (O.P.D./Ward) and Rheumatology O.P.D. and fulfilled the 2010 ACR:EULAR Classification Criteria. All the cases were subjected to a thorough history, clinical examination and relevant investigations. All patients underwent ECG and 2 Dimensional Echocardiography for cardiac assessment.

RESULTS AND OBSERVATIONS :

Cardiac structural and functional abnormalities were seen in 32 patients (39.5%). Left ventricular diastolic dysfunction was the most common and was seen in 20(24.69%) patients. Pericardial involvement was seen in 9 (11.11%) patients of whom 8 patients had pericardial effusion and 1 patient had pericardial effusion with pericardial thickening. Mitral valve regurgitation seen in 6 (7.4%), out of which mild MR was present in 4 patients and moderate MR was present in 2 patients. Tricuspid regurgitation with pulmonary arterial hypertension was present in 4 (4.93%) patients. Aortic valve regurgitation was found in 5 (6.17%) & Pulmonary valve regurgitation was found in 1 (1.23%). Ischemic heart disease was found in 2 patients (2.5%) and left ventricular systolic dysfunction was found in 1 patient (1.23%).

Table 1: Echocardiographic findings in patients of RA

Cardiac abnormalities	Number of RA patients	Percentage
TR with Pulmonary arterial hypertension	4	4.93
Pericardial effusion	8	9.87
Pericardial effusion with Pericardial thickening	1	1.23
Left ventricular diastolic dysfunction	20	24.69
Left ventricular systolic dysfunction	1	1.23
Mitral regurgitation	6	7.40
Aortic regurgitation	5	6.17
Pulmonary regurgitation	1	1.23
Ischemic heart disease	2	2.46
Regional wall motion abnormality	2	2.46

12 (14.81%) out of 81 RA patients had abnormal ECG. Nonspecific ST-T changes was found in 5 (6.17%) patients and was the most common finding.

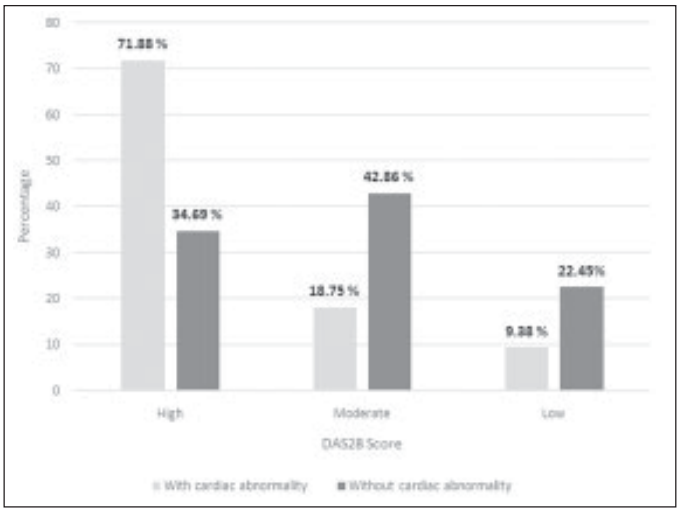
In our study, the mean duration of disease in RA patients was 3.13 years and mean duration of disease in patients with cardiac abnormalities was 3.88 years and those patients without cardiac abnormality was 2.66 years. The mean duration of disease of patients with LVDD was found to be 4.25 years.

Maximum no. of patients, 23(71.9%) with cardiac abnormality were with high disease activity, 6(18%) patients were with moderate disease activity and only 3(9.4%) patients with cardiac abnormality were with low disease activity.

Table 2: Association of DAS28 score with RA patients with cardiac abnormality and patients without cardiac abnormality,

DAS28 Score	Patient with cardiac abnormality	Patient without cardiac abnormality	Total
High (>5.1)	23 (71.8%)	17 (34.69%)	40 (49.38%)
Moderate (3.2 – 5.1)	6 (18.75%)	21 (42.88%)	27 (33.33%)
Low (<3.2)	3 (9.8%)	11 (22.45%)	14 (17.29%)
Total	32	49	81

Figure : Bar Diagram showing relation of cardiac abnormality in RA patients with Disease Activity



DISCUSSION :

The mean age of patients with cardiac abnormalities was 45.56 years and those without cardiac abnormalities 39.73 years. This corroborates with Guedes et al (2001) who also reported that the number of patients with echo abnormalities increases with advancing age[2]. In a study by Maione et al (1993), the maximum number of patients with cardiac abnormalities (66%) was seen in the 30-60 years age group.[3]

In our study out of 81 study subjects 20 patients (24.69%) were male and 61 patients (75.31%) were female with a female to male ratio of 3.05:1. Patients with cardiac abnormalities had 12 (60%) male and 20 (32.7%) female. And those without cardiac abnormalities had 8 (40%) male and 41 (67%) female. It shows that males

are more likely to develop cardiac disease than females in RA. Bacon PA, Gibson DG, (1974) had documented male sex as a risk factor for cardiac involvement in RA patients.[4] Mutru et al, (1989), reported that RA was associated with a higher rate of cardiovascular mortality in males.[5] So our study is comparable with the above studies.

In our study, the mean duration of disease in RA patients was 3.13 years and mean duration of disease in patients with cardiac abnormalities was 3.88 years and those patients without cardiac abnormality was 2.66 years. The mean duration of disease of patients with LVDD was found to be 4.25 years. This is comparable with Kaushal et al (1988) who also found that the mean disease duration in their patients was 3.65 years.[6] Our study also found that LVDD increases with increase in duration of disease which corroborates with Franco et al(2000)[7] and Montecucco C et al (1999).[8]

In our study CRP was high in 81.25 % of RA patients with cardiac abnormalities. So high CRP was associated with cardiac abnormalities in RA patients. This is also statistically significant (p = 0.0005). Similar studies conducted by Van Doornum S et al (2002)[9], Raya et al(2005)[10] and Hannawi S et al (2007)[11] also found that high CRP level is associated with increased risk of cardiovascular disease in RA patients.

In our study, there was significant correlation between the high disease activity and occurrence of cardiac abnormalities.(p=0.0014)This is comparable to Kobayashi et al (2009), who also reported that myocardial involvement was frequent in RA patients and associated with higher DAS28 score.[12]

In our study, there was significant correlation (p=0.0001) between presence of subcutaneous nodule and occurrence of cardiac abnormalities. Wislowska M et al (1999) evaluated echocardiographic findings in RA patients with subcutaneous nodules and compared them with RA patients without subcutaneous nodules.[13] Their study revealed a significantly increased incidence of cardiac abnormalities in RA patients with subcutaneous nodules (p<0.0002).

In our study cardiac structural and functional abnormalities were seen in 32 patients (39.5%). Left ventricular diastolic dysfunction was the most common and was seen in 20(24%) patients. Pericardial involvement was seen in 9 (11.11%) patients of whom 8 patients had pericardial effusion and 1 patient had pericardial effusion with pericardial thickening. The thickness of pericardium was 5 mm. Mitral valve regurgitation was seen in 6 (7.4%) patients, out of which mild MR was present in 4 patients and moderate MR was present in 2 patients. Tricuspid regurgitation with pulmonary arterial hypertension were present in 4 (4.93%) patients. Aortic valve regurgitation was found in 5 (6.17%), Pulmonary valve regurgitation in 1 (1.23%). Ischemic heart disease was found in 2 patients (2.5%) and left ventricular systolic dysfunction in 1 patient (1.23%).

Maione et al (1993) studied 39 RA patients and compared them with 40 matched control subjects.[3] The most common abnormality in their study was LV diastolic dysfunction (26%). Pericardial involvement was seen in 9% and valvular lesions in 8%. Dawson et al (2000) in their study of 146 RA patients have described a high incidence (21%) of pulmonary hypertension and 1% pericardial effusion in their series of patients. In Dawson et al moderate MR was present in 4% and mild MR in 17%.[14] Levendoglu et al (2002) evaluated forty patients with rheumatoid arthritis for ventricular function using Doppler echocardiography. They found a significantly increased incidence of left ventricular diastolic dysfunction. Diastolic function was impaired in both ventricles in patients with active RA.[15]

In the study group, ECG were seen in 12(14.81%) patients. One patient had Left ventricular hypertrophy (LVH), one patient had left bundle branch block, one patient had incomplete right bundle branch block (RBBB), one patient had left anterior hemi block (LAHB) and five patients had nonspecific ST-T changes, one had first degree AV block, two patients had ischemic changes. Raof R Merza(2008) in their study of 55 RA patients identified abnormal electrocardiographic findings in 10(18.18%) patients including partial bundle brunch block and non-specific T wave changes.[16] Dasgupta S et al (2007) had found ECG abnormalities in 10% of patients.[17]

CONCLUSION :

From our study it is concluded that cardiac abnormalities were found commonly above 60 years in RA patients and it increases with increase of age. It is more common in males than females and its occurrence increases with duration of disease. Cardiac abnormalities also increases with increasing DAS28 score, increased

CRP level and presence of subcutaneous nodule. LVDD is the commonest abnormality found. The early detection of cardiac abnormalities can be very important in the correct assessment and management of the RA patients, especially in light of the fact that, the most common cause of mortality in RA patients is cardiovascular disease. Therefore, every patient should be submitted to a cardiological assessment (in particular ECG and echocardiography) in order that cardiac involvement can be detected early and treated and the incidence of morbidity and mortality reduced. However a prospective study with larger sample size is required to arrive at the definite conclusion regarding association of cardiac abnormalities in RA patients.

