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Echocardiography in ESRD patients on CAPD

Mriganka Shekhar Chaliha*

Cardiovascular mortality is significantly increased in patients with Chronic Kidney Disease(CKD) leading to earlier atherosclerosis, valvular and pericardial disease, arrhythmias and heart failure. Use of echocardiography plays a crucial role in the evaluation of these patients. Over time, a combination of CKD and other medical conditions such as hypertension and diabetes leads to myocardial fibrosis and development of LVH. The term known as ‘cardiorenal syndrome’ (CRS) includes a broad spectrum of diseases in which both heart and kidney are involved. A consensus conference of the Acute Dialysis Quality Initiative Group1 has proposed the term ‘cardiorenal syndrome’ to define a clinical overlap between kidney and heart dysfunction. Left ventricular hypertrophy (LVH) represents the key feature in uremic cardiopathy and it is related to CRS type 4 (chronic renocardiac/cardiorenal syndrome).

Essentially three pathophysiological factors have been identified in relation to LVH of CKD and ESRD patients: (1) related to afterload, (2) related to preload, and (3) not related to afterload or preload2,3,4. The factors in the first category are represented by an increase in systemic arterial resistance, elevated arterial blood pressure, and reduced large-vessel compliance2-5. All these three factors result in myocardial cell thickening and concentric LV remodeling often together with activation of the intracardiac renin-angiotensin system4,6. Oxidative stress and xanthine oxidase activation as well as the phosphodiesterase-5 pathway may also be involved in the development of LVH7.

Among the preload-related factors, the role of intravascular volume expansion (salt and fluid loading) has to be underlined, as well as secondary anemia8-10, resulting in myocardial cell lengthening and eccentric or asymmetric LV remodeling. Both afterload- and preload-related factors operate with additive and synergistic effects. As a result, myocardial hypertrophy induces the activation of cellular apoptotic signals and activates metabolic pathways to increase extracellular matrix production up to fibrosis,11,12. Fibrosis leads to progressive impairment in contractility with stiffening of the myocardial wall, systolic and diastolic dysfunction, dilated cardiomyopathy and congestive heart failure13. Renin-angiotensin-aldosterone system activation induces hyperaldosteronemia promoting cardiac fibrosis through the generation of signals leading to profibrotic transforming growth factor production6. LVH can also be promoted by iron and/or erythropoietin14 or vitamin D deficiency15. Recent studies have pointed out novel biomarkers involved in the pathogenesis of LVH.

One of these is represented by FGF23, a member of the fibroblast growth factor family primarily involved in CKD-mineral and bone disorder (MBD) and secondarily to hyperparathyroidism. The pathogenesis of CKD-MBD has always been ascribed to a decline in 1,25-dihydroxyvitaminD [1,25(OH)2 D3] levels leading to increases in serum parathyroid hormone(PTH) and subsequent alterations in calcium and phosphorus metabolism16,17. Vitamin D deficiency, together with secondary hyperparathyroidism and hyperphosphatemia, was reported as a main factor contributing to high cardiovascular risks in CKD patients18.

In the present study, published in this issue, LVH
was found in 60% of cases (at the beginning) and 43.3% of cases (1 year after CAPD). It is seen that iPTH level > 300pg/ml was significantly associated with LVH compared to iPTH level < 300pg/ml (P < 0.048 and 0.019). Vit-D level of <30 ng/ml was associated with LVH (P < 0.02). Earlier experimental studies showed association between vitamin D deficiency and impairment of cardiac contractile function, increased myocardial collagen content, and increased cardiac mass19-21. In the present study, published here, there was appreciable reduction in LVH cases after 1 year of CAPD. The reduction in the degree of LVH can be achieved by fluid balance and blood pressure control together with anemia control22. Foley et al.23 found that improvements in LV mass and systolic function 1 year after the initiation of dialysis. Covic et al.24 reported a regression of LV mass in hemodialysis patients associated with improvements in anemia, serum phosphate level, and calcium-phosphate product.

In the present study (published in this issue) diastolic dysfunction (66% at baseline and 60% at 1 year of CAPD) and systolic dysfunction (33% at baseline and 30% at 1 year of CAPD) have been noted as common abnormalities in CKD patients. Cardiac alteration in patients with CKD leads to dysfunction in both diastolic and systolic properties. Echocardiographic abnormalities (impairment of EF and increased end-systolic and end-diastolic LV volumes) are frequently reported from the early stages of CKD to ESRD. Diastolic function was determined in the present study by measuring E/A ratio by special doppler inflow velocity (E is peak early diastole velocity and A is peak atrial filling velocity of left ventricle across mitral valve). E/A ratio less than 0.75 and more than 1.8 was considered as diastolic dysfunction. However, the accurate assessment of diastolic function in these patients is challenging as the wide variations in volume status makes mitral inflow velocity measurements difficult25. Therefore the ratio of early mitral flow velocity to early mitral annulus velocity (E/E′) has been found to be a reliable measure of LV filling in ESRD patients26. In CKD patients, Tissue Doppler Imaging (TDI) is more sensitive to detect diastolic dysfunction than conventional echocardiography27-30.

One question that comes here under the context is – Is it relevant to measure systolic and diastolic function of LV in uraemic population? In a previous study by Hsiao et al. LV dysfunction, LVH and LV diastolic dysfunction were found to influence prognosis31. In the same way, in a study by Kim et al. diastolic dysfunction was a significant marker of rapid decline in residual renal function and the occurrence of cardiovascular events in patients placed in CAPD32. Diastolic dysfunction has been observed in patients receiving renal replacement therapy for ESRD in many studies33,34. In a study by Duran et al., diastolic function of LV was not significantly altered after maintenance of haemodialysis treatment. They demonstrated that in the long run, the acute changes of volume, electrolytes and autonomic regulation due to haemodialysis session does not affect left diastolic function35. For Lee et al., the prevalence and severity of diastolic LV dysfunction is higher in PD patients36. Some authors suggest that Left ventricular mass and diastolic function are closely related to each other in all dialysis patients37. Similarly, fractional shortening, a measurement of global LV systolic function, could over estimate contractility in patients with concentric hypertrophy. In dialysis patients, tissue velocity and strain imaging can detect changes in LV function better and are less affected by the volume status of the patients38. The present study in reference did not find any improvement in cardiac function with treatment of 1 year. Perhaps a longer duration of study and use of TDI could have shown such an improvement.

REFERENCES:
Echocardiographic Changes in Patients with ESRD on CAPD with special reference to iPTH and Vit-D level - A Single Centre Study


Abstract

Background: Cardiac function abnormalities are common in CKD patients. We conducted this study: 1. to assess the cardiac function in ESRD patients on CAPD. 2. impact of CAPD on iPTH and Vit-D level and their association with changes in the echo-cardiographic parameters. 3. influence of CAPD on anemia and hypertension in patients with ESRD.

Material and Methods: We included 30 (thirty) ESRD patients on CAPD who were on 4 exchange per day irrespective of underlying etiology in our study, which was conducted in a tertiary centre in eastern UP, India. All patients were clinically evaluated thoroughly and subjected for complete blood count, renal function test, serum calcium, phosphate, albumin, iPTH, Vitamin D and 2-D echocardiography at the time of initiation of CAPD and at 12 months.

Results and observations: Out of thirty patient male to female ratio was 1.7:1 (63.33 vs 33.66). Mean age of presentation was 45.66±24.34. Mean iPTH level at the beginning and at the end of study were 223.12 ± 140.21 pg/ml and 214 ± 111.68 pg/ml respectively. Vit-D level were 26.71 ± 11.11 ng/ml and 31.85 ± 14.60ng/ml respectively at 0 and 12 months. LVH, systolic and diastolic dysfunctions were present in 60% (n=18), 33% (n=10), 66% (n=20) at the beginning and 43.33% (n=13), 30% (n=9) and 60% (n=18) at the end of the study respectively. iPTH level > 300pg/ml was significantly associated with LVH and diastolic dysfunction as compared to iPTH level < 300pg/ml (p=0.048 and 0.019). Vit –D level of <30 ng/ml was associated significantly with LVH (p=0.02) and diastolic dysfunction (p=0.04). Significant association of LVH (p= 0.04) and systolic dysfunction (p=0.02) was seen with hemoglobin level of < 10gm/dl. Mean BP changes were significant upon completion of the study. Conclusion: Diastolic dysfunction is the commonest echocardiographic abnormality in ESRD patients on CAPD followed by LVH and systolic dysfunction. Significant BP control was seen at the end of study, though it was short term study. High iPTH level > 300pg/ml were significantly associated with LVH and diastolic dysfunction. Vit-D level < 30 ng/ml were correlated well with the LVH and diastolic dysfunction.

Key Words: ESRD, LVH, systolic dysfunction, diastolic dysfunction, iPTH, Vit-D.

INTRODUCTION:

Advances in the renal replacement therapy had changed the outlook of ESRD patients in a significant way. Continuous ambulatory peritoneal dialysis is increasingly accepted treatment modality for RRT amongst ESRD patients worldwide. It has been suggested that patients on CAPD are fairly better in terms of fluid and hypertension control but are at the greater risk for developing atherosclerosis due to more production of atherogenic lipids, which in turn had adverse impact on cardiovascular morbidity and mortality. Cardiac alterations develop early in the course of CKD, which tend to progress with time in majority of patients with ESRD and these alterations can be efficiently demonstrated by echocardiography. The presence of LVH (48-75 %) in ESRD patients increases the risk for cardiac ischemia, congestive heart failure and arrhythmias and a strong predictor of cardiovascular mortality. These alterations in LVH and LV dilatation is principally mediated by hemodynamic factor like chronic pressure, volume overload or both and anemia, though other factors like metabolic and neurohormonal mechanism are also seen to contribute. CAPD exerts beneficial effects on cardiovascular system in ESRD patients by preventing the volume overload, lack of intra and interdialytic volume changes, better control of BP, constant electrolyte and acid base balance. The prevalence of CV risk factors has been found to change with time during follow up. Significant decreases in hypertension and left ventricular hypertrophy have been observed in the first year of therapy; but after 5 years, the risk factors are found in same proportions noted at the start of the...
We designed a prospective study to analyze various echocardiographic alterations of cardiac function in ESRD patients on CAPD.

