

ORIGINAL ARTICLE

Etiology of Ischemic Stroke and Correlation with Common Risk Factors in a Tertiary Care Centre

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ABSTRACT

Introduction: Stroke is the third leading cause of mortality worldwide and a matter of grave public importance in India. Ischemic stroke accounts for 80% of all cases. This study aims at classifying patients of ischemic stroke according to TOAST system.

Aims and objectives: The specific objectives of the study are to document various etiology of ischemic stroke and correlate clinical presentations and risk factors with the different subtypes.

Methodology: An observational study was carried out among 100 ischemic stroke patients using both prospective and retrospective data. History, clinical examination and different laboratory and radiological investigations were carried out. Etiology was classified by Trial of Org 10172 in Acute Stroke Treatment criteria and clinical presentations grouped by NIHSS score. Comparisons were done between groups stratified by stroke subtype.

Results: Among the 100 patients 25 had cardioembolic, 13 large artery atherosclerosis, 21 small vessel stroke, 33 undetermined and 8 others type of stroke. Among the risk factors there was significant preponderance of hypertension, diabetes, ischemic heart disease, dyslipidemia, ECG, Echocardiographic abnormality, propensity for basal ganglia and paraventricular involvement among certain subtypes. There was no substantial relation between the subtypes and addictions, past history of stroke, and other territorial involvement.

Conclusion: The etiological diagnosis of stroke in young adults has changed over time as a result of improvements in diagnostic workup. A notable portion of these patients remains without an evident stroke mechanism according to TOAST criteria.

Keywords: ischemic stroke, TOAST classification, cardioembolic, NIHSS score

INTRODUCTION

A stroke (previously known as a cerebrovascular accident) is rapidly developing clinical symptoms and/or signs of focal, and at times global (applied to patients in deep coma and to those with subarachnoid haemorrhage) loss of brain function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin (Hatano 1976)-WHO. Its importance as a public health matter can be envisioned from the fact that worldwide after coronary heart disease (CHD) and cancer of all types combined strokes are the third leading cause of death. And among Asians the prevalence of stroke is more than that of CHD. In the early 1980s the prevalence rates of stroke were around 500-700 per 100,000 in the western countries¹ and 900 per 100,000 in Asia.² Stroke can be broadly classified into ischemic and haemorrhagic type and among them 85% are of ischemic etiology. Accurate definition of the mechanism of stroke is

crucial as this will guide the most effective care and therapy. Ischemic stroke can be classified based on etiology according to various classification systems. A good stroke classification system is the key to select patients for genetic phenotyping, conduct epidemiological studies, and make treatment decisions and prognostic predictions. One of the most popular classification systems is the TOAST classification which was originally formulated for the purpose of investigating any potential efficacy of the anticoagulant danaparoid for treatment of various types of ischemic strokes but has been used extensively for other purposes, such as identifying new genetic markers and risk factors.³ So we studied 100 patients of ischemic stroke and classified them according to TOAST classification based on etiology and studied the correlation of the important risk factors with the individual subtypes.

METHODOLOGY

This observational study was carried out at Medical College Kolkata in the period from January 2014 to 2015. Approval for this study was granted by Institutional Ethics Committee for human research. 100 patients of ischemic stroke who were admitted in the wards or had attended outpatient department were chosen initially based on clinical features and in cases where the diagnosis was confirmed based on CT scan they were included in the study as per the inclusion criteria. Patients with other causes of stroke like intracerebral haemorrhage, subarachnoid haemorrhage, and transient ischemic attack were excluded. The selected patients were informed about the research protocol and written informed consent was taken from 85 patients. In the remaining 15 patients with moderate to very severe stroke who had altered consciousness written consent was taken from next of kin.

Procedure: On admission or during first visit the clinical features of the patient was noted and assigned a value according to National Institute of Health Stroke Scale (NIHSS). Detailed history was taken from the patient or relatives particularly history of diabetes, hypertension, atherosclerotic risk factors, prior history of stroke or Transient Ischemic Attack, addictions like smoking, alcohol intake. The patients were then subjected to different laboratory investigations namely complete haemogram, platelet count, serum urea, Creatinine, fasting blood sugar, lipid profile, coagulation profile (in some cases). They also underwent radiological investigations namely ECG, Echocardiography, bilateral carotid artery Doppler, MRI of brain and Magnetic Resonance Imaging in few selected cases. Based on the results of these clinical and laboratory parameters the patients were categorised into one of 5 etiological subtypes of ischemic stroke based on TOAST classification. After classifying these patients according to etiology correlation analysis was carried out as per their NIHSS score.

Statistical Analysis: - Categorical variables were expressed as Number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes. Continuous variables were expressed as Mean \pm Standard Deviation and compared across the groups using one way ANOVA Test. The statistical software SPSS version 20 was used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it was considered as significant.

RESULTS

100 patients of ischemic stroke who fulfilled the inclusion criteria were included in the study. Among them 66 were male and 34 were female patients. As

for other basic demographic data 63 patients were from rural areas and 37 from urban areas. Occupation wise non manual skilled workers were highest 21%, followed by 19% elderly, 16% unemployed, semiskilled workers 14%, manual workers 13%, unskilled 12%, and 5% were semi-professionals. From the history, clinical examination findings, laboratory and radiological reports the patients were divided into one of the 5 categories of TOAST Classification. Among 100 patients, 25 had cardioembolic variety, 13 had large artery atherosclerosis, 21 had small vessel stroke, causes of 33 was undetermined and 8 patients had other etiology of stroke.

Next statistical significance was determined between each subtype of stroke and different risk factors of cerebrovascular accident. The mean age was 45.76 among patients of cardioembolic variety, 59.92 among large artery atherosclerosis, 64.10 among patients with small vessel stroke, 36.38 among stroke due to other causes and 62 among patients whose cause could not be determined. So it was found that stroke due to other causes tends to occur in younger population whereas small vessel stroke occurred in the older age group. There were 63 patients with hypertension and 37 were non-hypertensive. There was significant relationship between hypertension and incidence among different subtypes of stroke. Patients with stroke due to large artery atherosclerosis were more likely to be hypertensive with a P Value of 0.020. Conversely patients with stroke due to other causes were less likely to be hypertensive only 3.17%. There were 50 patients who were diabetic and 50 who were nondiabetic. It was found that there was significant difference between diabetes and incidence among subtypes of stroke. Small vessel stroke patients were more likely to be diabetic 85.7% with a P Value <0.001 . Patients with cardioembolic variety were more likely to be non diabetic 20%. There were 16 patients with ischemic heart disease and 84 patients who had not. Among 33 patients with stroke due to undetermined cause only 1 had ischemic heart disease (IHD) and among stroke due to other causes none had IHD. Among the various subtypes small vessel stroke had maximum incidence about 38% and 50% of all cases of IHD. 18 patients had past history of stroke while 82 had not. However there was no significant probability of having past history of stroke among the different subtypes. Among the 100 patients there were 55 people who were smokers and 45 had not. There was no significant relationship between smoking and incidence of a specific subtype of stroke among the 55 patients who smoked. There were 16 alcoholic patients and 84 who didn't drink. The incidence was maximum among cardioembolic variety, 31% whereas there was 18% with large artery atherosclerosis, 25% with small vessel stroke, 12.5% in patients with other causes and 12% in patients with stroke due to unde-

terminated cause. But there was no significant statistical relation between alcohol intake and propensity to have a specific subtype of stroke. There was significant relation between deranged lipid profile values and specific subtype of stroke. As evident from Table 1 high cholesterol was associated with large artery atherosclerosis and small vessel variety while other causes of stroke had the least values. An increased

level of triglyceride also was found among large artery atherosclerosis and small vessel subtype and least among others variety. Low density lipoprotein was associated with small vessel stroke having a much higher value 121+/-41 than other subtypes. But there was no significant association of the mean levels of Very low density lipoprotein with the different subtypes of ischemic stroke.

Table 1: Relation of different subtypes of stroke with lipid profile (Mean ± SD)

Variables	TOAST					p Value
	Cardioembolic	Large Artery Atherosclerosis	Small Vessel	Others	Undetermined	
Cholesterol	140.56 ± 23.56	195.08 ± 39.47	192.24 ± 45.58	137.63 ± 25.29	143.91 ± 27.11	<0.001
Triglyceride	126.28 ± 29	174.77 ± 38.2	155.29 ± 35.57	108.5 ± 20.66	123.76 ± 27.54	<0.001
LDL	79.84 ± 20.69	115.46 ± 35.09	121.62 ± 41.64	82.88 ± 18.11	79.82 ± 17.7	<0.001
HDL	44 ± 6.71	32.62 ± 10.5	42.67 ± 5.84	43.25 ± 5.44	43.91 ± 4.99	<0.001
VLDL	33.16 ± 13.79	38 ± 21	32.24 ± 9.73	31.25 ± 11.21	34.7 ± 13.54	0.757

Table 2: Distribution of subtypes of stroke according to NIHSS subgroup

TOAST	NIHSS				Total	p Value
	Minor Stroke	Moderate	Moderate to Severe	Very Severe		
Cardioembolic	0(0)	22(27.85)	3(21.43)	0(0)	25(25)	0.066
Large Artery Atherosclerosis	2(33.33)	9(11.39)	2(14.29)	0(0)	13(13)	
Small Vessel	0(0)	15(18.99)	6(42.86)	0(0)	21(21)	
Others	2(33.33)	4(5.06)	2(14.29)	0(0)	8(8)	
Undetermined	2(33.33)	29(36.71)	1(7.14)	1(100)	33(33)	
Total	6(100)	79(100)	14(100)	1(100)	100(100)	

The relationship between the subtypes of stroke and various laboratory parameters were also carried out. Among 100 patients 57 had normal ECG findings. 13 patients had atrial fibrillation, 12 had ischemic changes, 10 had chamber enlargement or hypertrophy, 7 had different types of block and 1 patient had ventricular aneurysm. There was significant relation between any particular ECG abnormality and occurrence of a particular type of stroke. All patients with atrial fibrillation had cardioembolic type of stroke. There was similar incidence of ischemic changes (41%) among cardioembolic variety and small vessel stroke. There was also similar incidence of chamber enlargement (20%) among cardioembolic and stroke due to undetermined causes. In the patients with stroke due to other causes only one patient had an abnormality and rest 7 had normal ECG findings. Among 100 patients 42 had normal ECHO findings, 13 had valvular heart diseases, 9 had cardiomyopathy, 32 had chamber enlargement or hypertrophy and 4 had other abnormalities. There was significant relation between cardiac abnormality on ECHO and occurrence of a particular subtype of stroke. All 13 patients with rheumatic valvular abnormality had cardioembolic stroke. 55% of patients with cardiomyopathy had cardioembolic variety and 46% of patients having some chamber enlargement had stroke

due to undetermined cause. Significantly none of the patients with stroke due to other causes had any ECHO abnormality. Then the association of different types of stroke with site of involvement based on MRI findings was determined. It was seen among 100 patients 34 patients had some affliction of the basal ganglia while 66 had no such. There was significant relation between basal ganglia involvement and possibility of occurrence of a particular subtype of ischemic stroke. Cardioembolic variety had the maximum occurrence about 44% among the subtypes, while undetermined variety had least about 8% as evident by only 3 out of 33 patients had basal ganglia involvement. Among 100 patients 47 patients had Paraventricular infarct while 53 had no such. It occurred maximally about 49% in undetermined causes and there was no patient with other causes who had Paraventricular infarcts. Also it was found that cardioembolic variety had very less occurrence of such stroke, only 2 out of 25. Conversely in undetermined causes 23 out of 33 patients had Paraventricular infarct about 69.6%. Arterial territory wise also there was significant association between Middle cerebral artery infarcts and particular stroke subtype. Among 100 patients 50 had middle cerebral artery (MCA) involved and the rest had not. In the cardioembolic variety 19 among 25 patients (76%) had MCA stroke,

conversely only 10 patients out of 33 in the undetermined variety had MCA stroke.

After admission the NIHSS score was calculated for each patient and plotted in tabular form. Out of 100 patients 6 had minor stroke, 79 had moderate symptoms, 14 had moderate to severe symptoms and 1 had very severe stroke. By statistical analysis there was no specific relation between any types of stroke having a specific NIHSS symptom of severity. All subtypes had equal propensity of majority presenting with moderate symptoms.