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Review Article

Patient satisfaction-Factors and its evaluation

B. Khandelwal[*] V. P. Singh[**]

INTRODUCTION :

Identifying factors which promote patient's compliance with treatment is an area of research & concern as it has a tremendous effect in improving the quality of health care. Two major determinants of quality of care are patient outcomes and patient satisfaction. Patient satisfaction is an attitude and one satisfied consumer will share his positive experience with many others and a dissatisfied patient will share with many more. Health care industry which was traditionally known as a noble profession has evolved into a service industry due to increased awareness and expectations of the patient, introduction of third party payers and increasing litigations. With the healthcare market turning from a seller's market into buyer's market, health care providers are turning more and more towards marketing of their services. Patients are consumers and have ample opportunity to compare between the hospital quality metrics and choose the one, which in their opinion would provide the best care at an affordable cost.

Professional job satisfaction is equally important as patient's satisfaction but they might not always be complementary. As a doctor, we enhance our job satisfaction by enhancing our professional competency by attending conferences, mastering new skills and updating ourselves regarding latest technologies. Though this goes a long way in delivering quality health care but to a patient might not always be relevant.

What is patient satisfaction?

In spite of growing concern regarding assessment of patient satisfaction in health care, there is neither definite definition of the concept nor systematic consideration of its consequences and determinants. Some define it as individual perceptions of the quality of health care delivered. Many definitions have been proposed. "Patient satisfaction is a highly desirable outcome of clinical care in the hospital and may even be an element of health status itself".[1] The quality of hospital care in all of its aspects can be judged by patient's satisfaction or dissatisfaction."Patient satisfaction is the healthcare recipient's reaction to aspects of his or her service experience". [2] "Patient satisfaction belongs to the service dimension as opposed to the technical dimension of quality of care. Most patients report few problems related to technical quality of care in hospitals and moreover do not feel qualified to judge technical quality and therefore assume technical competence". [3]

There is a complex interaction between patient perception and expectation and the understanding of this relationship between the two is the basis of understanding patient satisfaction. A useful simple mathematical model of satisfaction provided by the "First law of Service" is Satisfaction = Perception minus Expectation. [4]

It is impossible to quantify or mandate expectations as it is a psychological phenomena and it varies not only from patient to patient but also changes with time. Past experiences, current needs and individual preferences are factors modulating the expectations. According to Kano model, patients have a set of subconscious expectations from any health care delivery system and take them as granted.[5] They do not recognize them as quality factors but if they are missing, the patients get dissatisfied.

Factors affecting patient satisfaction :

Patient satisfaction is a multi – attribute model with various aspects of care. Institute of Medicine (IOM), in its report "crossing the quality chasm" published in 2001, specified six aims for a quality health care system patient

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safety, equitable, evidence based, timely, efficient and patient centred. Patient satisfaction is directly influenced by the last three factors. Efficient, timely and patient centred delivery of quality health care affects the patient's satisfaction. Several discrete functional services such as house – keeping, dietary services, pharmacy, laboratory etc. and hospital policies, work culture and attitude may be a hurdle to satisfy a patient even if the doctor is competent and compassionate. The aspects concerned with patient satisfaction are multi factorial including General Satisfaction, Technical, Interpersonal Manner, Communication, Financial Aspects, Time Spent with Doctor, Accessibility and Convenience.

Physician's verbal and non-verbal communication while interacting with the patient has a major role to play in patient's satisfaction. In the search for factors promoting patients compliance and in turn improving the effectiveness and quality of health care, the communication style of the physician has emerged as an important determinant.

A major factor in patient's evaluation is affective component of physician's communication. The patient starts the interaction with apprehension regarding the disease, its course of treatment and outcome. When a physician communicates effectively, the patient feels like a person attended to and cared for rather than a case being studied. Each individual should be made to feel unique and important by acknowledging their feelings and concerns and paying undivided attention to both their verbal and non verbal communications. How we say a thing is as important as what we say. Patients should be updated about their disease, the tests planned, the further plan of investigation, the likely outcome and the final diagnosis. Reaching a diagnosis is important but how the patient was communicated while forming the diagnosis is equally important.

With widespread use and popularisation of internet, patients though more educated may often have lots of misconceptions regarding their illness and unrealistic expectations regarding the treatment. A doctor needs to explain the things with patience and compassion.

Staff satisfaction and patient satisfaction :

Consumers look for hospitals that balances cost, quality and service and it is the employees of the hospital that deliver on those expectations. Joe Giansante, UP, HR, Ellis Medicine says "The only way to make sure patients are satisfied is to make sure employees are satisfied".

Health care industry is undergoing massive changes. It is now preferred to be a quality – based care model rather than a volume – based care model. In order to adapt to these changes, healthcare organisations have to change their business strategy and this is reflected in their workforce management strategies.

Usefulness and limitations of patient survey as a tool of assessment :

Patient satisfaction survey is a relevant tool to measure patient satisfaction. There are many factors that may influence the ratings such as the respondent characteristics like age, educational status, socio economic status; level of expectation, socio psychological phenomena & gratitude.[6] Methodological factors such as sampling strategy, data collection procedure, questionnaire format and response rate also affect the accuracy of the ratings. It is important to note that the questionnaire that is being used for survey is satisfying the criteria of validity and reliability. In order that the instrument actually measures what it is supposed to measure, a clear representation of the factor under study and appropriate formats to measure those factors under study is a requisite To control for acquiescent responding, the instrument should contain both positively and negatively worded items. The questionnaire should be tested for general satisfaction, technical quality, interpersonal manner, communication, financial aspects, time spent with doctor, accessibility and convenience. The items of different subscales should not be in sequence; rather they should be placed randomly in the questionnaire. To get an explicit assessment of the patient satisfaction, each item should be calculated independently and subsequently the subscales should be calculated.

Patients feel actively involved in their own health care when they are asked to report their experiences. Most researchers feel that giving the patient an opportunity to participate in their care is a real time feedback for providers. The patient satisfaction survey helps to detect the deficiencies and take corrective measures. Surveys can prove beneficial only if there is proper use of the information received. Asking patient to report his experiences rather than answering yes/no or ratings on a Likert scale, gives a better insight into whether the patient's ratings are representative or reasonable.

There are many validated and reliable questionnaire but researchers who have studied conceptual and theoretical issues of patient satisfaction assert that the literal interpretation of a high satisfaction rating may actually not be representative of quality of health services. A matter of concern is the lack of awareness of study authors regarding proper method of survey. Credibility of research findings depends on the validity and reliability of the instrument

Use of self report questionnaire often results in evaluative data rather than descriptive and so ends up with evaluating quality of health service rather than patient satisfaction. A meaningful evaluative data must be considered against patient's expectation. [7,8] Van Mannenapthy described quality as an abstraction defining the margin between desirability and reliability. [9] When an existing instrument of measurement is modified, care should be taken that the validity and / or reliability of the instrument is not affected.

An issue for discussion is whether satisfaction is an appropriate measure of quality of care. Correlations may be strong between specific aspects of satisfaction and quality of care but may not be between the construct as a whole. Whether patient's compliance, response to treatment and progress frequency and length of hospitalisation can be used as indicators of satisfaction is a point of debate.

Some researchers have criticised the assessment of patient satisfaction by way of survey due to the gap between the clinical knowledge of patients and their health care providers.

Feedback from patients:

Feedback given by the patients show opportunities to improve services. Every hospital should have a mechanism for receiving complaints and patient must be informed of this mechanism and of their right to complain. Appropriate actions and honest response to the complaints should be taken and the same should be documented.[10] The void which is discovered should be accepted and acknowledged with grace but at the same time corrective measures for the same should be taken.

Hospital statistics and patient satisfaction :

The health care financing administration policy had made an effort to help patients in selecting hospitals by publicly announcing the hospital mortality rates. But the mortality and morbidity statistics do not seem to affect the patient as much as personalized care with respect and dignity. A question which often arises is "whether increasing patient satisfaction is important only for improving the hospital's statistics and revenue?" well, the answer should be a clear no. Achieving patient satisfaction should be the goal and continuous effort should be made to maximize it. A successful outcome is often interpreted by a clinician as success of the health care delivery system but it may not be so from the patient's point of view.

CONCLUSION :

Satisfaction trends in any health care setup will have its ups & downs but we should strive for an overall upswing trend. Quality is not static; it is linear and should be ascending. We need to improve ourselves continuously. A clinician should be caring and concerned. The qualities which can help the clinician in becoming so are attentiveness, effective communication, dignity and respect for the patient and shared decision making. Sir William Osler's words "Listening is unspoken caring" are of paramount importance in living up to a patient's expectation.

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Case Report

Takayasu's Arteritis - An Unusual Presentation

R. K. Kotokey[*], S. Kar[**], L. Bathari[***], K. B. Singh[***]

Abstract

Takayasu's arteritis (TA) is a chronic idiopathic vasculitis that variably involves the aorta and/or its main branches and the coronary and pulmonary arteries in 50–80%[1].The main pathology is the fibrosis in major arteries that results in obstruction. It is interesting to note that Takayasu's arteritis is sometimes present with aneurysm of the great arteries.