MATERIAL AND METHODS:
We included 30 (thirty) ESRD patients on CAPD who were on 4 exchange per day irrespective of underlying etiology in our study, which was conducted in a tertiary centre in eastern UP, India. A person was labeled as ESRD if his or her GFR was less than 15mL/min/1.73 m² as per Modified Diet in Renal Disease (MDRD) formula. No patients in our study group used icodextrin base exchange. Patient with obvious clinical evidence of coronary artery disease, valvular heart disease and rheumatic heart disease, congenital heart disease and primary cardiomyopathies were excluded from the study. All patients were clinically evaluated thoroughly and subjected for complete blood count, renal function test, serum calcium, phosphate, albumin, iPTH, Vitamin D and 2-D echocardiography at the time of initiation of CAPD and at 12 months. BMI and efficacy of CAPD was not correlated with this study though we performed KT/V in each and every patient as per protocol. 2D-Echocardiography machine GE LOGIQ 400 PRO was used with 3.5 MHz transducer probe. The M-mode recording perpendicular to the long axis through the centre of the left ventricle at the papillary muscle level was taken as standard measurements of the systolic and diastolic wall thickness and chamber dimensions. The left ventricular ejection fraction (LVEF) was taken as measure of left ventricular systolic dysfunction and ejection fraction <55% was considered as systolic dysfunction. Diastolic function was determined by measuring E/A ratio by special doppler inflow velocity (E is peak early diastole velocity and A is peak atrial filling velocity of left ventricle across mitral valve). E/A ratio less than 0.75 and more than 1.8 was considered as diastolic dysfunction. LVH was diagnosed when interventricular septum thickness or left ventricular posterior wall thickness was ≥ 12 mm. Hypertension was defined as BP ≥ 140/90 mmHg in right arm supine position and anemia was diagnosed with hemoglobin <13.5 gm/dl in male and 12.5 gm/dl in female. Vit-D insufficiency and deficiency were defined as Vit-D level ≤ 15-30ng/ml and ≤ 15ng/ml respectively. iPTH value of 150-300 pg/ml was the target range as per NKF/KDIGO guideline. Statistical analysis was done by SPSS software version 15 by using Fisher’s exact test. A ‘p’ value of < 0.05 were considered significant.

We conducted this study to evaluate the cardiac function anomalies in ESRD patients on CAPD, influence of CAPD on iPTH and Vit-D level and their association with changes in the echo-cardiographic parameters. Effects of CAPD on anemia and hypertension were also evaluated.

RESULTS AND OBSERVATIONS:
We studied 30 (Thirty) ESRD patients on CAPD irrespective of underlying etiology, who were on 4 exchanges per day and patients were followed up for 12 months. During this follow up periods we performed all necessary investigations in each and every patient. Results were analyzed by using SPSS-15 software version. We evaluated all the parameters in two separate occasions, one at beginning of the study and another at the end of 12 months.

Out of thirty patient male to female ratio was 1.7:1 (63.33 Vs 33.66). Mean age of presentation was 45.66±24.34. Diabetes account for 46.66% patients and was the most common cause of ESRD followed by hypertension in 26.66% and chronic glomerulonephritis in 16.66%. Basic demographic and laboratory parameters were presented in Table-1 and etiological profile in Figure-1. Mean iPTH level at the beginning of the study and at the end of 12 months were 223.12 ± 140.2 pg/ml and 214 ± 111.68 pg/ml respectively. Likewise Vit-D level were 26.71 ± 11.11 ng/ml and 31.85 ± 14.60 ng/ml respectively. No significant difference of iPTH and Vit-D level were noticed amongst the diabetic and non-diabetic ESRD population. Anemia was seen in each and every patient. A marked change in the serum albumin level was not seen at the end of the study. The mean systolic and diastolic blood pressure were 153.13 ± 53.2/ 93.13 ± 9.30 mmHg and 146.20 ± 34.6/77.06 ± 20.94 mmHg at start of the study and at the end of the study respectively and changes were statistically significant.

On analyzing the echocardiographic changes, LVH was present in 60% cases at the beginning and 43.33% at the end of the study. Systolic and diastolic dysfunction were seen in 33% and 66% cases at the start of the study. At the end of the study systolic and diastolic dysfunction were seen in 30% and 60% cases respectively. The
changes in these parameters were statistically insignificant. When iPTH level were correlated with echocardiographic changes it is seen that iPTH level > 300pg/ml was significantly associated with LVH and diastolic dysfunction as compared to iPTH level < 300pg/ml (p = 0.048 and 0.019). Vit –D level of <30 ng/ml was associated with LVH (p = 0.02) and diastolic dysfunction (p = 0.04).

**DISCUSSION :**

The relentless progressive nature of the CKD patients, by the time they reached ESRD confronted to wide variety of physiological and structural alteration that adversely affect the cardiac performance.6,7. These alterations could be because of hemodynamic factors, metabolic alteration or pre-existing heart disease or repeated uremic pericarditis. Not unexpectedly, alteration of cardiac structure and functions are common in CAPD patient. Maher estimated that 80% of patients referred for CAPD have some form of heart disease. Because of its steady state, hemodynamic and metabolic effects, CAPD would appear to possess comparative advantage over the hemodialysis as a renal replacement therapy in patients with ESRD and abnormal cardiac functions.8

In a study conducted by Singh S et al revealed a prevalence of LVH in 48% cases and diastolic dysfunction in 51.42% cases of studied population9. Agarwal S et al had observed diastolic dysfunction in 53.2% and systolic dysfunction in 30% patients with severe CKD10. Hunting et al, studied 55 normotensive patients receiving CAPD, using echocardiography to characterize cardiac morphology and function. LV hypertrophy was found in 84% of patients (including asymmetric septal hypertrophy). He also reported left atrial enlargement in 49% patients.11 Besides left ventricular hypertrophy a high prevalence of left atrial dilatation and abnormal left ventricular diastolic filling have been found in CAPD patients. Using echocardiography in a study of 16 CAPD patients with normal systolic function followed for an average of 35 months, Hutting and Acpert reported an increase in LV mass from 251g to 342 g and a decrease in LV volume mass from 0.73 to 0.54.12
In our study, we found LVH in 60% and 43.33% at the beginning and at the end of the study respectively. Systolic and diastolic dysfunction were seen in 33% and 66% cases respectively at the start of the study. At the end of the study systolic and diastolic dysfunction were seen in 30% and 60% cases respectively.

Hypertension was present in 83.33% cases in our study at the initiation of CAPD and at the end of the study it was present in 53% cases. Blood pressure control was statistically significant. In a study conducted by Lameire N observed that approximately 80% of patients are hypertensive at the initiation of dialysis; however, in hemodialysis the prevalence falls to 25 to 30% and in peritoneal dialysis to 40% by the end of the first year largely due to better blood volume control.

In our study serum iPTH level were not significantly influence by the CAPD, but there was a positive correlation between high serum iPTH and LVH. Serum iPTH level more than 300pg/ml was significantly associated with LVH (p=0.019). Serum PTH levels greater than versus less than 157 pg/mL were significantly associated with a greater likelihood of LVH (1.53; CI, 1.21 to 1.93) were significantly associated with diastolic dysfunction and elevated iPTH level >300 pg/ml was statistically significant in our study (p = 0.019).

This was supported by study done by Singh NP et al which shows that diastolic dysfunction seen in pre-dialysis CKD patients improved with calcitriol therapy.

In our study, we observed that Vit-D insufficiency (<30ng/ml) in 40% at the beginning of the study and 40% patients at the end of the study. LVH was significantly associated with Vit-D insufficiency in our study. In a study by Park CW et al shown that calcitriol caused a regression of LVH independent of changes in blood pressure.

In our study, we found LVH in 60% and 43.33% at the beginning and at the end of the study respectively. Systolic and diastolic dysfunction were seen in 33% and 66% cases respectively at the start of the study. At the end of the study systolic and diastolic dysfunction were seen in 30% and 60% cases respectively.

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pressure, suggesting a direct effect on attenuation of ventricular hypertrophy\textsuperscript{17}. Preclinical studies also support a role for vitamin D deficiency in the development of LVH in age related decline in kidney function and chronic kidney disease patients\textsuperscript{18}. Left ventricular diastolic dysfunction was significantly associated with Vit-D level of less than 30 ng/ml which contradicts to the study conducted by Hoorn et al and Anil Pandit et al. Whether this association was per se due to Vit-D insufficiency or diabetes mellitus and hypertension, it is difficult to ascertain because majority of our study population had both the disease, which in turn can influence the diastolic function. Despite growing medical literature suggesting Vit D deficiency is associated with cardiovascular disease, in a study conducted by Anil Pandit et al, involving a large number of unselected patients, Vit D deficiency is not associated with LV diastolic dysfunction and an abnormal LAV index\textsuperscript{19}. In his study lack of association may be due to exclusion of patients with serum creatinine of more than 2mg/dl and adoption of different echocardiographic parameter for diastolic dysfunction (LAVI). Recently, the Hoorn study showed in a prospective manner that Vit D levels at baseline were not associated with LAVI over a subsequent 8 years of follow-up\textsuperscript{20}.

**CONCLUSION:**

Some amount of cardiac function abnormality is common in CKD patient due to various factors. Diastolic dysfunction is the commonest echocardiographic abnormality in ESRD patients on CAPD followed by LVH and systolic dysfunction. Significant BP control was seen at the end of study, though it was a short term study. Anemia is well known association of various forms of cardiac function abnormalities. High iPTH level > 300pg/ml were significantly associated with LVH and diastolic dysfunction. Vit-D level of < 30 ng/ml was correlated well with presence of LVH and diastolic dysfunction. To establish the effects of iPH and Vit-D on heart in ESRD patients on CAPD needs further well designed randomized control studies with large number of patients.

**Drawback:**

Our study was a short term study with small number of patients. Echocardiographic findings were not evaluated in relation to the basic diseases. Adequacy of CAPD was not taken into account.

**REFERENCE:**


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Depression in Type 2 Diabetes Mellitus: Prevalence and Association with Clinical and Sociodemographic Parameters

K Saikia*, B Choudhury**, A Choudhury***, S K Agarwal***, A K Bhuyan****

Abstract

Aims and Objective: To study the prevalence of depression in patients of type 2 Diabetes Mellitus as well as to determine the association with different clinical and sociodemographic parameters. Material and Methods: Total 220 subjects with type 2 Diabetes Mellitus were enrolled into the study between August 2014 to October 2014 in Gauhati Medical College which is a tertiary care centre in North-East India. Detailed history was taken and clinical examinations with relevant investigations were done in all the subjects. Assessment of depression was done by the Assamese version of PHQ-9 questionnaire in each of the subjects. Binary logistic regression analysis was carried out to determine the association of different factors with depression. Results and Observation: The prevalence of depression was found to be 38.17% in our study. Out of this the prevalence of severe depression was 18.18%, moderately severe 8.18%, moderate 4.54% and mild depression 7.27%. The following factors were found to be associated significantly with depression – longer duration of the disease, higher HbA1c, being on insulin, presence of hypertension, presence of complications, unemployment, lower income and higher cost of medications. Factors that were not related to depression were – age, sex, BMI and use of OHA. Conclusion: A high prevalence of depression was found in patients with type 2 diabetes mellitus in North-East India. Several clinical and sociodemographic factors were identified which had a significant association with depression in these subjects.

Key Words: Depression, Questionnaire

INTRODUCTION:

The co-existence of diabetes and depression has been highlighted by several studies. The chronic nature of diabetes is associated with significant morbidity and mortality, as well as substantial financial burdens on the part of the patient. A more than co-incidental effect of the disease is observed in the mental dimension also, in fact the relation between depression and diabetes has been found to be bidirectional. People with diabetes have been found to have 1.4-3 times higher prevalence of depression as compared to healthy normal population. Different factors like age, duration of diabetes, glycaemic control, presence of complications, employment, use of insulin etc. are implicated to have associations with depression in people with diabetes. Although studies from different parts of the world have addressed this, issue reports from India are limited in number. The present study was therefore undertaken with the objective to study the prevalence of depression in type 2 diabetes mellitus and to find the association of clinical and sociodemographic parameters of diabetic patients with depression.