DISCUSSION

This study was an observational study with a modest sample size of 100 patients utilising both prospective and retrospective data. There were 66 male patients and 34 female. Among the males 15(22%) had cardioembolic, 10(15%) had large artery atherosclerosis, 16(24%) had small vessel stroke, 6(9%) had other causes, and cause was undetermined in 19 (28%) cases. Among the females 10(29%) had cardioembolic, 3(8%) had large artery atherosclerosis, 5(14%) had small vessel stroke, 2(5%) had other causes and 14(41%) had stroke due to undetermined cause. We observed no gender difference in those with cardioembolism or other determined etiology as was suggested by some studies^{4,5}. Similarly there was no predilection for a particular type of stroke based on occupation, religion, housing.

In our study we looked into prevalence of some common modifiable risk factors in our subjects and searched for any association with etiology. For this purpose we first segregated them into 5 subgroups according to TOAST system of classification. 25 had cardioembolic type, 13 had large artery atherosclerosis, 21 had small vessel stroke, 8 had other types (among which 1 had Moyamoya disease, 1 had Takayasu's Arteritis, 3 had SLE, 2 had dissection of cervical artery, and 1 had Cerebral sinus venous thrombosis) and cause was undetermined despite extensive evaluation in 33 patients. Then association with certain risk factors were tested separately with these subgroups by Pearson's Chi Square Test and we found the following results.

In our study 63 patients were hypertensive. Among the various subtypes it occurred in the highest frequency in large artery atherosclerosis patients and those with small vessel stroke which was similar to other studies⁶. Incidence tends to increase with age and was commoner among males.

As for association with ischemic heart disease 16 patients had evidence of such clinically or during investigations and majority of them had lacunar infarcts or small vessel stroke. A strong negative association was also found that none of the patients with stroke due

to other causes had ischemic heart diseases. This also correlated with the younger age trends in this type of ischemic stroke⁷. Trials like SAHLIS have shown past episode of stroke predispose to same events and it was highest among large artery atherosclerosis variety⁸. The same analogy could not be drawn from our study because of the small sample size and accurate records of past ischemic events could not be found out due to non maintenance of prescriptions. There were 50 diabetics and the most predominant stroke type among them was small vessel stroke. This is in accordance with the results of other large scale studies⁹. Smoking has been accepted as a traditional risk factor for ischemic stroke¹⁰. This was also shown in our study as the majority of patients 55 out of 100 were smokers. But there was no predilection for a particular stroke subtype among them. This may be due to the fact among the subjects very few women smoked and almost similar sex ratio between the subgroups led to these results. Similar scenario was seen in cases of alcohol intake and other drug addictions.

Dyslipidemia was consistently associated with ischemic cerebrovascular accident by traditional studies¹¹. Higher levels of cholesterol, triglyceride, Low density lipoprotein and low levels of High density lipoprotein were seen in small vessel disease and large artery atherosclerosis. The reverse situation was found in cardioembolic and others variety. This situation tallied with traditional studies as regarding other subgroup. As for anomaly in cardioembolic variety this was because in our study most of the cases were of rheumatic heart disease not of cardiomyopathy. Furthermore it tallied with the results in the Iranian study which also had a higher proportion of rheumatic heart disease patients¹². As regarding non modifiable risk factors the mean age of the patients belonging to cardioembolic group was 45.76. This was due to the fact high prevalence of rheumatic heart disease as a cause of embolus which occurred in younger age group. The mean age of large artery disease is 59.92, small vessel stroke is 64.10, undetermined cause is 62 and other cause is 36.38. In accordance with other studies small vessel and large artery disease occurred in older patients while other causes occurred in younger age group¹³.

In our study the highest number was that of undetermined causes 33 out of 100, followed by cardioembolism 25, small vessel stroke 21, large artery atherosclerosis 13 and lastly 8 cases of stroke due to other causes. Now the proportion differed considerably in various studies worldwide. In a large scale European study Stroke etiology was reported in detail for 3331 patients aged 15-49 years with first-ever IS according to Trial of Org in Acute Stroke Treatment (TOAST) criteria: large-artery atherosclerosis (LAA), cardioembolism (CE), small-vessel occlusion (SVO), other determined etiology, or undetermined

etiology. CE was categorized into low- and high-risk sources. Other determined group was divided into dissection and other non-dissection causes. Comparisons were done using logistic regression, adjusting for age, gender, and centre heterogeneity. The results were etiology remained undetermined in 39.6%. Other determined etiology was found in 21.6%, CE in 17.3%, SVO in 12.2%, and LAA in 9.3%³. In a similar Indian study at Sri Chitra Tirunal Institute of Medical Sciences and Technology (SCIMST), Trivandrum, patients of ischemic stroke were classified based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria; 25.2% patients had cardioembolic stroke, 12.6% had large artery atherosclerosis and 7.5% had lacunar infarcts. Strokes due to other determined etiology were 11.2% (7.0% arterial dissection, and one patient each with lupus erythematosus, primary antiphospholipid antibody syndrome and protein S deficiency). Four patients had stroke due to other causes (one case each of Moyamoya disease, Takayasu's arteritis, fibro muscular dysplasia and nephritic syndrome)¹⁴. Our study had undetermined category as maximum. Because treatment options are influenced by a presumed cause, an evaluation on a case-by-case basis is warranted. If strict diagnostic criteria are used, the diagnosis of stroke of undetermined etiology considerably increases. While such strict criteria are important in clinical trials that test new interventions, the value of the application of such methodologies to stroke in adults, needs clarification. In particular, the usefulness of categorizing a stroke as undetermined when two or more possible causes are identified needs to be explored.

In our study left hemisphere strokes were more frequent compared with right hemisphere strokes. This observation is in accordance with the observations from the large German Stroke registry¹⁵. The side preference reflects the poor recognition of right hemisphere stroke as aphasia is generally absent.

Most of the infarcts affected anterior circulation (80), whereas a minority 13 had posterior circulation or infarcts in both territories (7). Nearly a one-fourth of our patients had multiple visualized infarcts in MRI including both silent and current lesions. In our patients 46 out of 100 of them had evidence of leukoriosis. They were quite prevalent in small vessel and undetermined variety. These patients with small vessel stroke also had higher prevalence of hypertension and diabetes so a positive correlation with leukoriosis was found. As the availability and quality of imaging techniques improve, doctors are identifying more patients with no history of transient ischemic attack or stroke in whom imaging shows brain infarcts. Until recently, little was known about the relevance of these lesions. In a systematic review, Vermeer S et al gave an overview of the frequency, causes, and consequences of MRI-defined silent brain

infarcts, which are detected in 20% of healthy elderly people and up to 50% of patients in selected series. Most infarcts are lacunes, of which hypertensive small-vessel disease is thought to be the main cause. Although silent infarcts, by definition, lack clinically overt stroke-like symptoms, they are associated with subtle deficits in physical and cognitive function that commonly go unnoticed¹⁶.

CONCLUSION

In our study consisting of 100 patients according to TOAST system of classification the etiology of stroke was determined and the highest prevalence was seen in undetermined causes followed by cardioembolic, small vessel, large artery atherosclerosis and other causes. Correlating these subtypes with the traditional risk factors hypertension was significantly associated with undetermined causes and large artery atherosclerosis. Diabetes and Ischemic heart disease was seen more often in small vessel stroke. Dyslipidemia was seen more often in large artery atherosclerosis and small vessel stroke. But there was no predilection for a specific subtype of ischemic stroke with respect to past history of cerebrovascular accident, smoking or alcohol addiction. There was a preponderance of left hemisphere stroke (57%) and anterior circulation affection (80%). On neuroimaging infarcts involving basal ganglia and ischemic leukoriosis were common which was seen maximally in cardioembolic and undetermined variety respectively. Larger population based studies should be carried out to determine the etiology of stroke because if we can address this issue in the primary preventive stage it will be rewarding for an important public health problem like ischemic stroke. Also utmost efforts should be carried out to minimise the proportion of undetermined variety by astute clinical and laboratory investigations and reassessment of diagnostic protocols.

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ORIGINAL ARTICLE

Patient Activation Measures in Type2 DM in Tertiary Care Hospital – Does it Differ between Male and Female

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ABSTRACT

Introduction: Type 2 diabetes is characterised by relative insulin deficiency caused by pancreatic β -cell dysfunction and insulin resistance in target organs. The Patient Activation Measure is a valid, highly reliable, uni-dimensional, probabilistic Guttman-like scale that reflects a developmental model of activation. The measure has good psychometric properties indicating that it can be used at the individual patient level to tailor intervention and assess changes.

Aim: To investigate whether the level of patient activation differs between men and women with T2DM.

Materials and methods: It is a cross-sectional study involving all the patients with T2DM from a tertiary care hospital. The following data were extracted: age, gender, BMI, smoking status, HbA1c, use of glucose lowering medication, and the presence of complications. In this study the Dutch version of the PAM was used which was validated by NIVEL (Netherlands Institute for Health Services Research). The questionnaire consists of 13 items. The association between gender and patient activation was investigated with multivariate linear regression using the continuous PAM score.

Results: 54.5% of the patients were male and 45.5% were female. Mean age was 61.54 (SD: 12.037) years in men and 57.41 (SD: 12.583) years in women, who were significantly older than women ($p < 0.019$). We have found that there is stastically significant difference between patient activation in men and women ($p=0.0006$).

Conclusion: Patient activation is more in male compared to female. Hence healthy behaviours should be educated for diabetic patients to reduce complications and improve their quality of life and activation.

Key words: PAM-patient activation measures; Type 2 Diabetes Mellitus, BMI

INTRODUCTION

Type 2 diabetes is characterised by relative insulin deficiency caused by pancreatic β -cell dysfunction and insulin resistance in target organs. Between 1980 and 2004, the global rise in obesity, sedentary lifestyles, and an ageing population have quadrupled the incidence and prevalence of type 2 diabetes¹. World Health Organization (WHO) estimates that more than 346 million people worldwide have DM. This number is likely to be more than double by 2030 without any intervention. Almost 80% of diabetes deaths occur in low and middle-income countries². According to WHO report, India today heads the world with over 32 million diabetic patients and this number is projected to increase to 79.4 million by the year 2030³.

Diabetes can cause micro vascular and macro vascular complications. Strict metabolic control can delay or prevent the progression of complications associated with diabetes. The needs of diabetic patients are not only limited to adequate glycaemic control but

also correspond with preventing complications; disability limitation and rehabilitation. Various studies done in India revealed very poor adherence to treatment regimens due to poor attitude towards the disease and poor health literacy among the general public^{4,5}

There are seven essential self-care behaviours in people with diabetes which predict good outcomes. These are healthy eating, being physically active, monitoring of blood sugar, compliance with medications, good problem-solving skills, healthy coping skills and risk-reduction behaviours⁶. Socio-demographic and cultural barriers such as poor access to drugs, high cost, patient satisfaction with their medical care, patient provider relationship, degree of symptoms, unequal distribution of health providers between urban and rural areas have restricted self-care activities in developing countries.

In a study to identify the barriers from the provider's perspective in regard to diabetes care; factors like affordability by the patient, belief by providers that

medications cannot cure patient condition, no confidence in their own ability to alter patient behaviour were identified⁷. Another study stressed on both patient factors (adherence, attitude, beliefs, knowledge about diabetes, culture and language capabilities, health literacy, financial resources, co-morbidities and social support) and clinician related factors⁸(attitude, beliefs and knowledge about diabetes, effective communication).

The Patient Activation Measure is a valid, highly reliable, uni-dimensional, probabilistic Guttman-like scale that reflects a developmental model of activation. Activation appears to involve four stages: (1) believing the patient role is important, (2) having the confidence and knowledge necessary to take action, (3) actually taking action to maintain and improve one's health, and (4) staying the course even under stress. The measure has good psychometric properties indicating that it can be used at the individual patient level to tailor intervention and assess changes. Therefore, the aim of this study was to investigate whether the level of patient activation differs between men and women with T2DM.

METHODOLOGY

The study population consisted of patients with T2DM. It is a cross-sectional study involving all the patients with T2DM from a tertiary care hospital. We excluded patients with recent history of severe sepsis requiring hospitalization, severe trauma, recent fracture and malignancy.

The following data were extracted: age, gender, BMI, smoking status, HbA1c, use of glucose lowering medication, and the presence of complications. (The presence of microvascular complications was defined as having microalbuminuria, diabetic retinopathy, and/or diminished sensibility of the feet. The presence of macrovascular complications was defined as (a history of) angina pectoris, myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, stroke or transient ischemic attack).