KEY WORDS : *Takayasu's arteritis(TA), Carotid aneurysm, macaroni sign.*

INTRODUCTION :

Takayasu's arteritis : Takayasu's arteritis is a rare inflammatory disease that often affects the ascending aorta and aortic arch, causing obstruction of the aorta and its major arteries. These includes the subclavian arteries that supply the arms, renal arteries to the kidneys, coronary arteries in the heart and carotid arteries in the head and brain. Because of its predilection for the brachiocephalic vessels, this arteritis has been labeled *pulseless disease* and *aortic arch syndrome*. The cause of Takayasu's arteritis, and why an individual develops the disease at any one time remains unknown. The disease is most likely to be the consequence of environmental factors and a susceptible genetic background. One common but unproven hypothesis is that it is precipitated by an infection. Identification of endothelial antibodies in 18 of 19 patients with this disease supports an autoimmune mechanism. Histologic examination during active stages of the disease discloses a granulomatous arteritis. In later stages, medial degeneration, fibrous scarring, intimal proliferation, and thrombosis results in narrowing of the vessel. Aneurysm formation is less common than stenosis, but aneurysm rupture is an important cause of death in patients with Takayasu arteritis. During the early or "prepulseless" phase, symptoms include fever, night sweats, malaise, nausea, vomiting, weight loss, rash, arthralgia, and Raynauds phenomenon. Splenomegaly may occur and laboratory findings may include acceleration of the erythrocyte sedimentation rate, elevated levels of C-reactive protein, anemia, and plasma protein abnormalities. Once arterial obstruction develops, upper-extremity claudication may occur as a consequence of subclavian artery stenosis. Stroke, transient cerebral ischemia, dizziness, or syncope usually indicates narrowing of the brachiocephalic arteries or subclavian steal. Cardiac manifestations result from severe hypertension, dilatation of the aortic root producing valvular insufficiency, or coronary artery stenosis.

Here we are reporting a case of Takayasu's ateritis , presented with carotid aneurysm.

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CASE REPORT

Brief History : A 35 year female presented with repeated episodes of transient loss of consciousness associated with headache, palpitation and easy fatigability. She also complained of a gradually progressive painful, pulsatile swelling on right side of the neck. She also complained of numbness of both the upper limbs and also had difficulty when working with hands. The complaints were gradually increasing in intensity during the last 9 months for which she attended the hospital.

Fig.1. Pulsatile neck swelling

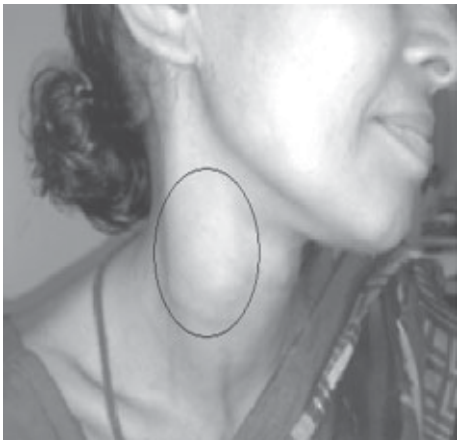
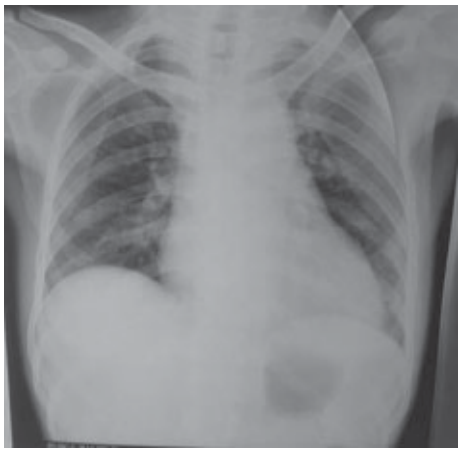


Fig.2. Chest X-ray



ON GENERAL EXAMINATION :

Patient was found to be afebrile; pallor was present; cyanosis, clubbing, oedema and lymphadenopathy were absent. Respiratory rate was 18/min, regular in rhythm. *Pulse was not palpable in both upper limbs,* but the peripheral pulses of both lower limbs was palpable. The rate was 90/min, regular, high in volume, normal in rhythm and character. Temporal arteries were normally palpable. *Blood pressure was not recordable in both upper limbs. But in the right lower limb the BP was 250/50 mmHg and 240/40 mmHg in the left lower limb.*

A 5 cm x 3 cm tender, firm, pulsatile swelling with thrill and bruit was present on upper one-third of the right sternocleidomastoid. Bruit was also present over the left common carotid artery.

On systemic examination, CNS, CVS and respiratory system were normal. There was cardiomegaly of left ventricular type. Abdominal examination revealed thrill and bruit over abdominal aorta.

INVESTIGATIONS :

Hb-5% ; ESR-55 AEFH ; TC-8400 ; DLC-$N_{70}E_1B_0L_{25}M_4$; RBS-91 mg/dl; Urea-13.4 mg/dl ; Creatinine-0.3 mg/dl ; T_3-0.82 ng/ml ; T_4-55 ng/l ; TSH-2.0 mIU/ml ; VDRL-non reactive ; Montoux test-negative ; Urine examination-NAD.

CXR - Aorta appears prominent, prominent bronchovascular markings, mild cardiomegaly.

USG Abdomen - Normal

Echocadiography - Global hypokinesia, moderate LV systolic dysfunction.

USG Doppler - Concentric diffuse thickening of the vessel wall with luminal narrowing (*Macaroni sign)* noted in bilateral common carotid, bilateral subclavian, visualized portion of the aortic arch and left internal carotid artery with an aneurysm in the right common carotid. Increased flow velocity noted in bilateral common carotid arteries with dampening of flow in the internal carotid artery. There was no renal artery stenosis.

Fig.3.Concentric diffuse thickening of the vessel wall Fig.4. Right common carotid arterial wall thickening with luminal narrowing (Macaroni sign)

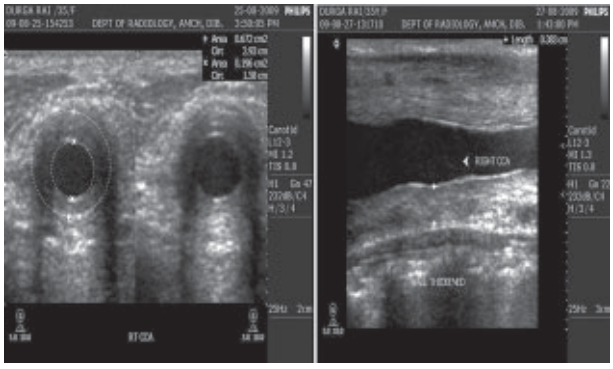
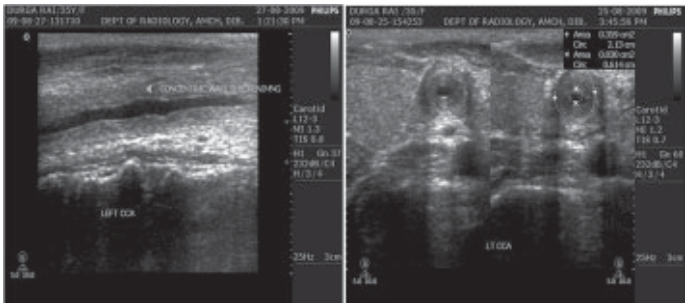


Fig.5. Left common carotid arterial wall thickening Fig.6. Concentric diffuse thickening of the vessel wall with luminal narrowing (Macaroni sign)



DISCUSSION :

The first report of TA was by Yamamoto R in 1830, while the first presentation on TA was in 1905 by Mikito Takayasu at the 12th annual meeting of the Japan Ophthalmology Society, describing a patient with a peculiar optic fundus abnormality, characterised by coronal anastomoses[2]. Ohnishi K and Kagoshima T also presented similar cases and noted their patients lacked a palpable radial pulse[2]. The first autopsy on a patient with TA was carried out in 1940 by Ohta K[3].

The classic form occurs with greatest frequency in Asian countries, but patients with a similar nonspecific aortitis are encountered worldwide. In 70 to 80 percent of cases, clinical manifestations of the illness appear during the second or third decade of life, but onset in childhood and in middle life have also been reported. Women are affected eight to nine times more often than men. The etiology is unknown; no infectious agent has been identified, and identification of endothelial antibodies in 18 of 19 patients with this disease supports an autoimmune mechanism[4]. Takayasu arteritis is the commonest cause of renovascular hypertension in India[5].

Aneurysm formation is less common than stenosis, but aneurysm rupture is an important cause of death in patients with Takayasu arteritis. Angiographically, the left subclavian artery is narrowed in approximately 90 percent of patients. The right subclavian artery, left carotid artery, and brachiocephalic trunk follow closely in frequency of stenosis. Thoracic aortic lesions occur in 66 percent of patients, the abdominal aorta is involved in 50 percent, and aortoiliac involvement is seen in approximately 12 percent. Pulmonary arteritis occurs in about half the patients and may be associated with pulmonary hypertension[4].

According to the vessels involved, the most recently proposed angiographic classification divides TA into six types[6,7]. Type I involves only the branches of the aortic arch. Type IIa involves ascending aorta, aortic arch and its branches. Type IIb affects ascending aorta, aortic arch and its branches, and thoracic descending aorta. Type III involves the descending thoracic aorta, the abdominal aorta and/or the renal arteries. The ascending aorta, the aortic arch and its branches are not affected. Type IV involves only the abdominal aorta and/or renal arteries. Type V has combined features of Type IIb and IV. In a study by Hata et al., Japanese patients showed higher frequency of involvement of the ascending aorta and its branches than the Indian in whom the frequency of involvement of the abdominal aorta and/or renal arteries was higher[6].

The American College of Rheumatology has identified six major criteria for the diagnosis of Takayasu arteritis[8]. Onset of illness by age 40 years avoids overlap with giant cell arteritis. Other criteria include upper-extremity claudication, diminished brachial pulses, greater than 10 mmHg difference between systolic blood pressure in the arms, subclavian or aortic bruit, and narrowing of the aorta or a major branch. The presence of three of these six criteria carries high diagnostic accuracy.

Corticosteroid therapy appears effective in suppressing inflammation during the active phase, and favorable results have been reported with immunosuppressive and cytotoxic agents[8]. Operative treatment may be employed to relieve symptoms caused by arterial obstruction, and percutaneous angioplasty and stenting are associated with favorable results. These procedures are best reserved for patients in whom the acute inflammatory stage of the disease has been controlled[9].