MATERIAL AND METHODS:

The present study was done between August 2014 to October 2014 in Gauhati Medical College & Hospital, which is a tertiary care hospital in Assam, India. Total 220 patients of type 2 diabetes mellitus, of all age groups and either sex, were enrolled into the study. A detailed history of the subjects including demographic profile, socioeconomic status and monthly cost of therapy was recorded. Thorough physical examination was done in all subjects. The Assamese version of PHQ-9 questionnaire was used to assess the presence as well as degree of depression. Scores of 5, 10, 15 & 20 were taken as cut off points for mild, moderate, moderately severe and severe depression respectively, as per PHQ-9 instruction manual. Patients having the inability to comprehend the written questionnaire were excluded from the study. BMI was determined in the subjects by using the formula weight (kg)/height (m²). Blood pressure
was measured by applying the cuff in right arm of the patient in supine position while measuring twice at 15 minute intervals and the average of the two values were taken. Retinopathy was diagnosed based on fundus examination. Spot urinary albumin to creatinine ratio (UACR) > 30 mg/gm or serum creatinine level more than 1.5 mg/dl in males and 1.4 mg/dl in females indicated presence of nephropathy. Neuropathy was diagnosed clinically by the presence of impaired vibration sense on testing by 128 Hz tuning fork, impaired response to testing with 10 gm monofilament, impaired response to pin prick and loss of ankle jerk. Whenever the results of nerve conduction results were available from the patient’s records they were used as additional data for the presence of neuropathy. ECG was done in all cases with echocardiography in selected patients. History of coronary artery disease, if any, was recorded. History of CVA was recorded when present, and previous records were reviewed. Peripheral vascular disease was assessed clinically by ankle brachial index along with Doppler study in selected patients. The estimation of HbA1c was done by HPLC method.

Statistical analysis was done by SAS 9.3. Data were expressed as mean, standard deviation and proportions. Binomial regression analysis was carried out to determine the association of independent factors with depression.

RESULTS & OBSERVATION:
A total of 220 cases were evaluated. The clinical and demographic characteristics of the study subjects are stated in table 1.

By applying the PHQ-9 questionnaire we derived 18.18% (40/220) prevalence of severe depression in our study subjects. Moderately severe, moderate and mild depression were found to have a prevalence of 8.18% (18/220), 4.54% (10/220) and 7.27% (16/220) respectively. The total prevalence of depression thus was 38.17%. The bar diagram in figure 1 illustrates the prevalence of different types of depression.

We found the following factor to be associated significantly with depression in patients of type 2 diabetes mellitus – longer duration of the disease, higher HbA1c, being on insulin, presence of hypertension, presence of complications, unemployment, lower income and higher cost of medications. Factors that were not related to depression were – age, sex, BMI and use of OHA.

DISCUSSION:
The prevalence of depression in subjects with diabetes demonstrates variable estimates ranging from 11.6 % to 92 % depending on the study population and the methodology adopted for defining depression. An early meta-analysis in 1993 found a prevalence of major depression in 14.6 % and minor depression in 26 % of patients of both type 1 and type 2 diabetes. Anderson et al in their meta-analysis found 31% prevalence of depressive symptoms in patients of diabetes. Studies on both type 1 and type 2 diabetes were included in the meta-analysis. The Indian data is limited in this regard; the study by Raval et al in a tertiary care centre of northern India showed the presence of major and moderate depression in 23% and 18%.

### TABLE 1. The clinical and demographic characteristics of the study cases.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years, Mean ± SD)</td>
<td>48.38 ± 9.89</td>
</tr>
<tr>
<td>BMI (Kg/m², Mean ± SD)</td>
<td>23.22 ± 3.15</td>
</tr>
<tr>
<td>Monthly income (INR, Mean ± SD)</td>
<td>8842.47 ± 7281.15</td>
</tr>
<tr>
<td>Duration of Diabetes (Years, Mean ± SD)</td>
<td>7.71 ± 5.30</td>
</tr>
<tr>
<td>Monthly cost of medications (INR, Mean ± SD)</td>
<td>1591.32 ± 920.34</td>
</tr>
<tr>
<td>HbA1c (Mean ± SD)</td>
<td>8.49 ± 2.61</td>
</tr>
<tr>
<td>Male subjects (%)</td>
<td>63.01</td>
</tr>
<tr>
<td>Female subjects (%)</td>
<td>36.99</td>
</tr>
<tr>
<td>Subjects having employment (%)</td>
<td>71.23</td>
</tr>
<tr>
<td>CVA (%)</td>
<td>22.83</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>35.16</td>
</tr>
<tr>
<td>PVD (%)</td>
<td>12.21</td>
</tr>
<tr>
<td>Neuropathy (%)</td>
<td>46.12</td>
</tr>
<tr>
<td>CKD (%)</td>
<td>30.14</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>72.44</td>
</tr>
<tr>
<td>Subjects on Insulin (%)</td>
<td>50.68</td>
</tr>
<tr>
<td>Subjects on OHA (%)</td>
<td>41.10</td>
</tr>
</tbody>
</table>
of patients of type 2 diabetes respectively\(^5\). Our observations are reflective of the pattern in a tertiary care centre of the north-eastern India – a prevalence of 38.17% with 18.18% severe, 8.18% moderately severe, 4.54% moderate and 7.27% mild depression.

We found that the presence of micro and macrovascular complications of diabetes have a significant association with depression. Several studies report similar findings. Roy et al found depression to be a risk factor for retinopathy in subjects of type 1 diabetes\(^6\). Lin et al in a prospective cohort study of 4623 subjects of type 2 diabetes found major depression to be associated with adverse microvascular and macrovascular outcomes\(^7\). In another longitudinal study by Clouse et al in women with diabetes a significantly increased risk of having clinically evident coronary heart disease was found in subjects with major depression\(^8\).

Poor glycaemic control, as reflected by a higher HbA1c, had a significant association with depression in our study subjects. Glycaemic control as a risk factor for depression is a conflicting issue, with non-uniform results of the studies seeking the relationship between the two. A meta-analysis by Lustman et al in 2000 found depression to be significantly associated with hyperglycaemia\(^9\). The study of Papelbaum et al demonstrated higher levels of glycated haemoglobin in patients of type 2 diabetes with depression\(^10\). Similarly Wagner et al showed the association of higher depressive symptoms symptoms with higher HbA1c\(^11\). Other studies have however found no significant association between glycaemic control and depressive symptoms\(^12\)-\(^16\). This difference might be attributed to the variation of study methodologies.

The duration of diabetes has been found to be associated with depression\(^17\). We observed a longer duration of the disease to be associated significantly with depression. We also found that the form of therapy also affected psychological health. The prevalence of depression was more among insulin users, whereas subjects who were on oral hypoglycaemic agents (OHA) did not show this association. The study of Peyrot et al demonstrates findings similar to this observation\(^18\).

Several demographic and psychosocial factors are implicated to have association with depression in subjects with diabetes - age, female sex, lower education and socioeconomic status, unemployment, lack of social support, presence of other medical diseases, smoking etc\(^19\)-\(^22\). We found the significant association of the following factors with depression - unemployment, lower income and higher cost of medications. Age, sex & BMI – these factors were not related to depression in our study.

There are certain limitations to our study. As the study was cross-sectional no prospective data could be obtained to observe the effect of different factors in the development of depression. The study sample was also small and hence the data may not be extrapolated to a larger sample size.

**CONCLUSION:**

The present study underscores the high prevalence of depression among patients of type 2 diabetes mellitus in north-east India and identifies the independent factors that are associated with it. The significant association of diabetes with depression stresses the need for careful consideration in the management of patients with diabetes mellitus.

**REFERENCES:**

Assessment of volume of bleed in Intra-cerebral Hemorrhage as a reliable and easy to use yardstick in prediction of 7 day mortality

D Das*, K Bhattachrjee**, S K Ghintala***

Abstract

Background: Intra-cerebral hemorrhage is extravasation of blood into the brain parenchyma and its mortality rates change depending on the volume, severity and site of bleed inside the brain parenchyma. The present study was undertaken to measure the volume of intra-cerebral bleed and correlate the same with mortality within 7 days of presentation to hospital.

Aims and objectives: To determine 7 days mortality according to volume of intra-cerebral bleed and to predict the prognosis using Glasgow Coma Scale.

Material and methods: The study was conducted in the Medicine department of a tertiary care teaching hospital of north eastern India. The admitted patients diagnosed as cerebrovascular accidents on the basis of CT brain as having intra-cerebral hemorrhage were included in the study. Study design: Hospital based single centered observational study.

Results and observations: In this study out of total 100 patients of intra-cerebral bleed, 60 were finally selected on the basis of inclusion and exclusion criteria, which constituted the study group and were analyzed. Of the 60 cases 78.3% were males and 21.7% were females. Maximum numbers of cases were between 65-75 years of age constituting 50% of cases. Hypertension, which is the major risk factor for intra-cerebral hemorrhage was identified in 75% cases of which males and females constituted 77.8% and 22.2% respectively. Bleeding volume more than 50 ml, 30-50 ml and less than 30 ml were found in 23.3%, 33.3% and 43.4% cases respectively. Upon observing the mortality pattern, patients who suffered bleed volume of >50 ml had 100% mortality. Hypertension can be considered as one of the risk factors because patients with an ICH volume >50 ml with hypertension showed higher mortality rate. Glasgow Coma Scale is also a good predictor of mortality though not statistically significant.

Conclusion: Hematoma volume is a significant yardstick which plays a role in influencing the functional outcome, prognosis and mortality. It may be worth mentioning that the ICH volume of 50 ml or more is probably as significant as a volume of 60 ml or more determining the clinical severity, final outcome including mortality in patients with ICH.

Keywords: Brain, Cerebral hemorrhage, Hematoma, Hypertension, Risk factor.

INTRODUCTION:

Intra-cerebral hemorrhage (ICH) is the extravasation of blood into the brain parenchyma and is most common in elderly and its incidence is more in those receiving anticoagulant therapy. The mortality rates change depending on the volume of bleed, severity and site of bleed inside the brain parenchyma. Hypertension and amyloid angiopathy are the primary causes while coagulopathy, trauma, intracranial neoplasm, drugs are the secondary causes for intracranial hemorrhage. The volume of bleeding depicted in CT scan brain has the potential prognostic capability to find the mortality rate in intra-cerebral hemorrhage cases. The CT scan imaging of the brain is the standard investigation to detect the presence or absence of intra-cerebral hemorrhage and it is more sensitive than MRI brain for the detection of acute bleed. The population studies reported 30 days mortality of 44% - 51% in Computed Tomographic era. The mortality of patients depend more on the volume of hemorrhage, lesser extent on the level of impairment of consciousness and other factors. If the volume of intra-cerebral hemorrhage increases in size after hospital admission, it may worsen the outcome. Studies have been correlating the volume of bleed and mortality. The present study was undertaken to measure the volume of intra-cerebral bleed and correlate the same with mortality within 7 days of presentation to hospital.

AIMS AND OBJECTIVES:

1. To determine 7 days mortality according to volume of ICH.
2. To determine the prognosis of patient using Glasgow Coma scale (GCS) for first 7 days.

MATERIAL AND METHODS:

STUDY SETTING:
The present study was conducted in the department of Medicine in a tertiary care teaching hospital in North Eastern India for a period of one year.