In this study the Dutch version of the PAM was used which was validated by NIVEL (Netherlands Institute for Health Services Research)⁹. The questionnaire consists of 13 items which measure knowledge, skills, confidence, and behaviours needed for self management. Each item has five different response categories: (1) disagree strongly, (2) disagree, (3) agree, (4) agree strongly, and (5) not applicable. In the current study, the same scoring rules as in the Dutch validation study of the PAM were used⁹. Patients who filled out less than 7 items or who answered all items with disagree strongly or agree strongly were excluded. Subsequently, mean scores for the PAM were calculated leaving out items

which were responded to with not applicable. The mean scores were transformed into a PAM score ranging from 0 to 100 based on scoring rules of Insignia Health¹⁴. Based on the same rules, the PAM score was also converted into the four levels of patient activation.

Statistical Analysis. Statistical analyses were performed using SPSS version 22

Multiple imputations were used for missing data on the independent variables, assuming that data was missing at random(MAR) or completely at random(MCAR).

Ten imputed datasets were created and the pooled results are described. The patient characteristics are expressed as mean with standard deviation (SD) or median with interquartile range (IQR) for normally distributed data, respectively. Categorical variables are described in numbers and percentages. Differences were considered to be significant at a p value of <0.05 . The association between gender and patient activation was investigated with multivariate linear regression using the continuous PAM score.

Four models were used: 1) a crude model, 2) model adjusted for drugs, HbA1c, veg/non-veg, 3) a model adjusted for drugs, HbA1c, veg/non-veg, complications, 4) a model adjusted for age, smoking, MVC, drugs, HbA1c, veg/non-veg and, 5) an explorative model with all variables in model(3) and BMI also.

These diabetes-related confounders were added to investigate whether the burden of T2DM may confound the relation between gender and PAM. The degree to which the different models determined the PAM score was evaluated by the explained variance, shown as adjusted R^2 .

Ethics: All patients gave written informed consent for the use of the survey data and the clinical data.

RESULTS

The patient characteristics are described in Table 1. 54.5% of the patients were male and 45.5% were female. Mean age was 61.54 (SD: 12.037) years in men and 57.41 (SD: 12.583) years in women, who were significantly older than women ($p < 0.019$). Men smoked more frequently and they had also more often complications compared to women. The BMI was slightly higher in women. In this study we have found that there is statically significant difference between patient activation in men and women ($p=0.0006$).

The median PAM score and the distribution of the PAM levels are described in Table 1. The median PAM score was 14 (IQR: 9.25-16.00) in men and 12 (IQR: 8.00-15.00) in women. Significant difference between PAM levels in men and women ($p = 0.006$).

Table 1: Patient Characteristics

Characteristics	Men	Women	p-value
Number of Patients (%)	109(54.5)	91(45.5)	
Mean age (years)	61.54(12.037)	57.41(12.583)	0.019 < 0.05
Median BMI	26(23.1-28.0)	27.5(23.1-28.0)	0.081 > 0.05
Smoking, n (%)	56(51.4)	16(17.6)	0.000 < 0.05
Use of glucose lowering drugs, n (%)	67(61.5)	57(62.6)	0.865 > 0.05
Use of insulin, n (%)	42(38.5)	34(37.4)	0.865 > 0.05
Median HbA1c (mmol/mol)	9.2 (7.85-11.4)	9.4 (7.8-11.5)	0.953 > 0.05
Complications, n (%)	60(55)	49(53.8)	0.865 > 0.05
Median PAM score	14(9.25-16.00)	12(8.00-15.00)	0.006 < 0.05
PAM level			
1	4(3.7)	5(5.5)	
2	16(14.7)	23(25.3)	
3	16(14.7)	15(16.5)	
4	73(67)	48(52.7)	

Values are depicted as n (%), mean (SD), or median (IQR).

Continuous data were analysed using independent t-tests or the Mann-Whitney Utest.

Categorical variables were analysed using Chi-square tests

Table 2a: Multivariate Regression Analysis for Patient Activation (Cont..)

Variable	Model(1) Adjusted R ² (%)= 0.040%		Model(2) Adjusted R ² (%)=0.038%		Model(3) Adjusted R ² (%)=0.034%	
	b (95%CI)	p value	b (95%CI)	p value	b (95%CI)	p value
Gender	-1.675 (-3.039,-0.311)	0.016	-1.838 (-3.235, -0.441)	0.010	-1.832 (-3.233, -0.431)	0.011
Age						
BMI						
Smoking						
Complications					-0.251 (-1.641, 1.139)	0.722
Drugs	-1.466 (-2.866, -0.67)	0.040	-1.824 (-3.617, -0.031)	0.046	-1.872 (-3.69,-0.055)	0.044
HbA1c			-0.145 (-0.532, 0.243)	0.463	-0.153 (-0.545 ,0.238)	0.441
Veg/Non Veg			0.829 (-0.625, 2.283)	0.262	0.806 (-0.656, 2.269)	0.278

Table 2b: Multivariate Regression Analysis for Patient Activation

Variable	Model(4) Adjusted R ² (%)=0.026%		Model(5) Adjusted R ² (%)=0.021%	
	b (95%CI)	p value	b (95%CI)	p value
Gender	-2.028 (-3.559, -0.497)	0.010	-2.034 (-3.570, -0.498)	0.010
Age	-0.021 (-0.090, 0.049)	0.562	-0.021 (-0.091, 0.049)	0.555
BMI			0.031 (-0.132, 0.158)	0.855
Smoking	0.308 (-1.252, 1.867)	0.698	0.312 (-1.252, 1.877)	0.694
Complications	-0.589 (-2.301, 1.122)	0.498	-0.606 (-2.331, 1.119)	0.489
Drugs	-1.938 (-3.771, -0.104)	0.038	-1.931 (-3.770, -0.092)	0.040
HbA1c	-0.147 (-0.541, 0.246)	0.461	-0.15 (-0.547, 0.246)	0.455
Veg/Non Veg	0.85 (-0.625, 2.325)	0.257	0.805 (-0.751, 2.361)	0.309

Table 3: Stratified Analysis for Men and Women

Variables	Men				Women			
	Model(4) aR ² (%)=0.030%*		Model(5) aR ² (%)=0.023%*		Model(4) aR ² (%)=0.013%*		Model(5) aR ² (%)=0.014%*	
	b(95%CI)	p#	b(95%CI)	p#	b(95%CI)	p#	b(95%CI)	p#
Age	-0.04 (-0.12, 0.03)	0.252	-0.05 (-0.14, 0.03)	0.22	-0.04 (-0.16, 0.09)	0.56	-0.04 (-0.17, 0.09)	0.572
BMI	-0.07 (-0.27, 0.12)	0.451	-0.07 (-0.27, 0.12)	0.467	0.12 (-0.11, 0.32)	0.341	0.11 (-0.11, 0.33)	0.344
Smoking	1.36 (-0.45, 3.17)	0.138	1.46 (-0.40, 3.32)	0.123	-1.81 (-4.83, 1.20)	0.235	-1.81 (-4.87, 1.25)	0.242
Complications			-0.52 (-2.68, 1.64)	0.633	-1.61 (-4.62, 1.39)	0.289	-1.62 (-4.66, 1.43)	0.294
Drugs	-2.63 (-4.82, -0.45)	0.019	-2.75 (-4.99, -0.50)	0.017	-0.84 (-3.11, 1.43)	0.465	-0.82 (-4.11, 2.47)	0.621
HbA1c	-0.29 (-0.77, 0.19)	0.24	-0.31 (-0.80, 0.18)	0.216			0.006 (-0.72, 0.73)	0.572
Veg/Non Veg	1.06 (-0.90, 3.02)	0.287	1.02 (-0.95, 2.99)	0.307	1.01 (-1.51, 3.54)	0.427	1.01 (-1.56, 3.58)	0.436

*aR²(%)=Adjusted R²(%); #p= p value

The results of the regression analyses are described in Table 2. In all models gender was has significant association with the PAM score. In the explorative model (model (5)), all diabetes-related factors (HbA1c, diabetes duration, use of oral glucose lowering drugs, and the presence of complications) were not associated with the PAM score.

Stratified analyses according to gender are described in Table 3. In men, lower age ($b = -0.044$; $p = 0.252$), and a lower BMI ($b = -0.074$; $p = 0.451$) were associated with a higher PAM score in models ($R^2 0.023\%$). In women, the absence of complications ($b = -1.614$; $p < 0.0289$) are associated with a higher PAM score in models ($R^2 0.013\%$). In the explorative model (model (5)), no associations were found between HbA1c, diabetes duration, use of oral glucose lowering drugs, the presence of complications, and the PAM score in men or women.

DISCUSSION

The study was conducted in south India in a tertiary care centre which constitutes mostly rural population. Diabetic care and PAM are mostly related to gender specific risk factors. In this study we have found that there is statically significant difference between patient activation in men and women ($p = 0.0006$) Since, India is a developing country there is a wide disparity in literacy rate. Men have higher literacy rate compared to women. So, PAM in men are slightly higher than women.

Women have slightly higher BMI compared to men since women in this study are mostly home makers with a sedentary life style. Women with T2DM have a lower degree of well-being, a lower health-related quality of life, and a higher BMI compared to men with T2DM^{16,17}. Use of drugs is slightly higher in men than women because educational status of men is higher compared to women in India. There is no much disparity of HbA1c levels in men and women.

Complications are higher in men compared to women even though women have higher BMI and low usage of insulin because of life style, nutritional and genetic factors. On account of the social stigma against females, which is prevalent in the Indian sub continent and per se, in rural India, females have a lack of awareness on their disease and its complications, and are non adherent to their medication and other self care activities. These factors contribute to a poor patient activation among females.

Healthy behaviours are higher in women compared to men since number of smokers are higher in men compared to women. A dutch study revealed that there is a slight degree of patient activation in men and diabetes⁹.

Some limitations need to be mentioned. Due to the cross-sectional design, causal conclusions could not be drawn. Although we have investigated important confounders, still some potentially important factors were not taken into account. We were not able to adjust for educational level, socioeconomic status, and marital status. Inclusion of those variables might increase the explained variance. Educational status and financial distress, which could be use as markers for socioeconomic status, were associated with patient activation in a previous Dutch study¹⁰

As noted by another study good glycaemic control was significantly associated with older age, higher education, higher patient activation, lower diabetes-related emotional distress, better diet and exercise behaviours, lower body mass index, shorter duration of disease and knowledge of HbA1c targets¹¹. Women may need additional support and specialized programs for encouragement and of self-management behaviours, problem solving, and addressing gender-specific barriers to self¹². Two studies found a higher level of patient activation in men^{9,10}, whereas three other studies did not find a difference between men and women in the level of patient activation^{13, 14, 15}.

A study revealed that there is no difference in the degree of patient activation of men and women with T2DM. Furthermore, no significant influence was found for well-being, quality of life, BMI, and smoking on the relationship between gender and patient activation¹³

Future studies should evaluate the importance of other factors, such as cognitive impairment, health literacy, motivation and self-efficacy with regard to self-management activation. Additionally, scientific efforts are needed to investigate causal pathways between these determinants and activation. This knowledge might help healthcare professionals to identify patients at risk of inadequate self-management behaviours, which is essential for the development of more individually targeted and tailored interventions.

CONCLUSION

Patient activation is more in males compared to females. Hence healthy behaviours should be educated for diabetic patients to reduce complications and improve their quality of life and activation.

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ORIGINAL ARTICLE

High Incidence of Advanced Stage Prostate Cancer in Riau Province of Indonesia

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ABSTRACT

Introduction: Indonesia is in the fifth position of the most prostate cancer incidence countries in Asia with the rate of 10.6 per 100.000 cases from all group of age and the mortality rate is about 8 per 100.000 cases. The objective of this study is to identify the characteristics of advanced stage prostate cancer patients.

Materials and Methods: We reviewed the medical records of 42 advanced stage prostate cancer men of all 103 prostate cancer men in Arifin Achmad Regional General Hospital Pekanbaru Riau Province, Indonesia, from January 2010 to December 2016.

Results: There were 103 adenocarcinoma of prostate patients from January 2010 to December 2016 consisting of 61 (59.2%) initial staging and 42 (40.8%) advanced stage prostate cancer patients in which included in this study. Most (40.5%) advanced stage prostate cancer patients were 61-70 years old. Most (88.1%) abnormal finding were found in digital rectal examination (DRE). Most (28.6%) patients had 61-80 ml prostate volume with Transrectal Ultrasound (TRUS). Most (47.6%) patients had initial Prostate Specific Antigen (PSA) >100 ng/ml with Gleason Score were mostly (81%) poorly differentiated. The bone scan results showed that 30 patients (71.4%) were positive for metastasis. The treatment with Androgen Deprivation Therapy (ADT) show the highest modality (78.6%).