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Case Report

Adrenocortical Carcinoma A Rare Cause of Ectopic ACTH Syndrome

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Abstract

Adrenocortical carcinoma (ACC) is a rare but important cause of Adrenocorticotrophic hormone (ACTH) independent Cushing's syndrome. The plasma ACTH level in these patients is usually low or undetectable. Paradoxically, plasma ACTH level has been found to be elevated, rather than being suppressed, in a few cases of ACC with Cushing's syndrome. We report a 10 year old boy who presented to us with Cushing's syndrome, hyperpigmentation and high plasma ACTH levels. Complete workup of the patient revealed a left sided ACC. Further imaging studies failed to localise any additional pituitary or an ectopic source of ACTH. Immunohistochemistry following partial excision of the tumour, was positive for ACTH. This case report highlights the fact that an elevated plasma ACTH can be found in patients with Cushing's syndrome due to an adrenocortical tumour. Adrenocortical carcinomas can thus be added to the list of rare causes of ectopic ACTH syndrome.

***KEYWORDS**: Adrenocortical Carcinoma, Acth, Ectopic Acth Syndrome.*

INTRODUCTION :

Adrenocortical carcinoma (ACC) is not a common entity. If the definition of a rare disease as proposed by the" National Institutes Of Health Office Of Rare Diseases Research" is followed , which means a prevalence of fewer than 200000 affected patients, then ACC becomes an even rarer one[1].

The tumours are aggressive with a high mortality rate. Adreonocortical carcinomas are functional in 80% cases, secreting glucocorticoid alone in 45%, glucocorticoid and androgens in 45%, or androgens alone in 10% cases[2]. 10% of adult cases of Cushing's syndrome are due to ACC[3]. However in children, 50% cases of Cushing's syndrome can be attributed to ACC[2]. Therefore ACCs are rare but important cause of ACTH independent Cushing's syndrome. It is therefore expected that the plasma ACTH level in these patients will be low or undetectable. Paradoxically, plasma ACTH level has been found to be elevated rather than being suppressed in a few cases of ACC with Cushing's syndrome[4,5]. We report a similar case of ACC presenting as Cushing's syndrome with inappropriately elevated plasma ACTH.

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CASE REPORT :

A 10 year old boy presented with a history of progressive weight gain and recurrent episodes of abdominal pain for 4 months. Patient did not have any other remarkable present or past history. Examination revealed a Cushingoid habitus, facial plethora, striae and hyperpigmentation without a palpable abdominal lump. The patient was hypertensive. His height was 135 cm (50^{th} – 75^{th} percentile) and weight was 32 kg (75^{th} – 97^{th} percentile). Sexual maturity rating was pre pubertal.

Investigations (TABLE 1) revealed a high serum cortisol level (morning 8 am - 45.1µg/dL, midnight-49.2 µg/dL) which was non suppressible after a 48 hour low dose dexamethasone suppression test (>50 µg/dL). 24 hour urinary free cortisol was 4334.2 µg (28.5-213.7 µg /day). Plasma ACTH was high (95.2 pg/mL).

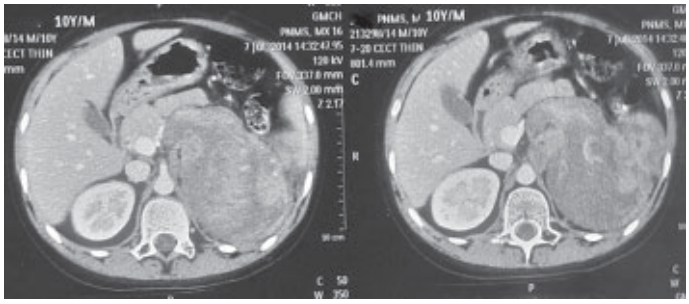
Table 1. Hormonal Investigations of the Patient

Assay	Result	Reference Range
Cortisol Morning(µg/dL)	45.1	5 -25
Cortisol Midnight (µg/dL)	49.2	< 7.5
Cortisol Post LDDST*(µg/dL)	>50	< 1.8
24hr Urinary Cortisol (µg /day)	4334.2	28.5-213.7
ACTH (pg/mL)	95.2	10 – 46
DHEAS (µg/dL)	412	80-560
24hr Urinary Metanephrine (µg /Day)	89.5	25-312
**48 Hour Low Dose Dexamethasone Suppression Test*		

Dehydroepiandrosterone sulfate (DHEAS) was 412 µg/dL (80-560 µg/dL) and 24 urinary metanephrine was 89.5 µg (25-312 µg).Thyroid function tests were within normal limits. Liver function and renal function tests were normal. His bone age was 10.8 years.

In view of the presenting complaint of pain abdomen an ultrasonography of abdomen was done which revealed a well defined solid mass lesion in the left suprarenal region (9.6x7.8 cm). Computed Tomography(CT) scan abdomen (Figure 1) showed a large (9.1x10.2x6 cm) fairly well

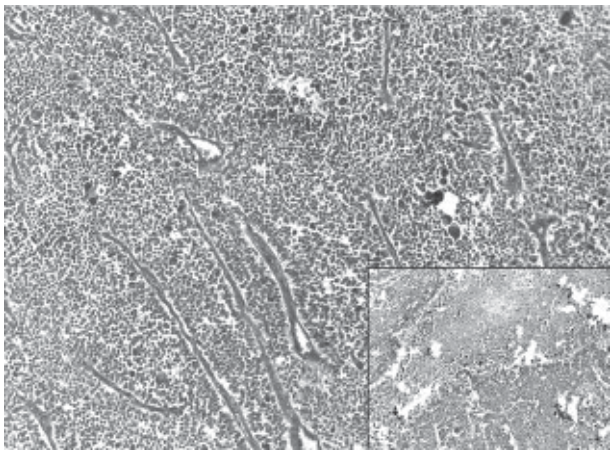
Figure 1. Contrast Enhanced CT Scan Abdomen Showing A Large Fairly Well Defined Lobulated Heterogeneously Enhancing Mass Lesion Arising From Left Adrenal Gland



defined lobulated heterogeneously enhancing mass lesion arising from left adrenal with internal haemorrhage along with enlarged and necrotic mesenteric lymph nodes and perilesional fat stranding. It had a density of 70 – 90 HU on plain scan. On post contrast study, the absolute and relative washout volume was 32 % and 21% respectively suggestive of adrenal carcinoma. The right adrenal gland was normal. In view of the high plasma ACTH a Magnetic Resonance Imaging (MRI) of the sella was done and it was found to be normal. Chest X Ray and CT scan of the thorax failed to detect any ectopic source of ACTH.

Patient was subsequently referred to the surgeon and he underwent left adrenalectomy with para aortic lymphadenectomy. The tumour was highly friable and was removed in piece meal. Lymph nodes measuring 1.5 – 2cm size seen anterior to the aorta were removed.

Figure 2. Photomicrographs from the Tumour Showing Sheets of Malignant Cells Exhibiting Diffuse Growth, Nuclear Pleomorphism, Hyperchromasia and Necrosis (Inset).



On gross examination, the external surface of the tumour was variegated with areas of necrosis. Microscopic examination (Figure 2) revealed tumour cells arranged in sheets and trabeculae separated by thin fibrovascular bands. The cells were polygonal, having moderate amount of eosinophilic cytoplasm, round to oval nuclei with coarse clumped chromatin and prominent nucleoli. There was marked anisonucleosis. Many tumour giant cells were seen. Few bizarre nuclei were noted at few places. Mitotic activity was brisk (Ã30/10 hpf). Large areas of coagulative tumour necrosis were seen. The findings were consistent with Adrenocortical carcinoma.

Immunohistochemistry (IHC) of the tumour for ACTH was done in view of high plasma ACTH, and for Chromogranin A, to exclude pheochromocytoma cosecreting ACTH. IHC was positive for ACTH (Figure 3) and negative for Chromogranin A (Figure 4) and hence a diagnosis of ACTH secreting ACC was made.

Figure 3. Immunohistochemistry of the Tumour Positive for Acth

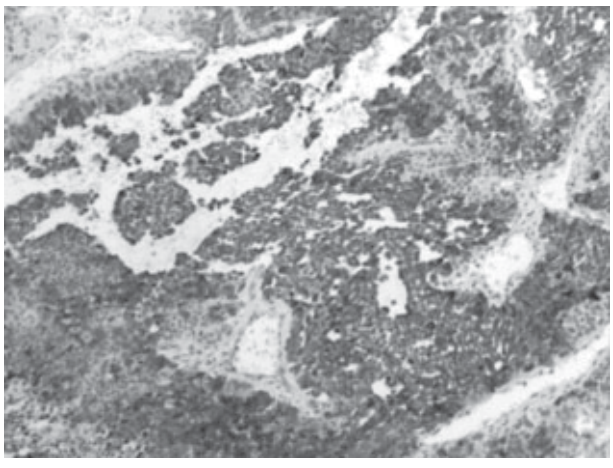
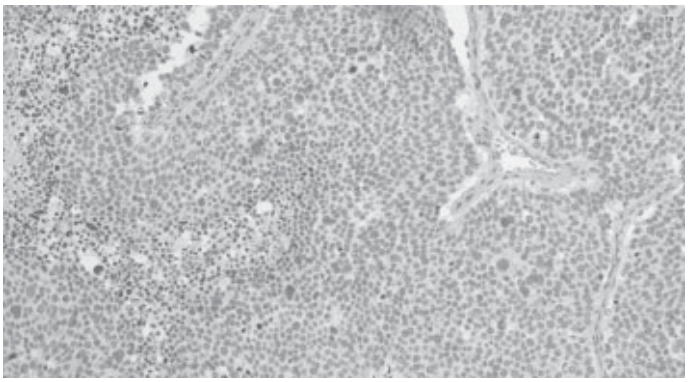


Figure 4. Immunohistochemistry of the Tumour Negative for Chromogranin A



The patient was referred to an oncology centre for further management. He succumbed to his illness 6 months later.