**STUDY DESIGN :**

The present study was a hospital based single centered observational study.

The patients who were admitted in the department of Medicine, Silchar Medical College with cerebrovascular accidents and diagnosed on the basis of CT brain as having intra-cerebral hemorrhage were included in the study. Each patient was followed up for a period of one week during which they were treated with anti-hypertensives, anti-cerebral edema measures as well as interventions to prevent aspiration pneumonia, bedsores and sepsis and other associated complications.

**Inclusion criteria :**

One hundred cases of new onset cerebrovascular accidents (onset within 2 days) diagnosed clinically and CT brain correlation as intra-cerebral hemorrhage, admitted in the Medicine department were included in the study.

**Exclusion criteria-**

Presence of factors which could alter the outcome like patients with intra-ventricular extension of the bleed, ischemic stroke, intra-cerebral tumors, presence of aspiration pneumonia or sepsis at the time of presentation or during the course of stay in the hospital, presence of concurrent subdural, extradural and subarachnoid hemorrhage, use of antiplatelet medication (Aspirin), anticoagulant medication (Warfarin), Diabetes Mellitus (DM), previous history of ischemic or hemorrhagic stroke, past or present evidence of coronary artery disease, acute or chronic kidney diseases, chronic liver disease, decompensated chronic pulmonary diseases and coagulopathies and malignancies anywhere in the body were excluded from the study.

Thorough clinical history and physical examinations were done in each case. Necessary investigations including complete blood count, fasting blood glucose, blood urea, serum(s.) creatinine, s. sodium, s. potassium, fasting lipid profile, liver function test, X-ray chest, ultrasound abdomen and fundoscopy based on indications were undertaken.

Hematoma size was calculated by using formula $\frac{ABC}{2}$, where $A$ is the greatest hemorrhage diameter by CT, $B$ is the diameter 90° to $A$, and $C$ is the thickness of hemorrhage, the total volume of hemorrhage is estimated. According to Luby et al. (2012), the ABC/2 method is the most sensitive, reliable and accurate of all.

Glasgow Coma Scale (GCS) was used to measure the neurological status. The patients’ GCS at day 1 and day 7 were recorded.

Statistical analysis was done and p value < 0.05 was taken as statistical significant.

**RESULTS AND OBSERVATION :**

In this study out of total 100 patients of intra-cerebral bleed, 60 patients were finally selected on the basis of inclusion and exclusion criteria, which constituted the study group and were analyzed. Of the 60 cases 47 (78.3%) were males and 13 (21.7%) were females. Three different age groups were <65 years which constituted 40%, between 65-75 years 50% and >75 years 10% comprises the study population. Hypertension, which is the major risk factor for intra-cerebral hemorrhage was identified in 45 (75%) cases of which males and females constituted 35 (77.8%) and 10 (22.2%) respectively (Table-1).

Bleeding volume > 50 ml were seen in 23.3% (14) cases, 30-50 ml in 33.3% (20) cases and < 30 ml in 43.4% (26) cases (Table-2). Total number of death observed was 24 (40%). Upon observing the mortality pattern, patients who suffered bleed volume of >50ml had 85.7% mortality with 100% hypertension. Hypertension can be considered as one of the risk factors because patients with a ICH volume

<table>
<thead>
<tr>
<th>Table 1. Demography of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>24</td>
<td>40%</td>
</tr>
<tr>
<td>65-75</td>
<td>30</td>
<td>50%</td>
</tr>
<tr>
<td>&gt;75</td>
<td>6</td>
<td>10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Number</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male- Hypertension</td>
<td>35</td>
<td>77.8% (p=1.000)</td>
</tr>
<tr>
<td>Female- Hypertension</td>
<td>10</td>
<td>22.2%</td>
</tr>
</tbody>
</table>

There was no significant association between incidence of hypertension and its occurrence according to gender of the patients (P = 1.000).
DISCUSSION:

Cerebrovascular diseases have recently emerged as a major health problem affecting the population including developing countries like India. Its incidence has increased many folds lately with the emergence of several risk factors like coronary artery diseases, diabetes mellitus, hypertension, dyslipidemia and significant contribution from increased life expectancy. Other factors influencing the incidences are smoking, stress and sedentary lifestyle and probably dietary habits. Intra-cerebral hemorrhage can be caused by a variety of etiological factors like head trauma, transformation of prior ischemic lesion, metastatic brain tumors, drugs like cocaine, amphetamine, arteriovenous malformations, amyloid angiopathy and capillary telangiectasias. A 60ml of blood volume is almost fatal to the patient and mortality rate in this group of patients are much higher than comparison with those with smaller volume of ICH. A blood volume of 3cm in diameter carries a poor prognosis, 3cm-1cm in diameter carries a moderate and <1cm in diameter carriers a favorable outcome. Thus volume of blood is one of the factors that can influence the outcome.

In the present series 78.3% cases were males and 21.7% were females, whereas Junshan Zhou et al. reported 64.2% males and 35.8% females in their series of 615 ICH patients.

In the present series 50% patients were in the age group of 65-75 years, which is almost in agreement with the series reported by Togha M and Bakhtavar K who found 69% of subjects between 60 to 80 years of age. In the present series mortality was observed in 40% cases, which is in agreement with the study by Joseph P. Broderick who reported 44% mortality in their series. Flaherty ML et al. in their study reported 31% mortality in 7 days.

In the present study patients with a ICH volume > 50 ml, 30-50ml and <30 ml showed mortality in 85.7%, 40% and 15.4% cases respectively. Joseph P. Broderick in their series reported 30 day mortality in 93%, 64% and 23% in patients with ICH volume >60 ml, 30-60 ml and <30 ml in their series. Salihovic D et al. reported mortality rate of 85%, 62.5% and 36% in ICH volume >60ml, 30-60ml and <30 ml respectively in their series. On literature search no data was found to compare the mortality according the ICH volume >50 ml, 30-50 ml and <30 ml.

According to Molshatzki et al. the mean hematoma volume for a severe stroke was 50.2 ml. The FUNC score by Rost et al. said that the hemorrhage size is used frequently in clinical decisions in patients with ICH, and scores predicting mortality and good functional outcome have been developed using ICH volumes categorized as <30 cm³, 30 to 60 cm³, and >60 cm³. Other number of studies have been undertaken considering 60 ml volume of bleed as a severe mode of stroke presentation, the present series observes that a volume of bleed equivalent to 50 ml or more worsens the prognosis towards a disastrous outcome and as such it was felt that for better awareness on the part of the clinician, a volume of bleed of 50 ml or more should be considered to
bear a fatal outcome especially in the developing countries. All these values are quite different from our observation. Our study suggests that 60 cm$^3$ hematoma volume is too high to call it a severe stroke, if the hematoma is as large as 50 cm$^3$, it can be stamped as severe stroke. This also supports the view of Hemphill et al. in “The ICH score” published in Stroke 2001 where they have mentioned that hematoma volume $>30$ cm$^3$ is an independent poor prognostic factor for 30-day mortality and morbidity$^{18}$. This proposition is in alignment with the views of Hemphill et al.$^{18,19}$ where hematoma volume exceeding 30cm$^3$ was considered an independent poor prognostic factor not only in terms of 30-day mortality and morbidity but also in the longer duration of 1 year functional outcome. However, the present series studied the outcome for shorter period.

In the present series hypertension was significantly associated with the cases having fatal outcome and was detected in all cases with ICH volume $>50$ ml and hypertension was present in 75% of the total cases irrespective of volume of bleed, whereas A H G Rasool et al.$^{25}$ reported hypertension in 90% of patients with acute ICH and reported it as one of the important contributor of mortality in ICH which is similar with the findings of the present study. However the contributing role of hypertension in influencing the presentation, prognosis and outcome in ICH needs to be evaluated in a series comprising of large number of cases vis-a-vis control over an extended duration.

**CONCLUSION :**

ICH is an extremely critical and life threatening condition which may alter the fate of the sufferer in seconds rather than minutes. It is prudent for the clinicians to develop strategies to cope with this menace. Hematoma volume is a significant yard-stick which play a role in developing treatment strategy and influence the functional outcome, prognosis and mortality. It may be worth mentioning that the ICH volume of 50 ml or more is probably as significant as a volume of 60 ml or more determining the clinical severity and mortality in patients with ICH.

**REFERENCES :**

Clinical Profile of Cryptococcal Meningitis: Hospital Based Study

S Bawri*, M Das**, A Kayal***, M Goswami***, L J Basumatary****, P Borah****

Abstract

Background: Cryptococcosis is a fungal infection caused by encapsulated yeast of the genus Cryptococcus and most cases are caused by Cryptococcus neoformans. Material and Method: The aim of the study is to study the clinical profile of cryptococcal meningitis. This is a prospective observational study conducted from September 2014 – September 2016 at Gauhati Medical College. Detailed neurological evaluation along with investigation was done in all the patients. Results and Observations: A total of 16 patients were included among which 10 patients were immunocompromised (7 were HIV positive, 3 on immunosuppressant drug) and 6 were immunocompetant. 13 were male and 3 were female. Mean age was 35 ± 4 years and duration of symptom was 2 weeks ± 4 days/3 weeks ± 5 days for immunocompromised / immunocompetant patients. Most common features were headache(81%), vomiting(75%), altered sensorium(62%), fever(56%), seizure(43%), neck rigidity(93%), Papilloedema(93%). Baseline investigations were normal and Cerebrospinal Fluid(CSF) analysis revealed low to normal sugar and normal protein with normal Adenosine Deaminase and Cryptococcal Antigen was positive in all patients. CD4 counts was <100 in all HIV patients. Computerized Tomography (CT) Scan revealed normal in 6, hydrocephalus in 6 & cerebral oedema in 4 patients. Magnetic Resonance Imaging (MRI) showed leptomeningeal enhancement in 4 & enlarged Virchow Robin spaces in 6 patients. Out of 16 patients, 6 patients succumbed. Conclusion: In the present study, patients presented with headache, vomiting, altered sensorium with positive meningeal signs. On evaluation cryptococcal antigen was positive and Patients were treated with antifungal. All cases of meningitis should be screened for cryptococcal antigen.

Key Words: Cryptococcal Meningitis, Immunocompromised / Immunocompetant patients.

INTRODUCTION:
Cryptococcosis is a fungal infection caused by encapsulated yeast of the genus Cryptococcus. Cryptococcus has a worldwide distribution. Most cases are caused by Cryptococcus neoformans. The incubation period is unknown and transmission is believed to result from inhalation of aerosolized organisms. The management of cryptococcal meningoencephalitis is discussed in 3 risk groups: (1) Human Immunodeficiency Virus (HIV)–infected individuals, (2) organ transplant recipients, and (3) non–HIV infected and non transplant hosts.

AIM OF THE STUDY:
The aim was to study the clinical profile of cryptococcal meningitis.