Conclusions: We found high incidence of advanced prostate cancers with high ages, high abnormality in DRE, high prostate volumes with TRUS, high PSA levels, high poorly differentiated adenocarcinomas, high Gleason Scores, high metastasis in bone scans and high treatment with ADTs.

Keywords: Prostate cancer, Prostate Specific Antigen, Digital Rectal Examination, Bone scan, Androgen, Deprivative Therapy

INTRODUCTION

Prostate cancer is the fourth most found case of malignancy on male after skin, lung, and colon cancers. ^{1,2} In 2012 there were 1,1 million cases diagnosed as prostate cancer in the world, with the highest incidence in Australia, New Zealand and North America (97,2 per 100.000).¹ The number of new case and death caused by prostate cancer are rising as the increasing number of elderly people. According to the data of 2009-2013 in the United State, the number of new prostate cancer are about 129,4 per 100.000 civilian and the mortality rate are 20.7 per 100.000 civilian each year.³ In European countries, prostate cancer is more likely suffered people at the age of 70 years old. Mostly prostate cancer incidence in Asia is lesser than the ones in industrial countries, but it seems to be showing some sign of increase.¹ The last data from Asia shows that there was an increasing trend of prostate cancer

incidence in several countries such as China, Japan, Philipines, Singapore, South Korea and Thailand compared to other high risk country (such as America and Europe).⁴

Indonesia is in the fifth position of the most prostate cancer incidence country in Asia, with the rate of 10.6 per 100.000 case from all group of age and the mortality rate is about 8 per 100.000. The prevalence of prostate cancer in Indonesia in 2013 were 0.2% or estimated 25.012 patients.⁵ Prostate cancers likely occur on male at the age of above 50 years and it's occurrence will increase as the person grow older.^{6,7} Other than the age factor, the risk of getting prostate cancer will rise with the history of family members having prostate cancer.⁸ Prostate Specific Antigen (PSA) test can be used to predict prostate cancer and the risk of long term metastasis.⁹

Transrectal Ultrasound (TRUS) can be used to find nodules on prostate malignancy and to determine the

volume size of prostate.¹⁰ Skeletal imaging examination such as bone scan which has the role of supporting diagnostic tool are more often used as an optimal method in evaluating the occurrence of bone metastasis.¹¹

Prostate cancer in early stage is almost always symptom-less so that there will be more likely found patient with advanced stage.¹² Especially in Asian countries, the rate of finding prostate cancer in advanced stadium are relatively higher than in USA and Europe, in which many of the cases did not do early screening.^{4,5} According to a study by Umbas (2011), it was reported that there were many advanced stage prostate cancer patients coming to the urology clinic, which was 50% (207 persons) of them were high grade and 66.7% patients (257 persons) are in stages four.⁶ The data from Global Burden Of Cancer Study (GLOBOCAN) data in 2012 showed that the death case from prostate cancer (307.000 cases) were much lower than the newly found cases (1.1 million cases), so it could be concluded that if those cases were detected and handled early the prognosis would be better.^{1,3}

According to the above data, we are interested to know how the characteristic of advanced stage prostate cancer that were being managed in Pekanbaru Riau Province Indonesia by looking in several variable such as age, digital rectal examination findings, PSA level, prostate volume, histopatology with Gleason Score and Grading, bone scan and the type of therapy given.

METHODOLOGY

This research is a descriptive epidemiological study with cross sectional design. The data were collected from medical records of Arifin Achmad Regional General Hospital Pekanbaru Riau Province Indonesia for 7 years in January 2010 until December 2016. The data collected consisted of age, digital rectal examination findings, PSA level, , prostate volume measurement using by Transrectal Ultrasonography (TRUS), histopathology with Gleason Score and grading, bone scan and the therapy. The sampling technique was total sampling fulfilled the inclusion criteria. Inclusion criteria were all advanced stage of prostate cancer according to the American Joint Committee on Cancer, and the histopathological findings from prostate biopsy and Transurethral Resection of Prostate (TURP).

RESULTS

There were 103 adenocarcinoma of prostate consisting of 61 (59.2%) initial staging and 42 (40.8%) advanced stage prostate cancer patients included in this study.

Table 1 shows the advanced stage prostate cancer patients were mostly (40.47%) found in the group age of 61-70 years old meanwhile the least (2.38%) are found in group age of 41-50 years old. The abnormal digital rectal examination findings were 88.10%. Prostate volume 61-80 ml were mostly (28.07%) found and PSA >100 ng/ml were mostly (47.6%) found. The histopathological Gleason Score (7-10) with poorly differentiated grade were mostly (80.96%) found, and the least (7.14%) were the Gleason Score 2-4 with well differentiated grade. The result of bone scan on the advanced stage prostate cancer patients are mostly 71,43% found with metastasis. The type of therapy used on those Advanced stage Prostate cancer patient are mostly (78,57%) Androgen Deprivation Therapy (ADT) and radiotherapy in 21,43.

Table 1. Characteristic of advanced stage prostate cancer patients (n=42)

Characteristics	Cases (%)
Age (years)	
41-50	1 (2.38)
51-60	14 (33.3)
61-70	17 (40.47)
71-80	7 (16.71)
81-90	3 (7.14)
Rectal Toucher	
Normal	5 (11.9)
Abnormal	37 (88.1)
Prostate Volume	
<20 ml	5 (11.9)
20-40ml	5 (11.9)
41-60 ml	9 (21.43)
61-80 ml	12 (28.57)
81-100 ml	7 (16.08)
>100 ml	4 (10.12)
Gleason Score (Grade)	
2-4 (well differentiated)	3 (7.14)
5-6 (moderately differentiated)	5 (11.9)
7-10 (poorly differentiated)	34 (80.96)
PSA level	
≤4	4 (10.12)
4,01-10	4 (10.12)
10,1-20	4 (10.12)
20,1-50	6 (14.28)
50,1-100	4 (10.12)
>100	20 (47.6)
Bone Scan	
No Metastatic	12 (28.57)
Metastatic	30 (71.43)
Therapy	
Androgen Deprivation Therapy (ADT)	33 (78.57)
ADT with radiotherapy	9 (21.43)

DISCUSSIONS

Prostate cancer usually attacks male with the age of 50 or above but it is symptomless. This statement suits the result of this study in which it is acquired

that the advanced stage prostate cancer patient is mostly in the group age of 61-70 years old about 17 patients (40,47%) and the least are in the group age of 41-50 years or 1 patients (2,38%). The result of this study are the same as the one found by Glady et al (2015) in Hasan Sadikin's Hospital Bandung Indonesia in which the most prostate cancer found were in 61-70 years old, 48% (75 patients) out of 156 patients in overall clinical stadium.¹⁴

Abnormal DRE findings are one of the indication for prostate biopsy needed to determine the diagnosis prostate cancer. In this study, the result of the DRE on those advanced stage prostate cancer as patients mostly abnormal findings namely 37 patients (88,10%). Other study by Palmeora et al (2012) had the same result in which the cohort study of 306 prostate cancer patients, 44% (293 patients) of them had abnormal DRE findings but 31% (167 patients) were normal.¹⁵ Some studies reported that DRE was an ineffective screening method, so that the result of those examination were still in controversy. Those studies showed abnormal DRE sensitivity which was only 44% and the specificity of 46% with 46% negative predictive value and 46% positive predictive value in detecting prostate cancer¹⁵. A study done by Wilbur (2008) also found only 25% prostate cancers detected with biopsy after the abnormal findings by palpating in the suspicious area of the prostate.¹⁶

Prostate cancer patients with the prostate volume of 44 ml or more has the risk of developing a high degree tumor, extension out of the capsule, vesicula seminalis invasion and smaller tumor volume.¹⁷ The result of this study shows that the prostate volume of advanced stage prostate cancer patients with TRUS mostly shows 61-80 ml group in 12 patients (28,57%) and the least are on the >100 ml group in 4 patients (10,12%). This result is different from the study done by Umbas et al (2010) that showed prostate gland with smaller volume tended to be more aggressive but the bigger one were not. According to their result of measuring the prostate volume in prostate cancer patients were mostly on the range of 20-40 ml in 47 patient (57,2%), in which 21 cases among them are in poorly differentiated of malignancy.¹⁷

PSA is an important sign in diagnosis, follow up, and to determine the prognosis of prostate cancer. The result of this study shows the PSA level on advanced stadium prostate cancer patients mostly are the group of >100 ng/ml namely 20 patients (47,6%). The same result published by Umbas et al (2011) showed 190 advanced stadium prostate cancers with the PSA level of more than 100 ng/ml were 66,55% from all prostate cancer in Cipto Mangunkusuma Hospital (RSCM) Jakarta and Jakarta's Darmas Cancer Hospital in January 1995 until December 2007¹⁸. Beside being an important sign on diagnosis, PSA follow up can also be rolled as marker of

prostate cancer progressivity such as if there is a possibility of bone metastasis seen from patient clinically. Such as in a study done by Park et al (2011), there were found metastasis on patient with PSA level > 50 ng /ml.¹⁹

Nowadays, gleason grading system is the most common classification used that helps to determine the histologic characteristics of prostate cancer. Prostate cancer patients with Gleason Score above 6 are likely to progress become advanced stage, as are patient with PSA value >10 ng/ml or higher.²⁰ In this study we found the grading of histopathology on the advanced stadium prostate cancer patients are mostly poorly differentiated (Gleason Score: 7-10) namely 34 patients (80,96%) and the least are well differentiated (Gleason Score: 2-4) about 3 patients (7,14%). These result were similar to the ones by Adam et al (2010) which found the degree of histopathology of advanced stadium prostate cancer with mostly poorly differentiated namely 21 patient (44,7%) from 47 patient samples²¹.

The diagnostic standard on bone metastasis which are commonly used nowadays are the bone scan with 99mTc methylene diphosponate (MDP). This study finds the bone scan results on the advanced stadium prostate cancer patients mostly shows metastasis which namely 30 patients (71,43%). This result suits the results with the one done in China by Dalin et al (2016) in which from 407 advanced stadium prostate cancer patients showed 340 patients (83,5%) had bone metastasis²². Other study done by Poussel et al (2006) showed most bone metastasis in 17 patients (68%) of 25 advanced stadium prostate cancer patients²³.

Androgen Deprivation Therapy (ADT) is a first line standard therapy for advanced stadium prostate cancer patient that commonly used today. The result of this study showed the type of therapy used to treat advanced stadium prostate cancer is ADT in 33 patients (78,57%). The same result gained by Lawrenson et al (2015) in a study on 234 prostate cancer with metastasis patients. The ADT therapies were mostly used in 105 patient (82,9%) followed by radiotherapies in 104 patients (44,4%).²⁴

CONCLUSION

We found high incidence of advanced prostate cancers with high ages, high abnormality in DRE, high prostate volumes with TRUS, high PSA levels, high poorly differentiated adenocarcinomas, high Gleason Scores, high metastasis in bone scans and high treatment with ADT's.

Conflict of Interest: The authors have nothing to disclose.