DISCUSSION :

Adrenocortical carcinoma is a rare disease with a high mortality rate. The median age of diagnosis is in the fifth to sixth decade[1]. The disease has a bimodal distribution with a childhood and a middle age peak. The early childhood peak is suggested from ACC being 1.3% of all childhood malignancies[1]. On the other hand the median age of the adult peak is reported as 46 years by the German registry and French data[6,7].

Patients with ACC may present with features of either hormone excess or with clinical manifestations of local tumour growth, such as abdominal pain or fullness of abdomen[1]. Around 20% to 30% of ACCs are diagnosed incidentally by imaging procedures[8]. 50%–80% of patients presenting with hormone excess have hypercortisolism and manifest as classical Cushing's syndrome[1]. Adrenal androgens are the second most commonly produced hormones in patients with ACC accounting for 40% –60% of hormone producing ACCs. Adrenocortical carcinomas are therefore rare but an important cause of ACTH independent Cushing's syndrome. Our patient had features of hypercortisolism alone without any evidence of androgen excess.

The presence of skin pigmentation in a patient of Cushing's syndrome is suggestive of an ACTH dependent cause and is concurrently associated with an elevated plasma ACTH level. It may be due to Cushing's disease but is more commonly seen in the ectopic ACTH syndrome[2]. The present child did not show any radiological evidence of a pituitary or ectopic source of ACTH. Elevated or normal plasma ACTH in a patient of ACC with Cushing's syndrome has been rarely reported in literature[4,5,9,10] and leads to a diagnostic dilemma as in our case.

Law A et al[4], has reported inappropriate ACTH concentrations in two female patients with functioning ACC. The first patient was a 19 year old girl who presented with secondary amenorrhoea, hirsutism, hypertension and Cushing's stigmata. There was no skin pigmentation. Cortisol, androgens, mineralocorticoid were elevated in both plasma and urine. Plasma ACTH concentration were found to be high (8 AM – 51ng/L; 12 AM – 25 ng/L). Abdominal computed tomography (CT) scan revealed a large right ACC. Chest and skull X rays were normal. High resolution CT scan of pituitary was also normal. The patient was treated medically as surgical resection was not possible due to invasion of the liver and vena cava. The patient died after 3 months.

The second patient reported by Law A et al[4] was a 74 year old woman presenting with Cushing's syndrome without skin pigmentation. The patient's plasma and urinary cortisol were elevated and were not suppressed after dexamethasone (8 mg/ day for 48 hours). Plasma ACTH levels were not suppressed (8 AM – 58ng/L; 12 AM – 24 ng/L). High resolution CT scan of the pituitary fossa was normal. Abdominal CT scan revealed a large left adrenocortical tumour which after resection and histological examination was suggestive of ACC. IHC of the tumour was negative for ACTH.

The presence of ACTH in plasma of Cushing's syndrome due to adrenocortical tumours is extremely rare. Law A et al[4] has put forward a number of hypothesis for this paradoxical observation – i) ACTH may be secreted by the adrenal tumour itself; ii) there may be a concurrent source of ectopic ACTH; iii) there may be a concurrent ACTH producing pituitary tumour; iv) there may be other steroids secreted by the adrenal tumour which may block the negative feedback effect of cortisol on pituitary and hypothalamus; v) there may be an abnormality in the cortisol receptor in the pituitary or hypothalamus.

Pollardo L F et al[5] in 1981 have reported a case of adrenal carcinoma producing ectopic ACTH. Bevan and Burke[9] have reported a case of adrenal carcinoma causing Cushing's syndrome with normal plasma ACTH levels. The patient was found to have an ACTH secreting bronchial neoplasm at autopsy. Anderson et al[10] had

described a patient of virilizing adrenal carcinoma with Cushing's syndrome and detectable ACTH levels. The contralateral adrenal of the patient had nodular hyperplasia and on autopsy a 5 mm pituitary basophil adenoma was detected.

Our patient had skin hyperpigmentation, which was absent in the two patients described by Law A et al[4]. He had a very ACTH level (95.2pg/ml) which is usually found in patients with ectopic ACTH syndrome[2]. Pheochromocytomas are known to cause ectopic ACTH syndrome[2]. Our patient did not have the typical pheochromocytoma spells, his urinary metanephrines were not elevated and the IHC of the tumour was negative for Chromogranin A. Hence a possibility of a pheochromocytoma co-secreting ACTH was ruled out. Imaging studies in this patient did not reveal a second tumour that might secrete ACTH. A concomitant pituitary tumour was not detected by the MRI of the sella. The source of the ectopic ACTH in our patient was the adrenocortical carcinoma itself as detected by the positive immunohistochemical staining of the tumour.

CONCLUSION :

This case report highlights the fact that an elevated plasma ACTH can be found in patients with Cushing's syndrome due to an adrenocortical tumour. Adrenocortical carcinomas can thus be added to the list of rare causes of ectopic ACTH syndrome.

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Case Report

Overlap Syndrome with Autoimmune Hepatitis and Primary Biliary Cirrhosis- an Uncommon Entity in Northeast India

N. Gogoi*, S. Islam, A. J. Talukdar**, S. Dutta*****

Abstract

The concurrent presence of main characteristics of two autoimmune conditions affecting the liver at the same time or during the course of illness is generally the basis for defining an overlap syndrome. Here we report two female patients aged 34 and 42 year old with clinical, biochemical and serological features consistent with diagnosis of overlap syndrome, who were put on ursodeoxycholic acid with steroids and showed gradual improvement.

KEY WORDS: *Primary biliary cirrhosis (PBC),Autoimmune hepatitis(AIH),Overlap syndrome(OS).*

INTRODUCTION :

OS is a condition in which patients had hepatitis of autoimmune etiology and also meet the clinical and histological criteria for PBC or PSC. The AIH-PBC combination is more common in adults, whereas the AIH-PSC overlap usually occurs in children, adolescents, and young adults[1]. OS mainly affects women belonging the age group of 50 to 60 years of age.

Clinical presentation of OS depends on predominant component of disease and is characterized by symptoms of pruritus, jaundice and fatigue, which in most cases are present from the onset. Other nonspecific symptoms such as arthralgia and myalgia are also present in this syndrome(1). Serum liver function typically shows mixed pattern of hepatitic and cholestatic features[2].

CASE SUMMARY:

CASE 1 : A 34 year old female hypertensive, non diabetic, non alcoholic presented with complaints of skin lesion of both the legs over the dorsum of foot for last 4 years and yellowish discolouration of sclera, generalised itching, pain abdomen on and off for last 2 year.

On examination her BP was 160/90,pulse 78/min, pallor and icterus was present. On abdomen examination hepatomegaly of >3cm below subcostal margin, firm, regular margin with tenderness with mild splenomegaly. Other systems were within normal limit.

On investigations RE blood showed HGB of 11gm/dl ,TLC 11.39 and platelet count of 378×10^3 and deranged LFT of AST/ALT 184/158and ALKP 1605, Albumin 3.7, total bilirubin 6.10, conj. 1.83, unconj.1.02, delta bil.3.25.

Viral markers for hepatitis A/B/C/E were negative.

She was on treatment with UDCA 300mg twice daily but her bilirubin and liver enzymes didn't show any improvement.

After further evaluation we found her antinuclear antibody(ANA) to be positive in 1:1000 titre and anti-mitochondrial antibody(AMA) to be positive in 1:100 titres ,serum total IGG was 27.20(6.5-13), MRCP findings were consistent with acute hepatitis with no obvious biliary obstruction.

She was treated as overlap syndrome with ursodeoxycholic acid 300mg twice daily and Prednisolone 40mg once daily.

CASE 2 : A 42 years old female hypertensive, non-diabetic, non-smoker, non-alcoholic presented with complains of skin discoloration for last 4 years, which

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initially started distally and then gradually involved the whole part of the body. It was associated with generalised itching followed by gradual tightening and was diagnosed to be a case of scleroderma with systemic hypertension. She developed jaundice 1 year before admission.

On examination her BP was high 180/100 mmHg with pulse rate of 86/min with icterus and pallor with hepatomegaly of 2cm below subcostal margin, firm ,regular margin and non tender and splenomegaly of 1cm below the subcostal margin, firm with prominent splenic notch.

On investigations RE blood showed Hb 9.3, TLC 5.9 and Platelet count 255×10^3 and deranged LFT of AST /ALT 165/156, ALKP 732, T.bil 3.8 Con. 1.1, Uncon.0.6, were persistent high for 1 year.

Viral markers were negative for hepatitis A/B/C/E.

She was on treatment with ursodeoxycholic acid 300mg twice daily for last 1 year but her bilirubin and liver enzymes were persistent high.

After further evaluation we found her ANA to be positive in 1:1000 titres and AMA to be positive in 1:100 titres ,total IGG was 26(6.5-13)and SCL- 70 positive with skin biopsy reveals scleroderma. MRCP suggestive of acute hepatitis with no obvious biliary pathology.

Then she was treated as OS with limited scleroderma and was started with UDCA 15mg/kg/day and low dose steroid 10mg/day.

DISCUSSION:

Patients with autoimmune liver disease present with a clinical, serological and histological picture showing characteristic findings of both AIH and PBC are labelled as OS.

Hepatic function tests show a mixed pattern with the presence of cytolysis (increased AST/ALT) and cholestasis (increased ALKP), while histological findings of interface hepatitis with florid bile duct lesions.

AIH criteria

1. ALT five times above its upper limit
2. IgG twice its normal level, or ANA/ ASMA should be present
3. Hepatic biopsy should show necrosis at the interface.