MATERIAL AND METHOD:
Inclusion criteria
All patients irrespective of age and sex presenting with features suggestive of meningitis with laboratory evidence of Cryptococcus antigen
Exclusion criteria
Patients with tumors, Trauma, previously diagnosed cryptococcal meningitis, bacterial meningitis and viral meningitis.
It is prospective observational study at Gauhati Medical College, Guwahati, a tertiary care hospital in the north east region
It is conducted from September 2014 – September 2016
Detailed neurological evaluation along with routine blood, liver function test, renal function test, electrolytes, VDRL, HIV and chest x-ray done in every patient.
CSF study including total count including differentiating count, sugar, protein, stains for acid fast bacilli, gram’s stain, fungal stain, Adenosine Deaminase, cryptococcal antigen done in every patients.
Neuro-imaging was performed in every patient.
including Computed Tomography (CT Scan) in every patient and Magnetic Resonance Imaging (MRI) done in some patient due to financial constrain.

RESULTS AND OBSERVATION:

- A total of 16 patients were included among which 10 (62.5%) patients were immunocompromised, 7 (43.8%) were HIV positive, 3 (18.76%) on immunosuppressant drug and 6 (37.5%) were immunocompetant.

Table 1: Age Distribution of Patients According To Gender

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Male</th>
<th>Female</th>
<th>All Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upto 20</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>21-30</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>31-40</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>41-50</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>&gt;50</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>3</td>
<td>16</td>
</tr>
</tbody>
</table>

- All immunocompetant patients were harbouring birds (mainly pigeons, hens) at their home, thus having risk of constant exposure.
- Out of 16 patients, 13 (81%) were male and 3 (19%) were female.
- Mean age of patients were 35 ± 4 years
- Mean duration of symptom was 2 weeks ± 4 days for immunocompromised, 3 weeks ± 5 days for immunocompetant patient.

Table 2: Duration of Symptom of Patients

<table>
<thead>
<tr>
<th>Mean duration of symptom</th>
<th>Immunocompromised</th>
<th>Immunocompetant</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks ± 4 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 weeks ± 5 days</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Among 16 patients studied, most common features were headache: 13/16 (81%), fever: 9/16 (56%), vomiting: 12/16 (75%), altered sensorium: 10/16 (62%), seizure: 7/16 (43%), neck rigidity: 15/16 (93%), Papilloedema: 15/16 (93%), paresis: 1/16 (6%).
- Baseline routine blood along with liver function test, renal function test and electrolytes were normal. Chest– X Ray showed increased Brocho-Pulmonary Vascular marking in 9/16 (56%) patients, fibrotic band in left upper zone in 1/16 (6%) patient and no abnormality detected in 6/16 (37%) patients.
- CSF analysis revealed pleocytosis with low to normal sugar and normal protein with normal Adenosine Deaminase and Cryptococcal Antigen was positive in all patients (more than 1000 in 11 patients (68%) and less than 1000 in 5 (31%) patients). CD4 counts among 7 HIV patients was below 100 in all patients.

CT Scan Brain revealed normal in 5 (31%), hydrocephalus in 6 (37%) and cerebral oedema in 4 (25%) patients. MRI Brain showed leptomeningeal enhancement in 4 (25%) and enlarged Virchow-Robin spaces in 6 (37%) patients.

Table 3: CSF Finding of Patients

<table>
<thead>
<tr>
<th>Average</th>
<th>Immunocompromised</th>
<th>Immunocompetant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total count</td>
<td>15/cu mm</td>
<td>20/cu mm</td>
</tr>
<tr>
<td>Differential count</td>
<td>Pred. Neutrophils</td>
<td>Pred.lymphocytes</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>30 ±6</td>
<td>55 ±6</td>
</tr>
<tr>
<td>Protein (mg/dl)</td>
<td>65 ±10</td>
<td>55 ±10</td>
</tr>
<tr>
<td>Stains</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Antigen titre</td>
<td>More than 1000</td>
<td>Less than 1000</td>
</tr>
</tbody>
</table>

A: CT Scan shows mild ventriculomegaly and sulcal effacement.
B: Contrast-Enhanced, Axial T1-weighted MRI shows Leptomeningeal enhancement.
Patients were started with inj amphotericin and maintained on fluconazole /voricanazole.

Out of 16 patients-Total 6 (37.50%) patients, 4(25%) patients among immunocompromised (HIV Positive) and 2(12.5%) patient among immunocompetant succumbed.

**DISCUSSION:**

Cryptococcus neoformans is encapsulated yeast first described in 1894, whose infection can induce a wide spectrum of clinical manifestations that range from a harmless colonization of the airways and asymptomatic infection to meningitis or disseminated disease. It is most commonly found in the debris around pigeon roosts, decaying wood and soil contaminated with pigeon or chicken droppings. This infection is fatal without treatment. Therefore, rapid diagnosis and treatment is required to decrease fatality.

In the present study, Out of 16 patients, 10(62.5%) patients were immunocompromised -7 (43.8%) were HIV positive, 3(18.7%) on immunosuppressant drug (2 patients were post renal transplant patients and 1 patient was Neuromyelitis Optica) and 6(37.5%) were immunocompetant. All immunocompetant patients were harbouring birds (mainly pigeons, hens) at their home thus having risk constant exposure.

Most common differentiating feature in the immunocompromised and immunocompetant group were headache (70% vs 100%), fever-(50% vs 60%), vomiting-(60% vs 100%), altered sensorium-(70% vs 50%), seizure(50% vs 33%), neck rigidity (90% vs 100%), Papilloedema (90% vs 100%), paresis (6% vs 0%).

On evaluation, patients had normal routine blood examination along with liver function test, renal function test and electrolytes. CD 4 count was below 100 in all HIV patients. CSF analysis revealed pleocytosis with low to normal sugar and normal protein with normal Adenosine Deaminase and Cryptococcal Antigen was positive in all patients (more than 1000 in 11 patients (68.75%) and less than 1000 in 5(31.25%) patients). All the immunocompromised group of patients had Cryptococcal Antigen more than 1000. One patient in the immunosuppressant group who had solid organ transplant (two years after post renal transplant had titre of more than 2500). Raised intracranial pressure was managed with repeated lumbar puncture, 20% Mannitol. Patients were started with an induction phase followed by maintenance therapy or secondary prophylaxis to prevent relapse on fluconazole /voricanazole. Acute (induction) regimen consists of amphotericin B (0.5 to 0.7 mg/kg/day) for 2 weeks and maintained on fluconazole 200mg twice daily in 12(75%) patients and 4(25%) patients were maintained on voricanazole 200 twice daily. But with treatment, renal profile and electrolytes become deranged in 10/16 (62.50%) in amphotericin group and liver profile was abnormal in fluconazole /voricanazole in 8/16(50%) patients.

One patient in the immunosuppressant group who had solid organ transplant (two years after post renal transplant had titre of more than 2500) was treated with liposomal amphotericin (4mg/kg/day) but the patient still had severe electrolyte imbalance (hypokalemia and hypomagnesaemia). Patient also received tacrolimus whose dose was decreased because of possible drug interaction after which electrolytes were improved. Out of the 7 HIV positive, one patient was put on antituberculous drug four months before the patient was diagnosed because of pulmonary tuberculosis and at time patient was screened for cryptococcal infection and CD 4 Count was 280/ml.

Out of 16 patients-Total 6 (37.50%) patients, 4(25%) patients among immunocompromised group and 2(12.5%) patients among immunocompetant succumbed.

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>81%</td>
<td>73%</td>
<td>88%</td>
<td>67%</td>
<td>80%</td>
<td>68.96%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>75%</td>
<td>42%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>51.72%</td>
</tr>
<tr>
<td>Fever</td>
<td>56.25%</td>
<td>45%</td>
<td>68%</td>
<td>86%</td>
<td>86.6%</td>
<td>58.62%</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>62%</td>
<td>28%</td>
<td>29%</td>
<td>29%</td>
<td>26.6%</td>
<td>37.93%</td>
</tr>
<tr>
<td>Neck rigidity</td>
<td>93%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Papilloedema</td>
<td>93%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Seizures</td>
<td>43%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6.89%</td>
</tr>
<tr>
<td>Motor deficits</td>
<td>6%</td>
<td>-</td>
<td>28%</td>
<td>-</td>
<td>-</td>
<td>1%</td>
</tr>
</tbody>
</table>

| Table-5: - Clinical Features in Immunocompromised and Immunocompetant of Patients |
|--------------------------------------|-------------------------|-------------------------|
| Features                             | Immunocompromised (n=10) | Immunocompetant (n=6) |
| Headache                             | 70%                     | 100%                    |
| Vomiting                             | 60%                     | 100%                    |
| Fever                                | 50%                     | 60%                     |
| Altered sensorium                    | 70%                     | 50%                     |
| Neck rigidity                        | 90%                     | 100%                    |
| Papilloedema                         | 90%                     | 100%                    |
| Seizures                             | 50%                     | 33%                     |
| Motor deficits                       | 6%                      | 0%                      | 6%                      |
patient among immunocompetent succumbed. Cause of Death in 4 (25%) was aspiration pneumonia, sepsis (3 in immunosuppressant and 1 in immunocompetent group), 2/16 (12.5%) had intractable seizure (1 each in immunosuppressant and immunocompetent group).

In the study by Satishchandra et al\textsuperscript{10,11}, the incidence of cryptococcal meningitis (31.9%) was at par with tuberculous meningitis (32.2%) in HIV patients. Mortality from HIV associated cryptococcal meningitis remains high in many countries due to multiple factors. Some of them include the insufficiency of antifungal drugs, and the complications such as raised intracranial pressure. The poor prognostic factors are depressed level of consciousness, signs of raised intracranial pressure, depressed CSF cell counts and glucose levels and CSF cryptococcal antigen titre > 1024.

In the present study, mortality was 37.5%. In the study done by Khanna et al\textsuperscript{12}, mortality was 32.18%. In the present study, the poor prognostic factors\textsuperscript{13,14} included altered sensorium, and CD4 count of less than 50/ml. This is in concordance with various other studies which have shown that altered sensorium is associated with poor prognosis. Response to therapy with amphotericin B and fluconazole was good and recovery was seen in 62.5% of the patients.

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1. Cryptococcal Meningitis: Claudia Fabrizio, Sergio Carbonara and Gioacchino Angarano Clinic of Infectious Diseases, University Of Bari, Italy.
4. Madhusudan NS “Demographic, Laboratory and Immunological Profile of HIV Seropositive Cryptococcal Meningitis”. Journal of Evolution of Medical and Dental Sciences 2014 March 17: 3(11): 2720-2726
Complication Profile of Diabetes Mellitus in a Tertiary care Hospital in Upper Assam

P Dihingia*, S M Baruah**, T K Das**, C Dutta***, T Karthikeyan****

Abstract

Background: Chronic complications are the major outcome of type 2 diabetes mellitus, which reduce the quality of life of patients, incur heavy burdens to the health care system, and increase diabetic mortality. The aims of this study were to describe the prevalence of chronic complications among both urban and rural population admitted in the ASSAM MEDICAL COLLEGE, a tertiary care hospital in upper Assam. Material & Methods: This cross-sectional hospital-based study was carried out in the patients admitted in a medical unit of a Tertiary care centre. The survey was conducted for a period of one year from March 2016 to Feb 2017 among the diabetes patients. The subjects were assessed clinically and informations were obtained from the routine Diabetic profile. Results: In our study, among the complications of Diabetes Mellitus, the most prevalent complication is Nephropathy (55.6%) followed by neuropathy (34.7%), retinopathy (19.1%), Cerebrovascular Accident (7.1%), Hyperglycaemic Hyperosmolar State (5.98%), Coronary Artery Disease (5.3) and diabetic Ketoacidosis (3.5%). Compared to other Indian studies nephropathy was found to the most common complication in our study. Conclusions: Chronic complications are highly prevalent among type 2 diabetic patients; in our part of the country. Nephropathy is found to be more prevalent. The glycaemic control of diabetic patients with chronic complications are poor, and future efforts should be directed at intensive blood glucose control, strengthening early diagnosis and improving case management to prevent and minimize the occurrence of complications. The high prevalence of Nephropathy alike rest of the world should be considered as a curtain raiser for a larger study in this regard.