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ORIGINAL ARTICLE**A Study on Attitude and Perception of Medical Students towards Rural Health Services in Hilly Region of Uttarakhand**Janki Bartwal¹, Amit K Singh²**Author's Affiliations:** ¹Assistant Professor; ²Prof. & HOD, Dept. of Community Medicine, VCSG Government Medical Science and Research Institute, Srinagar Garhwal**Correspondence:** Dr. Amit Kumar Singh, Email: hodpsmvcsgr@rediffmail.com**ABSTRACT****Background:** The wide disparities in health status exist within many countries worldwide. Lack of access to quality health-care providers is one of the primary root causes of health inequity and is disproportionately experienced by people living in remote and rural communities.**Aims & objectives:** To study the attitude and perception of medical students towards rural health service.**Materials and Methods:** A cross-sectional study was conducted in the government medical college in the state of Uttarakhand, India. A semi-structured, self-administered questionnaire was filled by 457 undergraduate medical students. Data were analyzed by using SPSS version 16. Chi square test was used for statistical analysis and $p < 0.05$ was considered significant**Results:** Of the 457 students, 261 (57.1%) were willing to work in rural areas after graduation. Mostly (33.9%) said they would work for 1-2 years. Majority (63.5%) of the students wants to contribute towards the betterment of health system of the state. 38.7% wish to join Government health facility. Limited infrastructure facilities, limited professional growth, delay in post graduation were the few reasons cited by the students for refusing to work in rural areas. Rural residence and schooling done in rural areas has significant association with willingness to work in rural areas after graduation.**Conclusion:** More than half of the students wished to work in rural areas but mostly for one to two years. The rural postings should be made attractive so that more of the undergraduates join rural health system.**Key words:** Medical students, rural, health service, Uttarakhand**INTRODUCTION**

Approximately one half of the global population lives in rural areas, but less than a quarter of the total physician workforce served this area. The situation is especially dire in developing countries where a critical shortage of trained health workers means an estimated one billion people have no access to essential health-care service.¹

The critical shortage of human resources in health service delivery and its unequal geographical distribution is documented in many studies.² According to a report, almost 69% of India's population lives in its villages while only about 26% of its doctors serve here.³

Uttarakhand (UK) is predominantly a hilly state (86% of the total geographical area).⁴ It is considered as a high focus state under National Rural Health Mission considering the poor health outcomes. The situation here is far worse with doctor per 1000 population ratio of 0.31.⁵

As per the Rural Health Statistics (RHS) 2016 report, 44.3% of the medical officer post lie vacant at Primary Health Centre (PHC) in UK while there is a shortfall 82.6% specialists at Community Health Centre (CHC) in the state.⁶

Hence, the state government has implemented a compulsory rural service after MBBS since the year 2008 when the first government medical college was established in the state. All the medical graduates from the Government colleges enter the government service under the 'bonded' contract and have to sign a bond at the time of admission to medical college that requires them to compulsorily serve in rural areas for 5 years. For the bonded category, the government heavily subsidizes the tuition fee. Such candidates are required to join the rural service after they finish their medical internship. In case of breaking this bond the student has to submit 30 lakhs which has been increased to 1 crore since the academic year 2017-18.⁷

OBJECTIVES

The objective of this research was to study the attitude and perception of medical students towards rural health service

METHODOLOGY

Uttarakhand is one of the hilly states situated in Northern India. There are three government medical colleges run by the state government and the present study was conducted in one of them. This cross sectional study was conducted among undergraduate medical students during Aug 2017 to Dec 2017.

Sample size – Considering a default prevalence (p) of 50% for favourable attitude towards working in rural areas after completing graduation and applying the formula of $4pq/d^2$, where d or absolute precision was taken as 5% and considering the non response rate as 10%. Sample size was calculated to be 440.

Sampling procedure – All the undergraduate medical students present on the day of study were briefed about the purpose of this study and were told that their participation was voluntary. They were not required to write their names to ensure confidentiality and to elicit correct responses from them. A pre-designed, pretested semi-structured self-administered questionnaire was used to collect the relevant information pertaining to study variables. Ethical approval was obtained from Institutional Ethics Committee before the commencement of study and written informed consent was obtained from the students.

Data collection and analysis – The data collected was coded, entered into Microsoft excel sheet and were analyzed using the Statistical Package for the Social Sciences version 16 software (SPSS Inc., Chicago, IL, United States). Statistical analysis was done using Chi square test and $p < 0.05$ was considered significant.

RESULTS

A total of 457 completed questionnaires were assessed. The mean age of respondents was 20.7 ± 1.76 years. The female students 285 (62.4%) outnumbered the males 172 (37.6%). Respondents' father and mother were graduate and above 370 (81%) and 298 (65.2%) respectively. 132 (28.9%) student's parents were working in rural areas. Majority 363 (79.4%) of the student's parent's residence was in urban area. Students mostly 383 (83.8%) had their secondary school in urban areas. 382 (83.6%) students made self - decision regarding choosing medicine as a career. 261 (57.1%) of students were willing to work in rural areas after graduation. 155 (33.9%) of the students would like to work only for 1-2 years in rural areas after completing graduation. [Table 1]

Table 1: Socio-demographic characteristics of the medical students (N=457)

Variables	Students (%)
Age group (years)	
17- 20	124 (27.1)
20-23	255 (55.8)
23-26	78 (17.1)
MBBS semester	
First	86 (18.8)
Third	99 (21.7)
Fifth	99 (21.7)
Seventh	95 (20.8)
Ninth	78 (17)
Sex	
Male	172 (37.6)
Female	285 (62.4)
Education of Father	
Below graduate	87 (19)
Graduate and above	370 (81)
Education of Mother	
Below graduate	159 (34.8)
Graduate and above	298 (65.2)
Any one of the parent working in rural areas	
Yes	132 (28.9)
No	325 (71.1)
Residence	
Urban	363 (79.4)
Rural	94 (20.6)
Secondary school	
Urban	383 (83.8)
Rural	74 (16.2)
Choosing Medicine as a career was decision made by	
Self	382 (83.6)
Parents	64 (14)
Others	11 (2.4)
Work in rural area after MBBS	
Yes	261 (57.1)
No	196 (42.9)
If at all one has to serve in hilly region, duration of service (in years)	
<1	8 (1.8)
01-02	155 (33.9)
02-03	151 (33)
03-04	101 (22.1)
04-05	42 (9.2)

Table 2: Factors perceived by the medical students for willingness to work in rural areas

Perceived factors for working in rural areas*	Students (N=457) (%)
To do private practice	39 (8.5)
Compulsory rural service bond	287 (62.8)
To join Government Health facility	177 (38.7)
Less work load in rural areas	103 (22.5)
Own residence in rural areas	50 (10.9)
Less stressful life	124 (27.1)
To contribute for betterment of health system of the state	290 (63.5)

*Multiple responses

Table 3: Factors perceived by the medical students for unwilling to work in rural areas

Perceived factors for unwilling to work in rural areas*	Frequency (N=457) (%)
Limited professional growth	288 (63)
Limited infrastructure facilities	297 (64.9)
Own residence in urban areas	113 (24.7)
Delay in Post graduation	265 (57.9)
Lack of educational opportunities for children and family amenities	219 (47.9)
Lack of recreational facilities	201 (43.9)
Less salary	111 (24.3)
Geographical location of health posts	187 (40.9)

*Multiple responses

Table 4: Incentives for encouraging the doctors to work in rural areas

Incentives the Government should provide for encouraging the doctors to work in rural areas*	Frequency (N=457) (%)
Reservation in PG seat	282 (61.7)
Appropriate career and postings	289 (63.2)
Salary and incentives should be regular and 1.5 times of current salary	328 (71.7)
Improvement of facilities	392 (85.7)

*Multiple responses

Table 5: Association between rural postings and socio-demographic profile

Variables	Rural posting		Total(N=457)%	χ^2 , p value
	Yes (n=261)%	No(n=196)%		
Age group (years)				$\chi^2 = 7.01$, p = 0.03*
17-20	81(65.3)	43(34.7)	124(27.1)	
20-23	132(51.8)	123(48.2)	255(55.8)	
23-26	48(61.5)	30(38.5)	78(17.1)	
MBBS semester				$\chi^2 = 10.3$, p = 0.036*
First	62(72.1)	24(27.9)	86(18.8)	
Third	56(56.6)	43(43.4)	99(21.7)	
Fifth	52(52.5)	47(47.5)	99(21.7)	
Seventh	49(51.6)	46(48.4)	95(20.8)	
Ninth	42(53.8)	36(46.2)	78(17.0)	
Sex				$\chi^2 = 2.93$, p = 0.087
Male	107 (62.2)	65 (37.8)	172(37.6)	
Female	154 (54.0)	131 (46.0)	285(62.4)	
Education of Father				$\chi^2 = 111$, p = 0.000*
Below graduate	52 (27.8)	135(72.2)	187(40.9)	
Graduate and above	209 (77.4)	61(22.6)	270(59.1)	
Education of Mother				$\chi^2 = 1.06$, p = 0.303
Below graduate	96(60.4)	63(39.6)	159(34.8)	
Graduate and above	165(55.4)	133(44.6)	298(65.2)	
Any one of the parents working in rural areas				$\chi^2 = 10.6$, p = 0.001*
Yes	91(68.9)	41(31.1)	132(28.9)	
No	170(52.3)	155(47.7)	325(71.1)	
Residence				$\chi^2 = 29.7$, p = 0.000*
Urban	184(50.7)	179(49.3)	363(79.4)	
Rural	77(81.9)	17(18.1)	94(20.6)	
Secondary school				$\chi^2 = 16.3$, p = 0.000*
Urban	203(53.0)	180(47.0)	383(83.8)	
Rural	58(78.4)	16(21.6)	74(16.2)	

*significant at p < 0.05

All the students were asked to state the factors they perceived to work as well as for unwilling to work in rural areas. Of the 457 students, majority 290 (63.5%) of the students want to contribute towards the betterment of health system in the state, followed by 287 (62.8%) intend to work in rural areas as a compulsory rural health service bond filled at the time of admission. 177 (38.7%) were keen to join Government health facility. [Table 2]

The factors which discourages the budding doctors from working in rural areas include, limited infrastructure facilities 297 (64.9%), limited professional growth 288 (63.0%), delay in post graduation 265 (57.9%), lack of educational opportunities for children and family amenities 219 (47.9%), lack of recreational facilities 201 (43.9%), geographical location of health posts 187 (40.9%), residence in urban areas 113 (24.7%) and less salary 111 (24.3%). [Table 3]

Few suggestions to the Government as stated by the students which can encourage doctors to work in rural areas includes improvement of facilities 392 (85.7%), regular salary and incentives & 1.5 times of current salary 328 (71.7%), appropriate career and postings 289 (63.2%), and reservation in post graduation (PG) seat 282 (61.7%). [Table 4]

Association between student's willingness to work in rural areas and factors such as age, semester in which students were studying, education status of father, any of the parents working in rural area, residence and schooling in rural areas has significant association while sex of the student and education status of mother was not found to be significant. [Table 5]

DISCUSSION

In the present study, 26(57.1%) were willing to work in rural areas after completing their graduation. Almost similar finding was reported by Kotha SR et al⁸ and Chuenkongkaew WL et al.⁹ In some studies prevalence was as low as 8%¹⁰ and as high as 72.4%.¹¹

In the present study, 163 (35.7%) were willing to work upto 2 years. In study conducted by Jain M et al¹² 66.2% want to work in rural areas for < 1year while in Saini NK et al¹³ 66.4% want to work for a few months to 2 years.

The major factor which was perceived to work in rural areas were compulsory rural service bond signed by medical students at the time of admission, others were contribution towards state health facility, to join Government job, less stressful life and workload, own residence in rural area and to do private practice. In studies done by Jain M et al¹² and Saini NK et al,¹³ 66% & 42.3% students respectively want to contribute towards state health system while 42% & 7.5% of the students respectively felt that in rural areas life was less stressful. Sultana A et al¹⁴ observed that 8.4% participants perceived less work pressure in rural while in study by Sinha RK¹⁵ 62.5% participants perceived less competition. Jain M et al¹² observed in her study that 15% medical students want to do private practice.

The factors perceived for not willing to work in rural areas were limited infrastructure facilities. Similar concerns were echoed by medical students in other studies.^{9, 11, 12, 13, 16, 17} Limited professional growth and lack of educational opportunities for children and family amenities were other factors cited by the students, similar findings were observed in other studies also.^{9, 12, 13, 16} Students were also apprehensive about rural postings as this would delay in doing post graduation as reported by students in other medical colleges.^{11, 17} Less salary and lack of recreational facilities were among other issues, as was also reported by other researchers.^{13, 14, 16}

Incentives as suggested by the medical students which Government should provide for encouraging the doctors to work in rural areas includes improvement of facilities whether it is health infrastructure facility, accommodation, transport, security etc. increase in salary, appropriate career opportunities and

postings along with reservation in PG seat for those who worked in rural areas. Similar findings were observed in other studies also.^{11, 12, 14, 16, 18}

Significant association with student's willingness to work in rural areas after graduation and rural residence was also reported in other studies.^{8, 9, 13-16} Chuenkongkaew WL et al,⁹ Jain M et al,¹² Sinha RK¹⁵ observed that students who had done schooling from rural areas were more willing to work in rural areas similar to the finding observed in present study.

CONCLUSION

More than half of the students intend to work in rural areas after graduation but mostly for a period of upto two years. Government should take certain steps for attracting and retaining the doctors in rural areas like providing better infrastructure, career opportunities and reservation in PG seat etc.

Limitation of the study: It could have been done on a larger scale involving all the undergraduate medical students in the three state run government medical colleges of Uttarakhand for better representation.

Relevance of the study: Since there is crisis of doctors, especially in remote areas, it is better to know what all factors influence the medical student's attitude and perception regarding rural posting. The suggestions can be helpful to the policy makers in attracting and retaining doctors in rural remote areas.