PBC criteria

1. ALKP of twice their normal levels and/or GGT at least five times the normal upper limit.
2. Positive for AMA
3. Hepatic biopsy should show biliary duct lesions.

PBC-AIH overlap syndrome: both 2 out of 3 PBC criteria are met and 2 out of 3 AIH criteria are met either simultaneously or consecutively.

	Case 1	Case2	
SEROLOGICAL			**Normal ranges**
AIH criteria			
1.ALT	>5 times(158)	>5times(156)	5-30 U/L
2.ANA	Positive (1:1000)	Positive (1:1000)	
3.IGG	>2times(27.2)	>2times(26)	6.5-13
PBC criteria			
1.ALKP	>13times(1605)	>6times(732)	38-120
2.AMA	Positive 1:100	Positive 1:100	
HISTOLOGICAL			
AIH criteria	Not done	Not done	Interface hepatitis
PBC criteria	Not done	Not done	Florid bile duct lesion

Table 1 : Paris criteria to define OS (Journal of hepatology 1998)

AIH criteria

4. ALT five times above its upper limit
5. IgG twice its normal level, or ANA/ ASMA should be present
6. Hepatic biopsy should show necrosis at the interface.

PBC criteria

4. ALKP of twice their normal levels and/or GGT at least five times the normal upper limit.
5. Positive for AMA
6. Hepatic biopsy should show biliary duct lesions .

PBC-AIH overlap syndrome: both 2 out of 3 PBC criteria are met and 2 out of 3 AIH criteria are met either simultaneously of consecutively.

	Case 1	Case2	
SEROLOGICAL			Normal ranges
AIH criteria			
1.ALT	>5 times(158)	>5times(156)	5-30 U/L
2.ANA	Positive (1:1000)	Positive (1:1000)	
3.IGG	>2times(27.2)	>2times(26)	6.5-13
PBC criteria			
1.ALKP	>13times(1605)	>6times(732)	38-120
2.AMA	Positive 1:100	Positive 1:100	
HISTOLOGICAL			
AIH criteria	Not done	Not done	Interface hepatitis
PBC criteria	Not done	Not done	Florid bile duct lesion

Most authors use the criteria established by Chazouilleres et al. (Journal of hepatology 1998)[3,4] to define OS also known as Paris criteria.

With reference to the above diagnostic criteria for OS, both our 2 cases met these diagnostic criteria for both conditions, thus labelled as OS.

Due to prolonged prothrombin time and poor general condition of both the patient liver biopsy was not done which was the drawback of our study.

Recommendations for the treatment of PBC–AIH overlap syndrome have not yet been standardized owing to the low prevalence of this autoimmune liver disease.

Because no randomized controlled therapeutic trials have been carried out so far, recommendations for treating PBC– AIH overlap syndrome are usually based on the methods used to treat the two main autoimmune liver diseases separately.

It is appropriate to start treatment with UDCA (13-15 mg/kg daily). However, if this therapy does not induce

an adequate biochemical response (decrease AST/ALT)in an appropriate time span of 3 months[5] or in patients with predominantly hepatitic serum liver tests, a corticosteroid should be added.

Liver transplantation is regarded as the treatment of choice for end-stage disease.

On the basis of fulfilling the above criteria both of our patients were diagnosed as OS. Case 1 was started with oral Prednisolone 40 mg once daily with Ursodeoxycholic acid 300mg twice daily. After 1 week of therapy she responded well and her AST/ALT ,ALKP were significantly dropped down to 138/113,1285 .Her liver enzymes were in decreasing pattern and at the end of 1st and 3rd month AST/ALT,ALKP were 98/80,900 and 57/40,540 respectively.

Case 2 was also started with low dose Prednisolone of 10mg once daily due to concomitant limited scleroderma of patient with ursodeoxycholic acid 300mg twice daily. She also responded well and on follow up with good results. Her AST/ALT, ALKP at the end of 1st and 3rd month were 95/86,640 and 76/58,356 respectively.

CONCLUSION :

Overlap syndrome is a rare entity whose frequency ranges from 7% to 18% among the autoimmune hepatic disorder[6]. These type of patients present as hepatitis with features of cholestasis and serological markers for AIH and PBC being present, respond better with combination with corticosteroids and UDCA and should be progressively tapered once ALT levels show a response.

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Case Report

Cutaneous involvement in lymphoma: A diagnostic clue

A. Jain[*], P. K. Doley[**], S. Prasad[*], A. Pandey[*]

Abstract

Cutaneous manifeststions of leukemia/ lymphomas are classified into Specific (infiltrates of leukemic cells) or Nonspecific (inflammatory, paraneoplastic, or secondary to marrow failure). These are important diagnostic clues and direct infiltration of malignant cells may be a bad prognostic marker. Integration of different diagnostic parameters, including immunohistochemistry (IHC) is essential to diagnose rare subtypes of lymphomas for which no definitive diagnostic criteria are available. Angioimmunoblastic T cell lymphoma (AITL) is a rare subtype of peripheral T-cell lymphoma, first described as a distinct clinicopathologic entity in the 1970s. AITL accounts for approximately 1% to 2% of non-Hodgkin's lymphoma. Typically, the architecture of the lymph node is effaced with perinodal extension of atypical cells and a proliferation of high endothelial venules. The neoplastic T cells are positive for CD2, CD3, CD4, CD10, CXCL-13, PD1, and often BCL-6. Cutaneous infiltration of AITL is confirmed by IHC of skin biopsy specimen. Here we are discussing an interesting case of a fifty year old male, who presented with complaints of high grade fever and rash on upper extremities, ultimately diagnosed as having AITL with cutaneous involvement.

KEYWORDS: *Angioimmunoblastic, immunohistochemistry, lymphoma, rash.*

CASE REPORT :

A fifty years old man was presented to our hospital with complaints of fever (on and off, high grade) for 2 months and generalized rash for 1 month. Physical examination revealed erythematous, itchy, maculopapular rash, confluenting at many places predominantly on upper extremities **(Figure1)**. Generalized lymphadenopathy was noted - B/L cervical, left axillary (medial group), B/L Inguinal lymph nodes which were firm, non tender, 1-2 cm in size, mobile, non matted. Abdominal examination was noteworthy for shifting dullness. Rest systems examination appeared to be normal. Differential diagnosis kept were as follows: tuberculosis with drug eruption, lymphoma / leukemia cutis, HIV with opportunistic infection, autoimmune vasculitis.

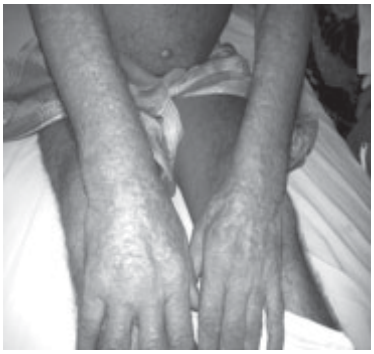

Figure 1: Erythematous, maculopapular rash predominantly on upper extremities

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On investigation hemoglobin was 11.2g/dL, Total and differential counts, platelets, peripheral blood film, renal and liver profile, lactate dehydrogenase, thoracic roentgenogram was within normal limits. HIV test was negative. Abdominal sonography showed mild splenomegaly and ascites. Ascitic fluid was low SAAG (serum ascitic albumin gradient) with 1019 cells/ml and 88% lymphocytes. Ascitic fluid was negative for malignant cells. Patient did not consent for lymphnode biopsy, however skin biopsy could be done, and he was discharged on request. He presented ten days later again with high grade fever and skin biopsy reports were available, which revealed dense perivascular and periadnexal, superficial and deep lymphohistiocytic infiltrates which was positive for CD3 and CD4 **(Figure2)**.

This time patient agreed for cervical lymph node biopsy which showed effacement of lymph node by

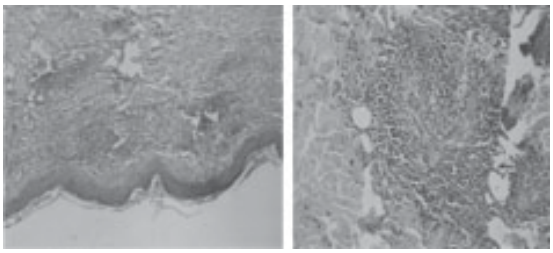

Figure 2: Skin biopsy showing dense perivascular and periadnexal, superficial and deep lymphohistiocytic infiltrates

variable sized atypical lymphoid cells, perinodal extension of atypical cells and proliferation of high endothelial venules. Immunohistochemistry showed neoplastic T cells were positive for CD3, CD4, CD10, CD30, and BCL-6 **(Figure3)**. Epstein Barr Virus encoded RNA (EBER) was

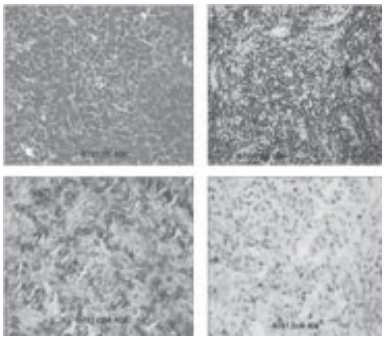

Figure 3: Lymphnode biopsy and immnohistochemistry : Effacement of lymph node by variable sized atypical lymphoid cells and proliferation of high endothelial venules, Immunohistochemistry showed neoplastic T cells were positive for CD3, CD4, CD10, CD30, and BCL-6.

positive. Bone marrow examination was normal. Computed tomography of thorax showed mediastinal and pretracheal and cervical lymphadenopthy. Final diagnosis of angioimmunoblastic T cell lymphoma (AITL) was made.