Keywords: Glycemic Control, Neuropathy, Nephropathy, Retinopathy.

INTRODUCTION:

Diabetes mellitus (DM) is a major public health problem depicting a rising prevalence worldwide. India is one of the epicentres of the global diabetes mellitus pandemic. Rapid socioeconomic development and demographic changes, along with increased susceptibility for Indian individuals, have led to the explosive increase in the prevalence of diabetes mellitus in India over the past four decades.

DM is the leading cause of end-stage renal disease (ESRD), nontraumatic lower extremity amputations, and adult blindness. It also predisposes to cardiovascular diseases. With an increasing incidence worldwide, DM will be likely a leading cause of morbidity and mortality in the future.

In prediction, India along with China will account for nearly a third of the estimated 300 million adult diabetics by the year 2025.

AIMS AND OBJECTIVES:

· To find the profile of complications of Diabetes mellitus
· To correlate HbA1c with disease duration.

REVIEW OF LITERATURE:

Diabetes-related complications affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease. Diabetes-related complications can be divided into vascular and nonvascular complications and are similar for type 1 and type 2 DM. The complications, affecting the eyes, kidneys, and peripheral nervous system, were collectively called microvascular complications, to distinguish them from the less diabetes-specific but highly prevalent macrovascular disease complications. Microvascular disease and peripheral neuropathy resulted in blindness, kidney failure, and amputations.

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The microvascular complications of both type 1 and type 2 DM result from chronic hyperglycemia. Evidence implicating a causative role for chronic hyperglycemia in the development of macrovascular complications is less conclusive. CAD events and mortality rate are two to four times greater in patients with type 2 DM and correlate with fasting and postprandial plasma glucose levels as well the hemoglobin A1c (HbA1c)\textsuperscript{6}.

The Diabetes Control and Complications Trial (DCCT) showed that keeping blood glucose levels as close to normal as possible slows the onset and progression of the eye, kidney, and nerve damage caused by diabetes. In fact, it demonstrated that any sustained lowering of blood glucose, also called blood sugar, helps, even if the person has a history of poor control\textsuperscript{6}.

**MATERIAL AND METHODS:**

**PLACE OF STUDY:**

Medical unit 5, Assam Medical College and Hospital.

**DURATION OF STUDY:**

One year (March 2016 to Feb 2017).

**DESIGN OF THE STUDY:**

Observational cross sectional study

**Inclusion Criteria:**
- All Diabetes Mellitus patients admitted in Medicine unit 5 at Assam medical College and hospital, who fulfill the American Diabetes Association criteria (2014), was taken up for the study.

**Exclusion Criteria:**
- Age less than 13 years
- Pregnancy
- Malignancy
- Secondary Hyperglycaemia
- Not giving consent for study

**Routine Investigation:**
- FBS
- PPBS
- RFT
- HBA1C
- Urine R/E
- NCS (optional)
- 24 hour urine protein (optional)

**RESULTS:**

The total population of the study was 167 individuals, aged 13 years and above who gave consent to participate in the study. Among them 117 were males and 50 were females. Mean age of males and females among the participants were 54 and 56.82 years respectively.

**DISCUSSION:**

Nephropathy is a common complication observed in our study in contrast to other similar studies in different parts of India like Ramachandran et al which showed retinopathy, nephropathy, neuropathy were common complications viz 23.7%, 5.5%, 27.5% respectively\textsuperscript{2}. Another study done in Uttar Pradesh showed prevalence of neuropathy was 20.26%, retinopathy 15.36%, and nephropathy 5.56%\textsuperscript{11}. A study done in rural Goa showed...
HHS, DKA 4 patients had neuropathy and 2 had nephropathy 1 had retinopathy. Also the increase in the prevalence of the complications had temporal correlation with the disease duration and the glycosylated haemoglobin level. One major limitation of our study is the high prevalence of the haemoglobinopathy in this part of the world, so the comparison of the HbA1c may not be of international standard.

The reason for the high prevalence of the Nephropathy in this region is not clear which need further interventional studies.

REFERENCES:


**Table 2: Prevalence of Various Complications**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of Cases</th>
<th>Percentage of Prevalance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephropathy</td>
<td>93</td>
<td>55.6</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>58</td>
<td>34.7</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>32</td>
<td>19.1</td>
</tr>
<tr>
<td>CVA</td>
<td>12</td>
<td>7.1</td>
</tr>
<tr>
<td>HHS</td>
<td>10</td>
<td>5.98</td>
</tr>
<tr>
<td>CAD</td>
<td>9</td>
<td>5.3</td>
</tr>
<tr>
<td>DKA</td>
<td>6</td>
<td>3.5</td>
</tr>
</tbody>
</table>

**Table 3: Correlation between disease duration (in years) and HbA1c (%) of patients with different complications:**

<table>
<thead>
<tr>
<th>COMPLICATIONS</th>
<th>r values</th>
<th>p value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephropathy</td>
<td>0.112</td>
<td>0.287</td>
<td>NS</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>0.160</td>
<td>0.167</td>
<td>NS</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>0.291</td>
<td>0.149</td>
<td>NS</td>
</tr>
<tr>
<td>CVA</td>
<td>0.111</td>
<td>0.732</td>
<td>NS</td>
</tr>
<tr>
<td>HHS</td>
<td>0.087</td>
<td>0.811</td>
<td>NS</td>
</tr>
<tr>
<td>CAD</td>
<td>0.320</td>
<td>0.402</td>
<td>NS</td>
</tr>
<tr>
<td>DKA</td>
<td>0.681</td>
<td>0.137</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Table 4: Correlation between disease duration (in years) and HbA1c (%) of patients with Triopathy**

<table>
<thead>
<tr>
<th>Patients with Triopathy</th>
<th>r values</th>
<th>p value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.171</td>
<td>0.484</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Nephropathy was found to be the most common complication in our study.
Physical Factors of Carcinogenesis

P S Roy* , A Inamdar** , T Nyodu*** , M Hazarika****

Key words: Environmental factors, physical factors, carcinogenesis.

INTRODUCTION:

The first observation in the natural history of carcinogenesis concerning the intervention of a substance in the appearance of a tumor belongs to Sir Percival Pott, from 1775, who understands that there is a relation between soot and the appearance of scrotal cancer in chimney-sweeps. In 1977, four researchers, Muir, Higginsi, Doll and Peto explained the evidences from epidemiological studies that 80% of all cancers were caused by environmental factors.

Current understanding of biological mechanisms of carcinogenesis suggests that all cancers are originated from both environment and genetics, implying that there are multiple external factors combined with internal genetic changes responsible for cancer. Prevention of the disruption of cellular signalling and protective pathways can be accomplished by preventing carcinogenic exposures from outside the body from any source. Prevention of carcinogenic exposures is still a major priority. Also, individuals with particular genetic predispositions may be more susceptible to the effects of environmental exposures than others.

Among the key environmental factors are chemical carcinogens, physical carcinogens, infectious agents and lifestyle. Physical carcinogens are highly variable in their chemical structure, and many of them are poorly understood. Some physical carcinogens are naturally occurring, while others are synthetic. Physical carcinogens include fibers, particulate matter, hard and soft synthetic materials and gels.

No specific pathway has been isolated that correctly identifies the way physical agents cause cancer. Most likely, cancer can be caused by a variety of different pathways. Primary targets for physical factors include cellular regulatory proteins which are essential for control of cell growth, DNA repair and programmed cell death. Among molecular targets on carcinogenesis are somatic mutation (genetic changes) and aberrant DNA methylation (epigenetic changes) at the genomic level and the post-translational modifications at protein level. To complicate matters, some physical carcinogens act in concert with genetic factors and other environmental agents to produce cancer. For instance, asbestos can cause cancer on its own; however, it has much stronger carcinogenic potential when combined with exposure to cigarette smoke.

Following are considered as physical factors of carcinogenesis: Ionizing radiation, Non-ionizing radiations (e.g., Ultraviolet light, Radiofrequency and microwave radiation, Electromagnetic fields), Asbestos and Nanoparticles.

Ionizing Radiation (IR):

Ionizing Radiation is defined as radiation that has sufficient energy to ionize molecules by displacing electrons from atoms. IR can be electromagnetic, such as X-rays and gamma rays, or can consist of particles, such as electrons, protons, neutrons, alpha particles, or carbon ions. Natural sources of IR make up about 80% of human exposure and medical sources make up about 20%. Of the natural sources, exposure to radon is the most significant exposure risk to humans.

It is clear from epidemiologic studies of radiation workers, survivors of atomic bomb and Chernobyl victims that IR can induce cancer*. The incidences of solid tumours, such as breast, ovary, bladder, lung, and colon cancers, were estimated to have increased by a factor of
in the exposed group during this time period. The epidemiology studies following the nuclear power plant disaster in Chernobyl showed a clear increase in thyroid cancer as early as 4 years after the accident. Young children were most vulnerable to radiation exposure. The largest source of radiation exposure to the population is radon, which is a natural radioactive gas. Another important source of human exposure to IR is medical X-ray devices, and there is a growing concern about the dramatically increased use of whole body CT scans for diagnostic purposes. For a typical CT scan, a patient will receive about 100-fold more radiation than from a typical mammogram. Cancer patients who receive radiation therapy are at risk of developing secondary tumours induced by the radiation therapy treatment. The most sensitive tissues for the development of secondary cancer have been found to be bone marrow (leukaemia), the thyroid, breast, and lung.

Electromagnetic radiation, such as X-rays or gamma rays, are sparsely ionizing and therefore classified as low linear energy transfer (LET) radiation, whereas particulate radiation, such as neutrons, protons, and alpha particles, are examples of high LET radiation. The biologic effects of IR are due to the local deposition of energy in radiation tracks. The distance between the depositions of energy is biologically very relevant and unique to the energy and the type of radiation.

The direct and indirect effects of radiation induce more or less identical types of lesions in DNA. Radiation-induced lesions consist of more than 100 chemically distinct base lesions, such as the mutagenic lesions thymine glycol and 8-hydroxyguanine. Furthermore, damage to the sugar moiety in the backbone of DNA and some types of base damage can result in single-strand breaks (SSB) or double-strand break (DSB). It has been estimated that 1Gy of ionizing radiation gives rise to about 40 DSBs, 1,000 SSBs, 1,000 base lesions, and 150 DNA-protein cross-links per cell. DSBs are the critical lesions that lead to cell lethality following exposure to ionizing radiation.