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ORIGINAL ARTICLE

Effectiveness of Triple Drug Fixed Dose Combination Inhaled Therapy in Severe COPD Patients

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ABSTRACT

Rationale: According to GOLD 2018 guidelines, inhaled corticosteroids are recommended along with long acting muscarinic antagonist (LAMA) and long acting beta-2 agonist (LABA) inhaler medications in Group D COPD patients who show frequent exacerbations and symptom severity. Therefore, the use of triple drug inhaled medication in such severe COPD patients become necessary.

Objectives: To know the effectiveness of inhaled triple drug medication in relation to spirometry, exercise tolerance, symptom control and prevention of exacerbations in severe COPD patients.

Method: 25 severe COPD patients were included in this hospital based study. Before initiating the triple drug inhaled medication the baseline parameters such as spirometry (FEV1), exercise tolerance (6 minute walking distance) and symptom control (CAT score, MMRC dyspnoea grading) are measured. 2 monthly follow-up till 6 months of the study period is done. At each visit all the baseline parameters are reassessed.

Result: There is statistically significant ($p < 0.01$) improvement in the FEV1, CAT scoring, MMRC grading, 6 Minute Walking Distance in the 25 subjects following initiation of treatment with the triple drug inhaler medication over 6 months observation period.

Conclusion: Triple drug inhaler medication in severe COPD patients is effective in improving airflow obstruction, symptom control, exercise tolerance and prevention of exacerbations.

Keywords: COPD, triple drug, MMRC, CAT Scoring

INTRODUCTION

GOLD 2018 defines chronic obstructive pulmonary disease (COPD) as a chronic, progressive and treatable disease characterized by persistent airflow limitation caused by damage to alveolar and or airway wall due to inhalation of environmental toxic noxious gas or particle.¹ Exacerbations and comorbidities contribute to the overall severity of patients.^{2,3} The destruction of lung parenchyma, increased by subtended inflammatory processes, leads to loss of alveolar attachments to the small airways and decreases lung elastic recoil; in turn, these changes the ability of the airways to remain opened during expiration.^{3,4}

COPD management is a major healthcare problem, and numerous recommendations/guidelines were created to increase appropriateness hence to address the unmet need of patients remaining symptomatic, so to improve patients benefit and reduce exacerbation risk,⁵ International guidelines such as the GOLD (Global Strategy for Diagnosis, Management and Prevention of COPD) provide guidance to physicians in treating COPD.⁴

COPD patients usually show neutrophilic inflammatory response to the environmental toxic gas or particle. However it is found that those patients who show atopy or has family history of atopy, asthma will show eosinophilic inflammatory response also.⁶ Therefore the idea of adding an inhaled corticosteroid as a medication in these patients comes into picture.

Till date, long acting muscarinic antagonist (LAMA) or LAMA and long acting beta 2 agonist (LABA) has served as a better treatment option in COPD patients³. The use of inhaled corticosteroids in addition to LABA and LAMA is seen to be effective in following patients:

- Allergy to dust, smoke and seasonal variation.
- Frequent episodes of exacerbations requiring emergency room visits.
- Spirometry showing post bronchodilator FEV1 reversibility but $< 12\%$ or $< 200\text{ml}$ ⁷.
- Family history of atopy, bronchial asthma.

Triple drug inhaled therapy delivered in a single inhaler dose reduces moderate to severe exacerbations

in COPD to a greater extent than dual inhaler therapy in patients at high risk for exacerbations, according to several studies such as IMPACT trial⁸ and TRINITY trial⁹.

METHODOLOGY

This is a hospital based study conducted from July 2017 to June 2018 in 25 severe COPD patients. These subjects were either not taking any inhaler therapy or were on dual drug inhaler medication. All the patients were male ex-smokers. Those already on dual inhaler medication were stopped from taking it and after washout period of those medications were put on single dose inhaler containing triple drug medication (LAMA+LABA+ICS). Those who were not taking any medications were directly initiated with the triple drug inhaled medication. Prior to this, baseline parameters like Spirometry, MMRC grading, CAT score, 6 Minute Walking Distance and BODE Index were assessed in all the subjects.

Patients were asked to come to the OPD every 2months for a total duration of 6months. During these 6months, patients were asked to report any time if they feel worsening of their symptoms and those episodes were considered as exacerbations. Patients’ frequencies of emergency room visits were noted. At each 2monthly visit, all the aforementioned baseline parameters were reassessed. At the end of 6months, the effectiveness of triple inhaler therapy was calculated by comparing the baseline values with the end of 6month values.

Inclusion criteria: Above 40 years male or female patients with smoking history >10pack years and stable severe COPD patients since past one month were included in the study

Exclusion criteria: Pregnant women or lactating mother; cases with history of allergy or hypersensitivity; who are not giving consent; cases requiring oral or parenteral steroids; who were vaccinated in a last year; who are on roflumilast as add on therapy; or cases having associated other severe co-morbid conditions were excluded from the study..

RESULTS

Minimum age in this study is 41yrs and maximum age is 74yrs. There are 11(44%) patients in age group

61-65 yrs followed by 7(28%) patients in age group 66-70yrs. There are 2(8%) patients each in the age group 41-45yrs, 51-55yrs and above 70 yrs. There is only 1 patient in the age group 56-60yrs (Table 1). All patients included in the study are male ex-smokers however depending on their smoking history in the past they are divided on the basis of their smoking index. There are 12(48%) patients having history of smoking index in the range 0-50 followed by 11(44%) patients with smoking index in the range 51-100. There are only 2(8%) patients with smoking index above 100 (Table 2). There is decrease in the frequency of emergency room visits by severe COPD patients after initiation of tripe drug inhaled medication as seen in table 3.

Table 1: Age wise distribution

Age group(years)	Patients (%)
41-45	2 (8)
46-50	0 (0)
51-55	2 (8)
56-60	1 (4)
61-65	11 (44)
66-70	7 (28)
>70	2 (8)
Total	25 (100)

Table 2: Smoking Index

Smoking Index	Patients (%)
0-50	12 (48)
51-100	11 (44)
101-150	2 (8)
Total	25 (100)

Table 3: Frequency of exacerbations

	Emergency Room visits (mean)
Before treatment	1.08
After treatment	0.8

Table 4: Baseline parameters

Parameters	Mean Values	
	Before treatmnt	After treatmnt
PFT	35%	44%
MMRC Grading	2.28	1.96
6 min walking distance	248.96m	270.88m
BODE Index	6.4	5
CAT Score	19.92	15.56

Table 5: Applying paired t test

	Mean	Standard Deviation	95%of CI	T	P value
PFT(0)-PFT(6)	-8.36	2.396	-9.35,-7.37	-17.45	<0.01
MMRC(0)-MMRC(6)	0.32	0.48	0.12,0.52	3.361	<0.01
6MWD(0)-6MWD(6)	-21.92	20.84	-30.52,-13.32	-5.258	<0.01
BODE(0)-BODE(6)	1.4	1.19	0.91,1.9	5.881	<0.01
CAT(0)-CAT(6)	4.36	2.94	3.15,5.57	7.409	<0.01

There is significant improvement in post bronchodilator FEV₁, Modified Medical Research Council (MMRC) grading system of dyspnoea, 6minute walking test, BODE index score and COPD Assessment Test (CAT) score in our study as seen in the table 4 and 5.

The change in mean from before starting treatment and at the end of 6 month follow up in spirometry, MMRC scale of dyspnoea, 6 Minute walking test, BODE Index, CAT Score is -8.36, 0.32, -21.92m, 1.4 and 4.36 respectively. The change in standard deviation in PFT, MMRC Scale, 6MWD, BODE Index and CAT Score is 2.396, 0.48, 20.84, 1.19 and 2.94 respectively. The p value for all the parameters are <0.01 which is statistically significant.

DISCUSSION

The goals of COPD therapy are to prevent and control symptoms, reduce the frequency and severity of exacerbations and improve exercise tolerance¹. Triple drug inhaled medication containing long acting muscarinic antagonist, long acting Beta- 2 agonist and inhaled corticosteroid has become an option for maintenance treatment of COPD and as a “step-up” therapy from single or double combination treatments⁸.

In my study, the mean value for the frequency of emergency room visits before triple inhaled medication was 1.08 and after 6months of triple inhaled medication was 0.8 which shows improvement in the exacerbations in COPD patients and this is comparable to other studies as follows:

IMPACT trial ⁸ has shown that triple therapy with fluticasone furoate, umeclidinium and vilanterol resulted in a lower rate of moderate to severe COPD exacerbations (0.91per year) than fluticasone furoate-vilanterol or umeclidinium-vilanterol (1.07 per year). Rate ratio with triple therapy, 0.85; 95%CI, 0.8 to 0.9; 15% difference; p value <0.001.

TRINITY trial ⁹ has shown moderate to severe exacerbation rates with extrafine fixed triple therapy (0.46; 95% CI 0.41 to 0.51). Fixed triple inhaled therapy was superior to tiotropium alone (rate ratio 0.80; 95% CI 0.69 to 0.92; p value=0.0025).

FULFIL trial ¹⁰ also showed statistically significant reduction in exacerbations with triple therapy versus dual ICS/LABA therapy (35% reduction; 95% CI 14 to 51; p value = 0.002).

In Rojas-Reyes et al trial included total 4 studies showed reduction in all cause hospitalizations with the use of combined therapy with tiotropium and LABA/ICS (0.61; 95%CI 0.4 to 0.92; 2 studies; n=961) ¹¹.

In Xie F et al review on Triple therapy for management of COPD which included 4 trials also concluded that hospitalization rates due to COPD exacerbations were significantly reduced with triple therapy compared to long acting muscarinic antagonist monotherapy (rate ratio 0.53; 95% CI 0.33 to 0.86 and 0.35; 95%CI 0.16 to 0.78) ¹².

In my study, improvement in mean value of FEV₁ was -8.36; 95% CI -9.35 to -7.37; p value <0.01 which is comparable to other studies given below. In TRINITY trial, for 52week pre-dose FEV₁, fixed triple dose inhaler was superior to tiotropium (mean difference 0.061L[95%CI 0.037 to 0.086]; p value <0.0001) ⁹. In FULFIL trial, mean changes from baseline in FEV₁ at 24 week for triple therapy (n=911) was 142ml (95% CI 126 to 158) ¹⁰. In Xie F et al review in Triple therapy for COPD improvement in lung function as measured by FEV₁was (with mean value 0.05L, 95% CI 0.00 to 0.11; 3 trials) ¹².

In our study we have used BODE Index as a measure of quality of life which showed mean value 1.4; 95% CI 0.91 to 1.9; p value <0.01. There was significant improvement in quality of life of COPD patients on triple inhaler medication which is also seen in the studies given below. In FULFIL trial, mean changes from baseline SGRQ (Saint George Respiratory Questionnaire) scores was -6.6 units(95% CI -7.4 to -5.7) ¹⁰. In Rojas –Reyes et al study, SGRQ scores showed statistically significant improvement in total scores with use of tiotropium and ICS/LABA compared with tiotropium alone (mean difference -3.46; 95%CI -5.05 to -1.87; 4 studies, n=1446) ¹¹. In Xie F et al review on Triple therapy for COPD showed significant improvement in quality of life (with mean difference 3.75; 95% CI 1.56 to 5.94; 2 trials) ¹².

CONCLUSION

Triple drug inhaled medication is effective in improving symptom control and frequency of exacerbations in severe COPD patients. This makes triple therapy an attractive combination in COPD.

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ORIGINAL ARTICLE

A Prospective Evaluation of Predictive Risk Factors, Severity of Liver Injury and Course of Anti –Tubercular Treatment Induced Hepatotoxicity

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ABSTRACT

Background: Hepatotoxicity is an established complication of Anti-tubercular treatment. However, there is limited information on the incidence, possible predictive risk factors and course of anti- tubercular treatment induced hepatotoxicity.

Objective: The study was planned to evaluate incidence, possible predictive risk factors and course of anti-tubercular treatment induced hepatotoxicity (ATTIH) .

Methodology: The present prospective study was conducted with Newly diagnosed pulmonary and extra-pulmonary tuberculosis patients admitted from may 2014 to may 2016. A sample size of 150 patients were put on ATT ranging from 6 months to 12 months depending on type of Tuberculosis. Their pretreatment clinical, biochemical and radiological parameters were recorded. These parameters were compared between cases and controls by appropriate statistical methods. Patients with abnormal base line LFT'S, Treatment defaulters, failure, MDR cases and patients with NASH, cirrhosis ,acute viral hepatitis &/or renal or cardiac disease were excluded from this study.