AITL accounts for approximately 1% to 2% of non-Hodgkin's lymphoma. In 1974, *Frizzera et al.* described AITL as a reactive lymphoproliferative disorder of T lymphocytes[1]. In 2001, the WHO classification of tumors of hematopoietic and lymphoid tissue listed AITL as a peripheral T-cell lymphoma.[2] Most patients with AITL are elderly; the median age of patients is older than 60 years, and the disease shows a male predominance[5]. At the time of diagnosis, almost all patients present with advanced-stage disease[3]. Cutaneous lesions vary widely and can be encountered in approximately half of the cases, presenting as a nonspecific rash, usually macules and papules, and less commonly purpura, urticaria, nodules or petechiae. A primary monoclonal and polyclonal T-cell proliferation secondary to Epstein-Barr virus infection has also been suggested[4]. Typically, the architecture of the lymph node is effaced with perinodal extension of atypical cells and a proliferation of high endothelial venules. The neoplastic T cells are positive for CD2, CD3, CD4, CD10, CXCL-13, PD1, and often BCL-6. Over expression of the chemokine CXCL13 and vascular endothelial growth factor-A in angioimmunoblastic T-cell lymphoma suggests that it may be derived from follicular helper T cells[6]. However CXCL13 was not done in this case. AITL has a moderately aggressive course, with occasional spontaneous remissions or protracted responses to therapy. The median survival is 24 months. The combination of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) has been used before or after prednisone and with or without interferon-a as consolidation. In retrospective analyses, CHOP and CHOP-based regimens have produced complete remission rates of about 60%[7]. Rodríguez et al described prolonged survival for patients with angioimmunoblastic T-cell lymphoma after high-dose chemotherapy and autologous stem cell transplantation[8]. The diagnosis of AITL is very challenging, given the lack of definitive diagnostic criteria. This case underscores the diagnostic challenges of AITL and illustrates the requirement for careful clinical evaluation and prompt integration of different diagnostic parameters.

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Case Report

USG Scrotum as an Important Investigating Tool for Lymphatic Filariasis

B. Thakuria[**], S. K. Baruah[*], P. Hatimota[***], S. Mitra[****], D. Raja[*****]

Abstract

A 58 year male patient with recurrent left leg and ankle swelling with redness was diagnosed to have filarial lymphangitis. The purpose of presenting this case is to highlight the importance of scrotal USG as a useful investigating tool in patients with suspected filarial lymphangitis, without scrotal swelling and with negative filarial antigen and DEC provocation tests.

KEY WORDS : *lymphangitis, DEC provocation.*

INTRODUCTION :

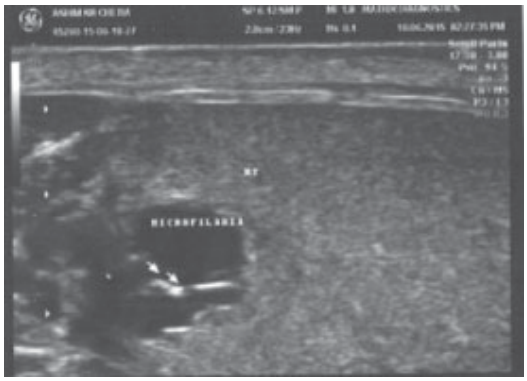
Lymphatic filariasis is an infrequently occurring condition with varied onset and clinical presentation. In 1997, it was estimated that at least 128 million individuals were infected with filarial parasites (115 million with *W. bancrofti* and 13 million with the *Brugia* spp.).[1] Most of these infections were in India (48 million) and sub-Saharan Africa (51 million). We are reporting a case of lymphatic filariasis which was diagnosed only by high resolution ultrasonography of scrotum. This proved as a very useful method of investigation as this patient had no scrotal swelling and other filarial tests were negative. Very few such cases have been reported so far.

CASE HISTORY :

A 58 year old male patient presented to us with recurrent cellulitis and swelling of left leg and ankle for 4 months. It was insidious in onset and gradually progressive. The swelling started in left inguinal region and gradually progressed from above downwards.

General examination of patient revealed non pitting edema of left leg and inguinal lymphadenopathy. His external genitalia were clinically normal. Systemic examination was also within normal limit.

Investigation: Routine examination of blood and biochemical profile were essentially normal. Doppler ultrasound of lower limb vessels was normal. Filarial antigen tests were negative. Diethylcarbamazine (DEC) provocation test was also done but it showed no microfilaria in blood after half an hour of DEC provocation. In view of recurrent cellulitis with above downward progression, there was high clinical suspicion of filarial lymphangitis; therefore, with no other options left to establish the diagnosis, high resolution ultrasonography (HRUSG) of scrotum was carried out on experimental basis, which showed presence of microfilaria in it and the diagnosis of filariasis was thus confirmed (fig)



Management: Patient was treated with DEC 6mg/kg body weight for 3 weeks and Tab Clindamycin 300mg 8 hourly for 7 days in view of superadded cellulitis, along with compression stockings for resolution of edema. At

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six months follow up, the patient is completely cured with near total resolution of the edema as well.

DISCUSSION :

Lymphatic filariasis is a deforming disease caused by the filarial nematode *Wuchereria bancrofti.* This parasite infestsabout 100 million people in many countries in the tropics and subtropics[2,3]. Approximately 10–30% of those infesteddevelop overt clinical disease (mainly hydroceles and/or lymphedema that can progress to elephantiasis). However,recent studies have shown that asymptomatic infestations are often associated with subclinical disease including lymphaticdamage demonstrable by lymphscintigraphy and nephritis manifested by proteinuria and hematuria[3,4].

Amaral and others have recently reported visualization of adult *W. bancrofti* in scrota of infected men by ultrasound[5].They reported that adult filarial worms are often found in dilated lymphatics in the scrotum and showedthat the location of worm nests in lymphatic vessels is highly stable over time. These investigators coined the term *filarial dance sign* to describe the ultrasound appearance of adult filariae. This technique has also been used with some success in India.[6].The ability to observe adult worms in vivo provides an opportunity to directly observe effects of chemotherapy on the worms and the host. In addition, this technique provides a potential window for observing early hydroceles and for improving understandingof the pathogenesis of this disease.

CONCLUSION :

As shown by this case, HRUSG of scrotum can serve as a useful non invasive investigation tool in the management of this treatable chronic deforming illness prevalent in the tropics.

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Case Report

Yellow Phosphorus Induced Acute Fulminant Liver Failure

M. Debbarma[*], A. Dasgupta[**]

Abstract

We report a case of 45 year old housewife woman, who was brought to hospital after 7 days of suicidal consumption of Ratol rat-poison paste (3% yellow phosphorus). She was previously discharged from a local hospital after 48 hours of observation from the time of consumption, where she was asymptomatic at the time of discharge. The clinical presentation and investigation at the time of presentation to our hospital showed that she developed hepatic failure. She was successfully managed conservatively and was discharged after 15 days of admission

KEYWORDS: *rat-poison, yellow phosphorus, hepatic failure*

INTRODUCTION :

Phosphorus is an inorganic substance. There are two varieties— (1) white or crystalline. It is used in fertilisers, insecticides, rodenticides, incendiary bombs, smoke screens, fireworks, etc. (2) Red or amorphous. Red phosphorus is reddish-brown in colour used on the sides of match box and is non-toxic. White phosphorus is white or yellow in colour and is highly toxic. It is a protoplasmic poison, which affects cellular oxidation. Fatal dose is 60 to 120 mg and fatal period 2 to 8 days.[1] The most readily available source of yellow phosphorus today is rodenticides. Rodenticides are available as powders or pastes containing 2 to 5% of yellow phosphorus. Our case is a case of acute yellow phosphorus poisoning by suicidal ingestion of ratol paste, presenting with acute fulminant hepatic failure. She recovered with conservative management and was discharged and followed up successfully. Acute fulminant liver failure following an acute poisoning with yellow phosphorus has been infrequently reported in literature.

CASE REPORT :

A 45 year old housewife was admitted to our hospital with altered sensorium for 2 days with alleged history of suicidal ingestion of rodenticide 7 days prior to admission. The amount ingested was unknown and the material brought by her family member revealed Ratol paste containing 3% yellow phosphorus. She was hospitalised in the local hospital immediately after ingestion for vomiting and pain abdomen, and was discharged after 48 hours when she became asymptomatic. She developed progressive alteration of sensorium 5 days following ingestion for 2 days and was taken to the same local hospital from where she was directly referred to our hospital. On examination, the patient was stuporous with temperature 101° F, pulse rate 130/min and respiratory rate of 28/min. Her blood pressure was 96/66 mm Hg in the right arm in supine position and SPO_2 95% in room air. Her Glasgow coma score was 8(Eye opening 2, Verbal response 1, Motor response 5) and there was icterus, mild pallor but no oedema. Abdomen was distended with soft and tender hepatomegaly. Investigations on the day of admission(7 days following ingestion) showed Total serum bilirubin 6.2 mg/dl, SGOT 839 IU/L, SGPT 903 IU/L, serum albumin 3.3 gm/dl serum ammonia 45 mg/dl and normal ABG. PT was raised to 24.4 (11.99-14.36) and INR 2.26(0.8-1.10). Haemoglobin was 9.9 gm%, platelet count 1.7 lakhs, TLC 9900/cumm. KFT and electrolytes level normal. CXR(P/A) normal and Sonography whole abdomen revealed enlarged fatty liver grade 3, with ascites and bilateral pleural effusion. Blood for malarial parasite, leptospirosis and all hepatotropic viral

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markers were negative. Based on the history, clinical and investigation findings, a diagnosis of Acute Fulminant Liver Failure due to yellow phosphorus was made. Accordingly patient was managed with 5 units of fresh frozen plasma, IV fluids, low dose dopamine, vitamin k injection, lactulose syrup and enema, injection ceftriaxone and pantoprazole. During the hospitalization, she required ventilation for 3 days from the day 3 of admission(10 days following ingestion). Her sensorium and blood reports improved gradually from day 6 of admission(13 days following ingestion). She recovered completely and was discharged after 15 days of admission(22 days following ingestion).