Terminally differentiated and stationary cells, such as kidney, lung, brain, muscle, and liver cells, are generally more resistant to radiation-induced killing than are cells with a high turnover rate, such as different epithelial cells, spermatogonia, and hair follicles. IR can induce cell death in tissues by many different mechanisms. Cell death induced by IR may in some cases be associated with autophagy, also called autophagocytosis, in which cells degrade cellular components via the lysosomal machinery. Finally, tissue can undergo necrotic cell death following exposure to IR.

**Medical exposure to ionizing radiation**

The medical applications of ionizing radiation have greatly expanded worldwide due to an increasing use of X-rays in diagnostic imaging and interventional radiology, the development of new technologies using radiopharmaceuticals for diagnosis and treatment in nuclear medicine, and the multiple applications of X-rays, gamma-rays and charged particles in radiotherapy. Radiation induced cancer risk increases with doses, with higher risk for children and young people, as they are significantly more sensitive to radiation exposure than adults. Epidemiological studies in humans demonstrate that ionizing radiation can give rise to cancer in multiple anatomical sites: leukaemia (short latency) and tumours in solid organs (long latency: bone, lung, liver, thyroid, breast, etc).

**Ultraviolet light**

Depending on the wavelength, UV light is categorized into UVA (320 to 400 nm), UVB (290 to 320 nm), and UVC (240 to 290 nm) radiation. Most of the UVC light emitted from the sun is absorbed by the ozone layer in the atmosphere, and, thus, living organisms are mostly exposed to UVA and UVB irradiation.

UVC light is more damaging to DNA than UVA and UVB because the absorption maximum of DNA is around 260 nm. The formation of these lesions results in the bending of the DNA helix, resulting in the interference with both DNA and RNA synthesis which in turn can form SSBs and base lesions in DNA of exposed cells.

The incidence of skin cancer, especially melanoma, is on the increase due to higher rates of sun exposure in the general population. Risk of contracting melanoma appears to be linked to high sunlight exposure during childhood. UV light can initiate carcinogenesis by inducing DNA lesions as well as suppressing the immune system, resulting in a greater probability that initiated cells survivability and growth into tumours. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the two most common skin cancer types. BCC and SCC occur predominantly in sun-exposed areas of the skin. The tumour suppressor genes p53 and p16 are frequently inactivated in BCC and SCC.
Radiofrequency and Micro wave radiation:

Radiofrequency radiation (RFR) is electromagnetic radiation in the frequency range between 3 kHz to 300 MHz; whereas microwave radiation (MR) is in the frequency range between 300 MHz to 300 GHz. RFR and MR do not have sufficient energies to cause ionizations in target tissues. Rather, the radiation energy is converted into heat as the radiation energy is absorbed. Sources of radiofrequency and microwave radiation include mobile phones, radio transmitters of wireless communication, radars, medical devices, and kitchen appliances.

Because human exposure to RFR has increased dramatically in recent years, it is important to know whether this type of radiation gives rise to genotoxic damage. One confounding factor when assessing the genotoxic effect of RFR, and MR, is the heating effect that affects the tissue when the radiation energy is absorbed. A recent study controlling for the potential heating effect of exposure found that RFR induces DNA damage in human spermatozoa in-vitro, which is an alarming finding. It has been suggested that MR may affect the folding of proteins in cells that promote new protein synthesis.

A number of studies have focused on the potential cancer risks from mobile phone usage, and some of these studies indicate that long-term mobile phone usage may be associated with increased risks of developing brain tumours. Some studies have shown a connection between proximity to mobile phone base stations and increased cancer incidence, whereas another study found no association between exposure to RFR from mobile phone base stations and early childhood cancers.

Electromagnetic fields:

An electromagnetic field (EMF) is a physical field produced by electrically charged objects that can affect other charged objects in the field. Typical sources of EMFs are electric power lines, electrical devices, and magnetic resonance imaging (MRI) machines.

A low frequency EMF does not transmit energy high enough to break chemical bonds therefore; it is not thought to directly damage DNA or proteins in cells. EMFs have been shown to induce nongenotoxic effects in cells, such as interference with cellular signalling pathways which could contribute to neurodegeneration.

There is no strong link between EMF exposure and increased risks of contracting adult leukaemia, brain tumours, or breast cancer. Furthermore, a study investigating whether EMF exposure was associated with heritable effects found no correlation between parental exposure and childhood cancer.

Asbestos:

Asbestos is the generic name for a group of naturally occurring inorganic fibrous silicates that have been widely used in building materials for its heat, sound, and electrical insulating qualities. Asbestos becomes a serious health hazard if the fibres are inhaled over a long period of time, and these health effects are increased dramatically if the exposed individual is a smoker. It was first reported in 1935 that asbestos might be an occupational health hazard that could induce cancer. The use of asbestos products peaked in the 1970s, yet remains a major health hazard in many places around the world today. Asbestos exposure account for the largest proportion of occupational cancers.

Asbestos fibres can enter cells and induce reactive oxygen species (ROS). ROS have been implicated to originate from affected mitochondria leading to induction of SSBs and base damage. If not successfully repaired, asbestos-induced DNA damage has been shown to result in chromosome aberrations, micronuclei formation, and increased rates of sister chromatid exchanges.

Lung Cancer:

Epidemiologic studies have found a strong link between asbestos exposure and lung cancer. It has been estimated that about 5% to 7% of all lung cancers are attributable to asbestos exposure; and asbestos and tobacco smoking act in synergy to induce lung cancer.

Mesothelioma:

After being taken up by lung tissues, asbestos fibres can translocate into the pleura which are covered with a protective lining, the mesothelium, which consists of squamous-like epithelial cells. Mesothelial cells can internalize asbestos fibres, resulting in the induction of ROS and inflammatory responses, subsequently leading to the initiation and progression of malignant mesothelioma.

Nanoparticles:

Nanoparticles are defined as ultrafine particles of the size range 1 to 100 nm in diameter. The production of nanoparticles has increased dramatically in recent years,
and they are found in many industrial and consumer products such as paint, cosmetics, and sunscreens. They also have many potential medical applications, such as delivery vehicles for specific drugs to specific target tissues or tumours.

Many of the cellular effects of nanoparticles are similar to the effects exerted by asbestos, such as the generation of ROS and inflammation. Nanoparticles have been shown to induce oxidative DNA damage, such as DNA strand breaks and 8-hydroxyguanine lesions both in cell culture and in vivo. Nanoparticles have also been found to affect the immune system and can induce the release of the pro-inflammatory cytokine TNF-α from cells. Some nanoparticles, such as titanium dioxide, which is used as pigments in paint, have been classified by the International Agency for Research on Cancer (IARC) as a group 2B carcinogen (possible carcinogenic to humans). However, rigorous epidemiologic data is lacking to fully evaluate the cancer-inducing potential of nanoparticles.

CONCLUSION:

Evidence from various studies either confirms or implicates role of environmental factors in the development of a wide range of malignancies by stimulating intracellular signaling pathways. Although, no specific pathway has been isolated that correctly identifies the way physical agents cause cancer, intracellular DNA is the target of most of the physical agents. Some physical carcinogens act in concert with genetic and other environmental factors to produce cancer. Prevention of the disruption of cellular signaling can be accomplished by preventing carcinogenic exposures. However, prevention of carcinogenic exposures is still a major priority and is considered as a major public health concern.

Acknowledgments: The authors declare that there is no conflict of interests.

REFERENCES:
Kartagener’s Syndrome: Case Presentation

B Hazarika*, R Korwa**

Abstract
Kartagener’s syndrome, a rare autosomal recessive genetic ciliary disorder is a part of the subset of Primary ciliary dyskinesias (PCD). It comprises the triad of situs inversus, chronic sinusitis, and bronchiectasis and has a variable genetic heterogeneity. We report a rare case of the syndrome in a female with preserved fertility.

Keywords: Primary ciliary dyskinesias, Situs inversus, Chronic sinusitis, Bronchiectasis

INTRODUCTION:
Kartagener’s syndrome (KS) belongs to group of primary ciliary dyskinesias (PCDs). A genetic condition with an autosomal recessive inheritance, comprising a triad of situs inversus, bronchiectasis and sinusitis. In 1904 Siewart first described this condition. Etiological correlation between the elements of the triad was recognised by Kartagener and reported four cases in 1933. The estimated prevalence of PCD is about 1 in 30,000, though it may range from 1 in 12,500 to 1 in 50,000. Ultrastructural genetic defect leads to impaired ciliary motility which is responsible for manifestations of disease including infertility. Here we report a case of female of Kartagener’s syndrome whose fertility was preserved, a rare entity which led to delayed diagnosis of the same.

CASE REPORT:
A 54-years-old female presented with complaints of productive cough with profuse expectoration, low grade fever since 1 month. She has recurrent rhinosinusitis and cough with expectoration and low grade fever since childhood which subsides on taking medication. The patient had been married for 30 years and she has two sons. There was no history of breathlessness, wheezing, hemoptysis or loss of weight. There was no history of similar illness in other members of his family. Clinical examination of the patient revealed average build with no pallor, pedal edema, clubbing or lymphadenopathy. Patient was febrile 99.6°F, pulse rate 104 beats per minute, respiratory rate 20 cycles/min and normal blood pressure 120/70 mmHg in right arm in supine position. Apex beat was localised to right fifth intercostal space (ICS) on mid-clavicular line; and liver dullness was on left side in 5th ICS on percussion–findings suggestive of situs inversus. On chest auscultation, bilateral, lower zone, coarse crepitations were present on inspiration as well as expiration. Routine blood tests did not reveal any significant abnormality except for leucocytosis and raised ESR. Sputum culture was negative for acid-fast bacilli, and microbiology. Chest radiography with bronchography after using diansol dye (propylidone) showed dextrocardia with the aortic arch lying on right side of the trachea with cystic bronchiectatic changes seen in both lower zones and midzones (Figure:1).

*Assistant Professor, **PGT, Department of Pulmonary Medicine, Assam Medical College, Dibrugarh Correspondence Address: Dr. Basanta Hazarika, Department of pulmonary medicine, Gauhati Medical College, Guwahati-781023 Assam, India. E-mail: drbasantahazarika@yahoo.com

Figure: 1: PA view chest with bronchography
CT scan of paranasal sinuses showed mucoperiostial thickening in the sinuses indicating chronic sinusitis (Fig:2)

HRCT (High resolution computed tomography) of chest showed bronchiectatic changes in left lingula, and right middle lobe. (Fig:3)

Spirometry of the patient showed FEV1/FVC to be 65% of predicted values, suggestive of obstructive pattern with little improvement after bronchodilators. The ‘nasal saccharin transit time’ test gave mucociliary clearance time of 60 minutes (Normal < 30 minutes). Ultrastructure study of nasal cilia via electron microscopy could not be carried out. Thus, Kartagener’s syndrome was diagnosed clinically. Patient was started on antibiotics, mucolytics and chest physiotherapy and improved dramatically.

DISCUSSION:
Primary ciliary dyskinesia (PCD) is a genetic disorder of cilia structure and function, chronic infections of the respiratory tract, fertility problems and disorders of organ laterality. Kartagener described four cases with features of bronchiectasis, sinusitis, and situs inversus in 1933, though the first case was described by Siewert in 1903.

The clinical features of PCD have been described in primary ultrastructural defects in cilia. Axoneme, key component of the cytoskeleton has a characteristic nine plus two arrays of microtubules. Nexin links and spokes seem to provide structural rigidity to the axoneme. Dynein arms contain most of the ATPase activity of the axoneme, and are important in releasing energy for sliding and bending of microtubules and ciliary motion.