Results: Out of 150 patients 22 patients (14.7%) developed ATTIH. Among 22 patients 15 (68.2%) were females and 7 (31.8%) were males. Higher incidence of ATTIH was seen in patients with low BMI of 18.99kg/m²(45.16%), pretreatment low serum albumin <2.5gm(65.21%), Corrected calcium < 7.9gm/dl(58.8%), Serum cholesterol < 200mg/dl (59.1%), Extra pulmonary TB(69.3%), concomitant paracetamol intake(77.7%). Age and consanguinity were statistically insignificant. In this study 18 patients (81.81%) developed ATTIH within 2 weeks of starting ATT with average of 9 days and severity of liver injury ranged from mild with ALT (51-250IU/L) in 12(54.5%), intermediate (251-500IU/L) in 7 (31.8%) and severe (ALT >500IU/L) in 3(13.6%). Normalization of LFTs after ATTIH was seen within first 2 weeks in 11(50%) patients with average of 11 days. ATTIH was associated with prolongation of expected treatment duration in 16 (72.7%) patients. Recurrence of ATTIH was not seen in any patient on reintroduction of treatment. Among 22 patients, 19(86.36%) were cured, 2(9.1%) expired and 1 patient lost follow up.

Conclusion: Early identification of predictive risk factors, modification of treatment with close monitoring and hospitalization are required for reducing morbidity, mortality and treatment completion in ATTIH.

Key words: Tuberculosis, Anti-tubercular treatment induced hepatitis (ATTIH), Prolongation of treatment.

INTRODUCTION

Tuberculosis is a global emergency. More than 90% of global tuberculosis cases and deaths occur in developing world. An effective control has been achieved by wide spread use of anti-tubercular drugs. Hepato-toxicity is well known with, anti-tubercular Treatment^{1,2,3}, severity of which ranges from mild alteration in liver enzymes to hepatitis and occasionally complicated by liver failure carrying high mortality unless transplanted. Drug induced hepatotoxicity is potentially serious adverse effect of currently used regimens containing isoniazid, rifampicin and pyra-

zinamide^{1,2,3}. Single agent prophylaxis in TB with Isoniazid resulted in transaminitis in 20% patients but only 1% had severe liver necrosis requiring withdrawal of drug ⁴. Several types of drug induced liver damages have been described; 1). Idiosyncratic damage, 2) Dose dependent toxicity, 3). Induction of liver enzymes, 4). Drug induced acute hepatitis, 5). Allergic reactions^{5,6,7}. Factors implicated in the development of ATTIH are; 1) Advanced age, 2) Female sex, 3) Alcoholism, 4) Underlying liver disease, 5) Acetylator phenotype, 6) N- acetyl transferase activity, 7) Glutathione S transferase activity, 8) HIV infection, 9) Extensive disease, and 10) Malnutrition⁸.

Criteria⁹ for ATTIIH includes at least one of them; 1) A rise of 5 times the upper limit of normal levels of AST/ALT. 2) A rise in the level of serum total bilirubin >1.5mg/dl. 3) Any increase in ALT/AST above normal levels with nausea, vomiting, anorexia and jaundice. If the transaminase levels are < 5 times upper limit, toxicity was considered mild, 5-10 times moderate and > 10 times as severe⁹. The present study was planned to evaluate incidence, possible predictive risk factors and course of anti-tubercular treatment induced hepatotoxicity (ATTIIH)

METHODOLOGY

The study was conducted in department of general medicine of Sheri Kashmir institute of medical sciences (SKIMS) Srinagar, Kashmir. A total of 150 Newly diagnosed pulmonary and extra-pulmonary tuberculosis patients admitted from May 2014 to May 2016 were studied. All patients were put on ATT ranging from 6 months to 12 months depending on type of TB. Patients who developed ATTIIH were considered as cases and those not, as controls. All patients had pre treatment evaluation for the evidence of liver diseases, body weight & BMI, history of alcoholism or concomitant drug therapy and laboratory evaluation including complete hemogram, albumin levels, serum cholesterol, LFTs and USG abdomen. Malnutrition was defined as BMI of < 18.99kg/m². Viral markers were considered to exclude viral hepatitis. Presence of fatty liver was excluded on the basis of USG. These parameters were compared between cases and controls. Patients with abnormal base line LFT'S, Treatment defaulters, failure, MDR cases and patients with NASH, cirrhosis ,acute viral hepatitis &/or renal or cardiac disease were excluded from our study.

Statistical Analysis: Statistical software SPSS version 20.0 and Microsoft excel were used to carry out the statistical analysis of the results obtained from the study. Data was analyzed by means of descriptive statistics viz, mean, standard deviation, percentages and presented by means of bar diagrams . For parametric data Students independent t-test was employed. Chi square test or Fishers exact test, which ever appropriate was used for non- parametric data. P – value of less than 0.05 was considered statistically significant.

RESULTS

A total of 150 Newly diagnosed pulmonary and extra-pulmonary tuberculosis patients were studied, 73 (48.7%) were males and 77 (51.3%) were females, out of 150 patients 22 (14.7%) developed ATTIIH. Higher incidence of ATTIIH was seen in females

15(68.2%), thus female gender was statistically significant risk factor for ATTIIH (p <.05)

Table 1: Incidence and Pretreatment characteristics with predictive value of ATTIIH

Variables	cases	controls	p value
Total patients	22(14.70%)	128(85.3%)	
Sex M:F	7:15	66:62	<0.05
Age	32 ±11.2	34 ±14.5	0.068
BMI ratio (M±2SD)	17.22 ±2.75	21.50 ±2.31	<0.05
Albumin (M±2SD)	2.8 ±1.12	4.1 ± 8	<0.05
Calcium (M±2SD)	7.2±1.6	9.8 ±1.2	<0.05
Cholesterol (M±2SD)	175 ±17.34	252 ±18	<0.05

Table 2: Alteration of liver function tests in patients of ATTIIH

Patients with ATTIIH	N (n= 22) (%)
ALT	
< 5 times	12 (54.5)
5 -10 times	7 (31.6)
>10 times	3 (13.6)
ALP	
150 – 250	3 (13.6)
251- 350	5 (27.3)
> 350	14 (63.6)
Bilirubin	
1.5 – 2	3 (13.6)
2-4	14 (63.6)
>4	5 (22.7)
Deranged	
1-1.5	16 (71.3)
>1.5	6 (32.7)

Table 3: Frequency of USG findings in ATTIIH cases

USG findings in ATTIIH	Cases (%)
Narrowing of hepatic veins	2 (8.6)
Reactive GB wall thickening	2 (8.6)
Hypo-echoic echo-texture	3 (13.5)
Peri-portal cuffing	6 (27)
Enlarged liver span with smooth borders	7 (34.6)

Table 4: pattern of normalization of LFTs

Duration for normalization of LFT	Cases with ATTIIH (%)
6 days	6 (27.3)
7 to 14 days	11 (50)
15 to 21 days	2 (9)
36 days	1 (4.5)

Table 5 Side effects other than ATTIIH were:

Other side effects	Cases (%)
Gastritis	13(8.7)
Rash	1(0.67)
Thrombocytopenia	1(0.67)
Hyper-uricemia	4(2.6)

In this study 18 patients (81.81%) developed ATTIIH within 2 weeks of starting ATT with average of 9 days. Follow up USGs in all 150 patients was done and out of 22 ATTIIH cases, 14 had acute hepatitis like picture.

Normalization of LFT was seen in 6 patients (27.3%) in 6 days, 11 patients (50%) in 7-14 days with median of 11 days, 2 patients (9%) in 15-21 days, 1 patient took 36 days, 2 patients expired of Acute liver failure. ATTIIH resulted in prolongation of expected treatment duration in 12 patients. Out of 22 ATTIIH patients 19 were completely cured, 2 Patients died of ALF one patient lost follow-up.

DISCUSSION

The use of multidrug regimens for the treatment of Tuberculosis such as the combination of Isoniazid, Rifampicin and Pyrazinamide has been associated with an increased incidence of hepatotoxicity when compared with Isoniazid monotherapy used as Anti-tubercular prophylaxis^{1,10}. In our study 14.7% of the patients developed ATTIIH, an incidence similar to reports from Asia (8-19.8%)^{11,12,13,14} and higher than those from the west (4.3%)¹⁵. Haung et al¹⁵ reported that in total of 224 patients, 33 patients (14.7%) were diagnosed with ATTIIH similar to this study. Similarly, in a study of Hoda et al¹⁶ a total of 100 consecutive TB patients were prospectively followed up both clinically and biochemically before and during the course of anti-Tubercular therapy with daily doses of Isoniazid, Rifampicin, Ethambutol and Pyrazinamide or Streptomycin ATTIIH developed in 15(15%) patients.

In this study 59% cases developed ATTIIH within 7-14 days (average 9 days). This is in agreement with the results of Mehmood et al¹², who reported that the onset of ATTIIH in almost two thirds of their patients (41/67) was within 10-14 days from the start of therapy. Similarly, Shakya et al¹³ reported an interval of 12-60 days (median=28 days). This emphasizes the importance of close and frequent monitoring of patients in first 2 months of anti tubercular treatment.

In the present study the interval from onset of hepatotoxicity to LFTs normalization was 2-46 days (median= 11 days). In almost 3/5th of patients, LFT normalized within 2 weeks which is consistent with Mehmood et al¹² who reported that in 4/5th of patients, LFTs normalized within 2 weeks. In addition, Shakya et al¹³ reported that liver enzymes returned to the normal level within few days of cessation of therapy.

Present study shows increase in the risk of treatment induced hepatotoxicity in females compared to males (19.8 vs 12.5%). Several studies have confirmed the same findings^{15,16,17}.

The higher vulnerability of females could be due to variations in pharmacokinetics and slow acetylation¹⁸ pattern and lower BMI. Malnutrition may be a risk factor for ATTIIH as detected by BMI < 18.99kg/m² and serum albumin levels < 3.5mg/dl. This may be due to depletion of glutathione stores, which makes patients more vulnerable to oxidative injuries and the slower pace at which their liver metabolize drugs. This study shows pretreatment low BMI (63.6%), Low Hb (63.2%), low serum cholesterol levels (59.1%) were associated with higher rates of ATTIIH with a significant p values. Kumar et al¹⁹ reported similar findings.

In this study, among ATTIIH cases concomitant paracetamol ingestion was reported in 77.7%. This factor of indiscriminate drug use may be responsible for higher rates of ATTIIH compared to west²⁰. Other side effects reported were gastritis (9.8%), Hyperuricemia (2.5%), Rash (0.4%), thrombocytopenia (0.8%) and optic neuritis (0.4%). 12(53.8%) patients had mild transaminitis,

Moderate in 7 (33.2%) patients and severe in 3(13%) patients. It was consistent with study of Iftikhar et al²³. We were safely able to reintroduce INH and RCIN in all cases after recovery from hepatitis. We introduced ATT in a stepwise manner²¹ both with regard to the specific drug and the dosage and this strategy proved to be fairly effective and safe.

Out of 22 ATTIIH patients, 20(90.9%) patients with ATTIIH were hospitalized. 3 female patients (9.3%) presented with ALF, among them two patients expired despite discontinuation of ATT and one patient was managed in ICU setting with NAC and her LFTs never normalized and was treated with alternate regimen for 24 months. INH was successfully introduced in remaining patients during hospitalization and these patients were discharged after successful re-challenge. Recurrence of ATTIIH was not seen on reintroduction. All these findings however need to be studied with greater number of cases for confirmation of results.

CONCLUSION

Anti-tubercular treatment induced hepato-toxicity influences the outcome of tuberculosis. It increases the morbidity and mortality. Early detection and pre-treatment risk factor identification, hospitalization and appropriate modification of treatment will definitely reduce the ATTIIH and will result in successful completion of ATT and better outcome.

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ORIGINAL ARTICLE

A Study on the Social and Medical Perspectives on Alcohol Consumption in Adults

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ABSTRACT:

Introduction: Alcohol use has been a significant part of a large number of adults, and can be assumed to be increasingly prominent in the future. Understanding alcohol consumption patterns and factors associated with risky drinking along with social and medical consequences aids in detecting adults who may suffer from the hazardous use of alcohol or alcohol use disorders.

Methods: This is a prospective hospital based study on patients with alcohol related disorders using a structured questionnaire. Study period was from February 2018 to July 2018.

Results: Social reasons were the most common reasons for alcohol consumption. Various economic and occupational factors are also responsible for alcohol intake.

Conclusion: The harmful effects of alcohol misuse are far reaching and range from individual health risks, morbidity, and mortality to consequences for family, friends, and the larger society. The present study assessed some essential issues in alcohol consumption among adults: the prevalence of consumption and associated factors, adults' own reasoning for their alcohol consumption, social and cultural influences on alcohol use and harmful medical consequences.