DISCUSSION:

Acute poisoning of phosphorus presents in three stages. In the First stage, due to local irritation, symptoms occur within few minutes to few hours after exposure and last from 8 hours to three days. Luminescent vomit and faeces are diagnostic. Second stage is a symptom-free period lasting for two to three days. In the Third stage, symptoms of systemic toxicity occur from absorbed poison. There is nausea, vomiting, diarrhoea, haemetemesis, liver tenderness, and enlargement, jaundice and pruritus. Haemorrhages occur into skin, mucous membrane and viscera. Renal damage and central nervous involvement also occurs. Death may result from shock, hepatic failure, central nervous system damage, haematemesis or renal insufficiency.[1] Fernandez and Canizares in a series of 15 patients have reported a mortality of 27%, confirming that yellow phosphorus is extremely lethal when ingested.[2]

There is no specific antidote for yellow phosphorus. Treatment is directed at removal of the poison and supportive therapy. Gastric lavage with potassium permanganate is recommended to convert the phosphorus to relatively harmless oxides. Careful monitoring of hepatic and renal function and management of their failure is required. Liver transplantation has been done in suitable candidates for acute hepatic failure.[3] Unless looked for specifically clinical evidence of icterus or an abnormality in liver function tests can be missed and elevation of prothrombin time can be wrongly attributed to a warfarin containing rodenticide.[4]

Santos et all. described three cases of white phosphorus intoxication with acute liver failure secondary to the consumption of firecrackers. In one case, liver injury improved with supportive care, in the other, the patient required liver transplantation and the third case had a fatal outcome.[3]

Anupama et al. reported a case of three year old girl, who was brought to hospital for accidental consumption of rat-poison (3% phosphorus), who was asymptomatic for first 48 hours but later on developed the symptoms of hepatic failure. She was managed conservatively and was discharged after 14 day.[5]

Karanth and Nayyar reported two cases of rodenticide induced severe hepatic dysfunction where one of the patient died due to acute hepatocellular necrosis and fulminant hepatic failure, and the other patient with ratol ingestion was successfully treated.[4]

Aniket et al. reported a case of ratol induced acute fulminant hepatic failure in a 21 year old woman who died despite all available measures taken. Prevention strategies by restricting access to the poison can be one of the best method to avoid complications. Public as well as clinicians should made aware of lethality of inorganic phosphorus in miniscule quantities.[6]

CONCLUSION :

Our patient presented in the Third stage of acute poisoning, who developed the symptoms of liver failure after five days of ingestion of the ratol paste. We would like to suggest that all patients with yellow phosphorous poisoning should be followed with LFT in at least a week time especially in patients with ingestion of unknown amount.

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Case Report

Conjunctival Squamous Cell Carcinoma A rare opportunistic neoplasm in HIV

A. P. Jog[*], P. Bhattacharjee[**], B.K. Nath[***], P. Das[***]

Abstract

Conjunctival Squamous Cell Carcinoma (SCC), is an uncommon disease, the average annual incidence of which has been estimated to be approximately 17-20 cases per million persons per year, across all age groups. Risk factors include a history of repeated intense sunlight exposure, male sex, advanced age, cigarette smoking, blonde hair, light complexion, xerodermapigmentosum, HPV 16 and 18 infection of the conjunctiva and HIV/AIDS[1].HIV infection/ AIDS is a global pandemic[2]. At a prevalence of 0.3 % India ranks third in the world, with a few North-Eastern states ranking amongst the highest in terms of prevalence[3]. HIV infection is associated with increased occurrence of certain neoplastic conditions[2]. Conjunctival SCC, is one such rare neoplasm. Though documented in other geographical areas, reports of SCC of the conjunctiva in association with HIV are lacking in Assam . Below, we present such a case of conjunctival SCC in a newly diagnosed HIV infected patient and its therapeutic outcome.

KEY WORDS : *Carcinoma, Squamous Cell, Conjunctiva, HIV*

INTRODUCTION :

Ocular surface squamous neoplasia (OSSN) describes a spectrum of benign, pre-malignant and malignant unilateral slowly- progressive epithelial lesions of the conjunctiva and cornea. Squamous cell carcinoma is one histological type of OSSN and may present as a leukoplakic, gelatinous or a papillomatous lesion[4]. After 1983 there was observed a marked increase in the occurrence of this SCC especially at a younger age. Parallel increase in atypical Kaposi's sarcoma and ophthalmic zoster, which are associated with HIV infection, suggested a similar association[5]. The oncogenesis is thought to be disordered epithelial maturation induced by various irritants[1].

CASE REPORT :

The patient XYZ, a 40 year old, unmarried heterosexual local shopkeeper was admitted in the Medicine Ward at SMCH, Silchar with complaints of low grade fever and weight loss since 4 months.History of sexual exposure to a female sex worker, two years prior to admission was given. He is a non-smoker/ non-alcoholic, but a habitual tobacco chewer. General examination was unremarkable, except for a bright red mass in the left eye.

The mass, measuring about 5 mm vertically and 4 mm horizontally, was located on the temporal side overlying the limbus and partly involved the conjunctiva and adjacent cornea. Patient had noted the presence of the mass since one year, but had not sought medical consultation due to lack of significant discomfort, despite it having grown in size over this duration. As the mass was not encroaching upon the pupil, the patient had no difficulty in vision. The right eye did not reveal any abnormality externally. No lymphadenopathy was present.

Patient tested positive for HIV-1. Routine blood investigations were normal (Hb=13.4 g/dl, TLC= 5970 cells/ mcL, Creatinine= 0.79 mg/dl, AST= 49 units/L, ALT= 54 units/L, RBS= 97 mg/dl, Chest X-Ray, abdominal ultrasound and CT Head were normal). CD4 count of the patient was 39 cell/mm^3. He was started on TMP-SMX and triple drug ART (Tenofovir, Lamivudine and Efavirenz).

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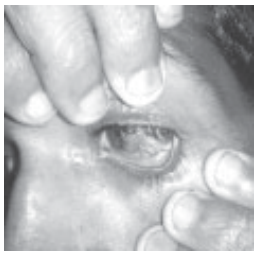

fig 1- picture of left limbal squamous cell carcinoma

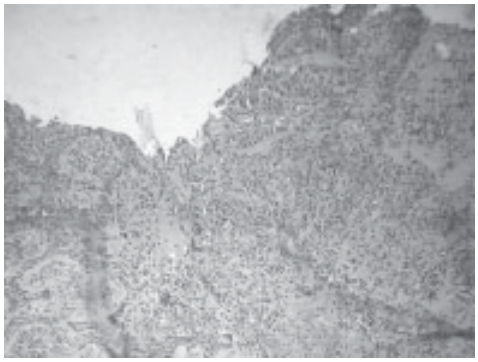

fig2-microscopic picture of conjunctival squamous cell carcinoma

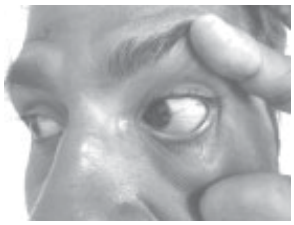

fig3- post operative picture of left eye

Ophthalmological consultation revealed a normal fundus, vision, IOP, gonioscopyand gave the differential of basal cell carcinoma, squamous cell papilloma andconjunctival SCC. An excision biopsy with amniotic membrane grafting was performed on the patient on 10/02/16. The section studied showed the presence of tumour cells arranged in sheets and nests. Individual cells had a high N:C ratio (nuclear: cytoplasmic) with distinct cell borders. Nucleii were moderately pleomorphic, vesicular with prominent nucleoli. At places, intracellular keratin was noted with a few mitotic figures. This picture was suggestive of a diagnosis of Squamous cell carcinoma of the conjunctiva.

A post-operative 10week course of topical mitomycin- c (0.02%) eye drops was given to the patient (1 drop in left eye, 6 hourly).On follow up at monthly intervals post-op, the patient has not shown any signs of relapse of the SCC.

DISCUSSION :

As seen in our patient, tumors of the conjunctival epithelium occur frequently as focal epibulbar lesions at the corneoscleral limbus[1]. Relative risk of conjunctival epithelial malignancies increases 13 fold in AIDS[6]. They are more common in elderly males, except in immunodeficient patients, where they may occur at an earlier age[1]. Accompanying cutaneous and visceral malignancies are seen at a rate of around 13% and 8% respectively, but were absent in this case. Corneal involvement, seen in about 50 % cases was present in our patient. Intraocular and orbital invasion is a feature in 2-8% and 12-16% cases respectively, but were absent in this patient[6]. Patients with AIDS are likely to exhibit rapidly progressive malignant conjunctival and corneal neoplasms of the stratified squamous epithelium and metastasis of those neoplasms[1]; but no evidence of the same was seen in this case.

Treatment modalities for conjunctival SCC range from simple excision to exenteration, based upon the size of the lesion, location, status of the fellow eye and age and health of the patient. Following surgery, topical chemotherapy in the form of mitomycin-c (0.02% to 0.04%) or 5-fluorouracil (1%) maybe used in patients with extensive involvement of cornea or conjunctiva[1].

CONCLUSION :

Ocular opportunistic disorders, infectious or neoplastic, maybe seen in HIV infected patients, especially with a CD4 count less than 200 cells/mm^3. Ophthalmological examination is not routinely done in HIV positive patients, unless any ocular complaint is provided. This may leave certain lesions, that could have otherwise been detected, undiagnosed. Thus, ophthalmologic screening should be given to all patients living with HIV/ AIDS on a routine basis, thus aiding in early diagnosis and treatment of any pathologies.

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