Mucociliary transport in the respiratory tract is important for normal respiratory function and resistance to respiratory infection. Abnormalities in dynein arms or radial spokes, microtubules or ciliary orientation prevent normal transport of mucus from the bronchial tree to the mouth and result in serious impairment of the lungs defence systems.

The mode of inheritance is autosomal recessive with variable phenotypic expressions. The diagnostic criteria recommended for this syndrome are history of chronic bronchial infection and rhinitis from early childhood, combined with one or more of following features: - (a) situs inversus or dextrocardia in a patient or a sibling, (b) living but immotile spermatozoa, (c) tracheobronchial clearance which is absent or nearly so, and (d) cilia that have ultra structural defects characteristic of the syndrome. About 50% of the people affected with primary ciliary dyskinesia have situs inversus, so fit in the criteria of Kartagener’s syndrome.
Screening tests like Exhaled nasal nitric oxide (ENNO) measurement (usually low in PCD) and Saccharin test to assess mucociliary function of nasal epithelium (which is delayed in Kartagener’s) can be done. Diagnostic tests like electron microscopic confirmation of the ultrastructural ciliary defect and video recording for ciliary beat pattern and frequency analysis are done. Adult females reported a range of fecundity, some achieving pregnancy with no difficulty, others reporting consistent infertility despite unprotected intercourse.7,8

Female patient in our case did not have fertility issues and had diagnosis of the syndrome considerably late representing the fact that kartagener’s syndrome has a variable phenotypic presentation. Due to lack of facilities for ENNO and electron microscopic study, in our case diagnosis was made clinico-radiologically.

CONCLUSION:

Kartagener’s syndrome (KS) is a rare disease belongs to group of primary ciliary dyskinesias (PCDs). This disease comprising a triad of situs inversus, bronchiectasis and sinusitis. Treatment with antibiotics, physiotherapy and appropriate surgical intervention has improved the prognosis in these patients and, in many cases, lifespan may be normal. Early diagnosis is important. Once bronchiectasis is established, prognosis worsens significantly.

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Sheehan’s Syndrome Presenting as Cardiac Tamponade

R Choudhury*, J. Idiculla**, R Pradeep***

Abstract
Cardiac involvement in Sheehan’s syndrome is rarely observed. We report a case of massive pericardial effusion in a patient with partial empty sella secondary to post-partum necrosis of the pituitary.

INTRODUCTION:
First described in 1937, Sheehan’s syndrome occurs due to pituitary necrosis consequent to severe blood loss and hypovolemia’. Though the prevalence rate of this condition was as high as 10-20 per 100,000, half a century ago, with advancements in medicine, it has come down in developed countries. In India, a study from Kashmir estimates that more than 3% of women above the age of 20 years may be affected with post-partum pituitary necrosis’. The various hormone deficiencies may result in multitude of symptoms ranging from lactational failure to pancytopenia’.

CASE:
A 33 year old presented with abdominal distension 2 weeks after a lower segment Caesarean section. The surgery was at 8 months of gestation in view of pre-eclampsia. She had two more children from her previous pregnancies which were uneventful. On examination, her pulse rate was 102 per minute and blood pressure 100/70 mm Hg in the right upper limb and the saturation at room air was 98%. The jugular venous pulse was elevated (7 cm) above the sternal angle. The heart sounds were muffled on auscultation and there was shifting dullness in the abdomen. She gave a history of failure to lactate since delivery. The initial investigations revealed mild anaemia (Hb 10.8 gm%) with normal white cell and platelet counts. The serum creatinine and liver enzymes were normal. There was hypoalbuminemia and hyponatremia. The X-ray Chest showed cardiomegaly and in the electrocardiogram low voltage complexes were seen with T wave inversion in all the leads. The echocardiogram revealed massive pericardial effusion with cardiac tamponade (Fig 1). Table 1 presents analysis of the aspirated pericardial fluid. On evaluation of hyponatraemia, the thyroid hormones were low: free

<table>
<thead>
<tr>
<th>Table 1: Pericardial Fluid</th>
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<tbody>
<tr>
<td>TC: 2100</td>
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<tr>
<td>DC: N1 L99</td>
</tr>
<tr>
<td>Total protein: 3.3 g/dl (&gt;0.5 times serum total protein)</td>
</tr>
<tr>
<td>Albumin: 1.7 g/dl</td>
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<tr>
<td>Glucose: 130 mg/dl</td>
</tr>
<tr>
<td>LDH: 146 U/L</td>
</tr>
<tr>
<td>ADA: 1.5T U/L (0-40)</td>
</tr>
<tr>
<td>AFB: Negative</td>
</tr>
<tr>
<td>C &amp; S: No growth</td>
</tr>
<tr>
<td>Malignant cells: Negative</td>
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Figure 1: Chest X-Ray
Cardiomegaly
T3 1.65 (2.3-4.2 pg/ml normal) and free T4 0.65 (0.8-1.7 ng/dl normal) with an inappropriately normal TSH of 0.71 (0.3-5.5uIU/l normal). This along with low a.m. Cortisol 1.04 ug/dl along with l-thyroxine. She improved symptomatically and a repeated echo prior to discharge showed resolution of the effusion. Though the patient did not undergo imaging of the pituitary gland during the hospital stay, this was done at the first OPD visit (Fig 2) which showed a partial empty sella with thinned out pituitary gland. She remains euthyroid now with normal electrolytes and blood pressure.

**DISCUSSION:**

The case described above demonstrates a very uncommon presentation of Sheehan’s syndrome. The cardiac manifestations of hypothyroidism include diastolic hypertension, coronary artery disease, narrow pulse pressure and pericardial effusion. When there is co-existent Hypocortisolism this may be a low pressure phenomenon with absent pulses paradoxis and mildly elevated JVP. Our patient had similar features with low levels of thyroxine and cortisol.

Pericardial effusion in central hypothyroidism is extremely rare and only few cases have been described and Sheehan’s syndrome with such a clinical picture is even more uncommon. The mechanisms include increased capillary permeability, slow lymphatic drainage and enhanced avidity for salt and water. The fluid is straw coloured with high lymphocyte count and protein content as in our patient.

The response to treatment is dramatic on replacement of deficient thyroxine. While replacing this, it is extremely important to ensure steroid replacement in adequate doses to prevent adrenal crisis in patients with dual hormone deficiency. Rarely cholesterol crystals can precipitate while on treatment with thyroxine, resulting in pericarditis.

**CONCLUSION:**

Though Sheehan’s syndrome is a relatively common cause of hypopituitarism in women, pericardial effusion is a rare presenting manifestation of the same. Appropriate history and hormonal assays with timely replacement of hormones will be life-saving in such patients. One should keep in mind the diagnostic short-coming of screening for thyroid dysfunction solely with thyroid stimulating hormone level.

**REFERENCES:**

Case Report

Cryptogenic *Burkholderia cepacia* Sepsis in A Haemoglobin E Disease Patient with Splenic and Hepatic Abscesses

S Baruah*, B Thakuria**, T Das***, S Kalunkhe****

**INTRODUCTION:**

We report a case of *B. cepacia* sepsis with hepatic and splenic abscesses in a haemoglobin E disease patient who had no pneumonia or any other identifiable source of infection. Such a case has never been reported in standard literatures till date.

**CASE REPORT:**

A 32-year-old male presented with fever and chills for two months; and cough with expectoration for a month. He did not have any neurological, cardiovascular, gastrointestinal or musculoskeletal symptoms. His past medical history revealed multiple hospital admissions for anaemia with frequent blood transfusions.

On examination, he was febrile 101°F, heart rate of 126/minute, respiratory rate of 22/min and blood pressure of 100/70 mm Hg. He was thin built, poorly nourished and was not in distress. His abdominal examination detected splenomegaly; neurological, respiratory and cardiovascular system examinations were essentially normal.

His laboratory tests showed abnormal blood counts; total white cell count was normal, red blood cells were reduced, haemoglobin was 4.1 gm/dl, mean corpuscular volume was 63.9 fl and platelets were reduced at admission. Earlier reports showed a reduced total count (Table 1). The peripheral blood smear showed anisocytosis, microcytosis and target cells. Haemoglobin electrophoresis revealed haemoglobin E homozygous state.

Ultrasonographic examination of the whole abdomen showed an enlarged spleen with heterogeneous echotexture and multiple small hypo to anechoic lesions, and a normal sized liver with multiple hypo to anechoic lesions (Figure 1 & 2). A subsequent computed tomography scan of the abdomen revealed...
splenomegaly, multiple splenic infarcts with splenic abscesses, hepatomegaly and multiple hepatic abscesses (Figure 3). A guided splenic aspirate was obtained and sent for culture and sensitivity testing.

His urine culture was sterile and X-ray of the chest was normal.

After sending samples for blood culture; patient was empirically started on Piperacillin-Tazobactum and Metronidazole infusions.

On day 3, blood culture showed profuse growth of *B. Cepacia*, sensitive only to Meropenem, Ceftriaxone and Co-trimoxazole. The splenic aspirate too showed growth of *Burkholderia cepacia* sensitive only to Meropenem.

Serology for HIV, Hepatitis B and C, Dengue, Malaria and Salmonella species were negative.

The patient gradually responded to Meropenem injections; started after the culture report. He received 3 units of packed cells transfusion too. His chills and fever subsided, and was subsequently discharged after 20 days in-hospital care.

However he got readmitted again after a few days with renewed fever and weakness and collapsed due to septic shock.

**DISCUSSION:**

A search of literature did not reveal case reports of *Burkholderia cepacia* sepsis in a patient with haemoglobin E disease with no pneumonia or any other apparent source of infection.

Clinical manifestations of *B. cepacia* infection varies from asymptomatic colonization to necrotizing pneumonia and sepsis1.

Reports of *B. cepacia* sepsis in patients with cystic fibrosis were plenty2. Colonization in cystic fibrosis patients has been reported to be as high as 3%3.

Some reported catheter-induced *B. cepacia* bacteremia in hemodialysis patients2 and also in peritoneal dialysis4.

Immunocompromised patients are at particular risk4. There were reports of *B cepacia* sepsis in children with sickle cell disease5.

There have been reports of pseudo-contamination of blood products by *Burkholderia cepacia* because of the use of contaminated disinfectant during quality control, especially when quarternery ammonium compounds or chlorhexidine were used. With the use of alcohol as disinfectant, it is now rare6. Our patient too had multiple transfusions, both during and prior to the current hospital stay, hence making it difficult to identify as the source of infection.

*Burkholderia* species are often multi-drug-resistant, and treatment is challenging. The organisms are often sensitive to Trimethoprim-Sulfamethoxazole, Meropenem and Ceftazi-dime7. The optimal treatment regimen is not established. Intravenously administered antibiotic therapy, often in combination, has been successful.

**CONCLUSION:**

As *B cepacia* is known to cause catastrophic sepsis only in patients with known immunodeficiency; and our patient had solely Hemoglobin E disease as a comorbid
condition; this case report might prove as a good stimulus to study the associated abnormalities in Hemoglobin E disease patients to immunohematologic cell lines other than red blood cells.

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