Key words: alcohol use, prevalence, risky drinking, society, cultural, medical.

INTRODUCTION

Alcohol has been a part of human culture since the beginning of recorded history because of its expected beneficial effects, in search of pleasure or to avoid negative emotional states¹. However, alcohol intake has been identified as an important risk factor for many chronic diseases and injuries². Alcohol consumption is related to cohort life styles, gender, the course of life, social patterns, physiology, cultural heritage, the health condition and moral principles^{3,4,5}. This study provides information on alcohol consumption among community-dwelling adults. It explores the prevalence of alcohol consumption among adults, associated characteristics and their own reasoning for alcohol consumption.

OBJECTIVES

The study was conducted to examine the prevalence and at-risk drinking patterns in community-dwelling adults and their associations with socio-demographic factors; to investigate what the adults themselves consider to be the reasons for their alcohol consumption and also to investigate the health related effects of alcohol.

MATERIALS AND METHODS

We conducted this prospective observational hospital based study on patients with alcohol related disorders. . Both indoor and outdoor patients visiting the Department of Medicine at GNRC Medical, North Guwahati were included in the study. Study period was from February 2018 to July 2018. A written informed consent was taken from the relatives.

A structured questionnaire was developed for this study. A large proportion of the questions were retrieved from previous epidemiological studies in which the questions had been validated^{6,7,8}. The alcohol-related questions included in the inquiry were retrieved from the clinical guidelines and questionnaire for alcohol use in adults⁹ which is adjusted from NIAAA guidelines¹⁰ and AUDIT¹¹.

At-risk drinking for both males and females was defined by taking into account the frequency of use and the portions consumed on one occasion. An at-risk drinking status was defined as consuming 1) >7 drinks per week or 2) >3 drinks several times per week or 3) >5 drinks on a typical day when alcohol is consumed (Clinical guidelines for alcohol use disorders in adults). Categories of alcohol use other than

at-risk drinking included moderate drinking defined by drinking alcohol at least once a month and using at least one portion of alcohol on a typical alcohol-consuming day. Others were defined as minimal/non-users.

RESULTS

Of the 344 respondents investigated most of the subjects were in the 40-59 year age group (181, 52.6%). Prevalence of alcohol use was more among males (77.62%) as compared to that in females (22.97%). Prevalence of problem drinking was more among the married patients(78.48%) as compared to single(13.95%), divorced(1.45%) or widowed(6.10%).

Illiteracy and lower education level(75.87%) was associated with increased alcohol consumption. Prevalence of alcohol consumption was higher among daily wage earner(26.16%) followed by those involved in agriculture(18.02%), factory(16.56%) and service-man(15.40%). Majority of alcohol users belonged to middle class and low middle class family.

Of the 344 respondents while 7.84% (n = 27) exceeded the defined at-risk drinking limit while 56.39% were moderate users.

Among the respondents, the younger age groups reported more often than the older age groups that they used alcohol for having fun, celebration, and for social reasons. Report using alcohol for medicinal purposes increased with age, being 5.23%.

Hypertension (51.74%) was common among the alcohol users followed by diabetes (20.93%) and depression (9.59%). Of 344 respondents, 47.96% and 42.15% presented with fatty liver disease and alcoholic hepatitis respectively whereas 13.37% progressed to chronic liver disease.

DISCUSSION

A study which was done in Faridabad showed the prevalence of alcohol use to be 24.6% among men, while none of the women had used alcohol¹². Similarly, our study showed that prevalence of alcohol use was 22.97% among females.

Male gender and adult age group were found to be independently associated with an increased risk of alcohol use in another study¹³. Similarly, it was found that illiteracy and lower educational levels were associated with an increased risk of alcohol use in the general population ¹⁴.

A study from Vellore reported that hazardous alcohol use was 14.2% as compared to a 7.84% use in our study ¹⁴. A study among industrial workers in Goa showed the prevalence of hazardous drinking to be 21%¹⁵.

Table 1: Population Composition

Variables	Patients (%)
Age(in years)	
<30	17(4.94)
30-39	56(16.27)
40-49	97(28.19)
50-59	84(24.41)
60-69	46(13.37)
70+	44(12.79)
Sex	
male	265(77.62)
female	79(22.97)
Marital status	
single	48(13.95)
married	270(78.48)
divorced	5(1.45)
widowed	21(6.10)

Table 2: Socio Economic Status

Variables	Patients (%)
Education	
Illiterate	101(29.36)
1st to 10 th standard	160(46.51)
>10 th standard	83(24.12)
Occupation	
Agriculture, livestock, forestry.	62(18.02)
Factory, mining, construction or similar work.	57(16.56)
Office work, mental work, service	53(15.40)
Daily wage earner.	91(26.16)
Education services.	28(8.13)
Others.	53(15.40)
Monthly Per Capita Income(in rupees)	
>2756(Class I)	38(11.04)
1376-2755(Class II)	123(35.75)
826-1375(Class III)	86(25)
411-825(Class IV)	85(24.70)
<411(Class V)	12(3.48)

Table 3: Pattern of Alcohol Consumption

Pattern	Patients (%)
Minimal users	123(35.75)
Moderate users	194(56.39)
At risk users	27(7.84)

Table 4: Reasons for Alcohol Consumption

Reasons	Patients (%)
For social reasons	136(39.53)
Fun, celebrations	123(35.75)
As a pastime	16(4.65)
Medicinal purposes	18(5.23)
With meals	9(2.61)
Relieving loneliness	6(1.74)
Relieving depression	5(1.45)
Relieving anxiety	5(1.45)
Because everybody else uses it	15(4.36)
Meaningless life	11(3.19)

Table 5: Associated Co Morbidities

Co-morbidities	Patients (%)
Hypertension	178(51.74)
Coronary heart disease	22(6.39)
Prior myocardial infarction	10(2.90)
Prior stroke	3(0.87)
Asthma	23(6.68)
Osteoarthritis	19(5.52)
Diabetes	72(20.93)
Dementia	11(3.19)
Depression	33(9.59)
Prior or current diagnosis of cancer	8(2.32)

Table 6: Alcohol Related Disorders

Alcohol use disorders	Patients (%)
Alcohol intoxication	56(16.27)
Alcohol withdrawal	29(8.43)
Ugi bleed	24(6.97)
Fatty liver disease	165(47.96)
Alcoholic hepatitis	145(42.15)
Chronic liver disease	46(13.37)
Liver cancer	2(0.58)

Contrary to this study, being divorced or single, or living alone has in some earlier studies been associated with a higher prevalence of problem drinking¹⁶. In the present study, social reasons were the most common reasons for alcohol consumption, which is in line with prior studies performed among young people¹⁷. Coping motives appeared particularly in the at-risk user group; a larger proportion of reported that they use alcohol because of their meaningless life, in relieving anxiety, relieving loneliness, and relieving depression.

CONCLUSION

Alcohol consumption, including at-risk consumption, is prevalent among community-dwelling adults, particularly among males, despite advanced age, comorbidities, and the multiple use of medications. Health care professionals should be aware of this occurrence. Prevalence of alcohol use is high, especially among males. Health educational interventions among those who are at a higher risk and management of alcohol dependent subjects, may help in reducing the burden of alcohol use in this area.

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ORIGINAL ARTICLE

An Observational Study on Implication of Educational Level on Control and Long-Term Complications of Diabetes Mellitus In a Tertiary Care Hospital of Eastern India

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ABSTRACT

Introduction: The strongest environmental risk factor for diabetes, obesity, is related to socio-economic status. Due to lack of education in India, several myths and social stigma add to the problems of managing Diabetes Mellitus. The purpose of the project is to establish association of educational of the patient with complications and control of diabetes mellitus.

Materials and Methods: An epidemiological cross sectional study of descriptive observational nature was conducted at the Diabetic OPD in a tertiary care centre in Eastern part of India on 303 patients. Patients of both sexes suffering from diabetes mellitus attending the Diabetic OPD in the tertiary care hospital and selection on random basis. The patients were asked to fill a pretested predesigned questionnaire prepared by Stanford Patient Education Research Centre.

Observations and Results: Though the timing of taking pill regularly is high of lower socioeconomic classes, regular exercise and probability of complications is higher for the lower education level and it gradually decreases as the Education level increases.

Conclusion: Treatment can be improvised by spreading awareness about the disease and its complications along with proper education on exercise, following diet plans and treatment regimens

Keywords: Observational Study, Educational Level, Long-term Complications, Diabetes Mellitus.

INTRODUCTION

Diabetes mellitus is defined as a multimetabolic syndrome, characterized by chronic hyperglycemia associated with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both¹. Complications of Diabetes can be microvascular (neuropathy, retinopathy, nephropathy); macrovascular (coronary artery disease, Peripheral vascular disease, cerebrovascular disease) and infections. A high percentage of this cost is related to the treatment of its complications.^{2,3}

Adverse lifestyle behaviours, such as smoking, unhealthy diets and lack of exercise, social implications associated with income inequalities, and to the adverse effects of stress in the workplace, including job insecurity can worsen the life expectancy^{4,5}. The strongest environmental risk factor for diabetes, obesity, is related to socio-economic status. Socioeconomic status may influence access to and quality of care, social support, and community resources, diabetes-related knowledge, communication with providers, treatment compliance, regular follow-up, ex-

ercise, and dietary regimens, treatment choices, monitoring of blood glucose concentrations, adjustment of insulin and oral antidiabetic agents in response to blood glucose readings and intercurrent illness. Due to lack of education in India, several myths and social stigma add to the problems of managing Diabetes Mellitus. Regarding administration of insulin, Patient-centred issues focus on the fear of weight gain, social embarrassment/stigma, hypoglycemia, lifestyle changes/restrictions, and painful injections⁶.

In addition, communities may play an instrumental role in the health status of the residents through availability of health care services, neighbourhood characteristics that promote health and prevailing attitudes towards health⁷.

The purpose of the project is to establish association of educational level of the patient with complications and control of diabetes mellitus. Correspondingly, the reduction of socioeconomic disparities in health may have a profound impact on the morbidity and mortality associated with diabetes.^{8,9}

OBJECTIVES

The objective of this study was to distribute the study population according to educational status, to explore the association between the educational level and the complications and to find out the association between education and control of diabetes mellitus.

MATERIALS AND METHODS

An epidemiological cross sectional study of descriptive observational nature was conducted at the Diabetic OPD in a tertiary care centre in Eastern part of India on 303 patients. Patients of both sexes suffering from diabetes mellitus attending the Diabetic OPD in the tertiary care hospital and selection on random basis (ADA criteria: HbA1c > 6.5% or fasting Plasma glucose > 126mg/dl or 2 hour plasma glucose during OGTT(75g) > 200 mg/dl or random plasma glucose > 200 mg/dl)¹⁰ were included. Patients of Extremes of age, Pregnant and with complications leading to acute morbid state excluded from the study group.

The patients were given informed consent forms in 3 languages (Bengali, Hindi and English) and their informed consent was duly obtained. The patients were asked to fill a pretested predesigned questionnaire prepared by Stanford Patient Education Research Centre. The questionnaire had been modified according to the requirements of the project. Selection was done on a random basis. Those patients who had been included in the study were excluded when they attended to the OPD for further visits. It took approximately 15 minutes per patient to fill the provided questionnaire. The questionnaire included the following: Sociodemography(name, age, sex, religion, income, residence, occupation), background(education, marital status, family type, number of family members, addiction, presence of chronic diseases, family history of diabetes), mental health, daily activities, physical activities, diet, regular glucose testing, medical care along with measurements of height, weight, waist circumference, blood pressure). Along with the questionnaire, clinical examinations and laboratory investigations were done.

For clinical examinations, the following parameters were examined--- Height, Weight, BMI, Waist circumference, Hip circumference, Waist hip ratio, Blood pressure in standing and lying position(to check postural hypotension), Anemia, Oedema, Clubbing, Pulse on both sides, Neuropathy testing by monofilament or tuning fork.

The laboratory investigations that were done are--- Fasting blood glucose, Oral glucose tolerance test, Post prandial blood glucose, HbA1c, Lipid profile(total cholesterol, LDL, HDL, Lp(a)), Test for ketone bodies and Proteins in urine, Serum urea and Creatinine, Ophthalmoscopy.

The laboratory investigations were done at a NABL accredited laboratory. Ophthalmoscopy was conducted at the Institute.

The confidentiality of the study was maintained throughout the study duration. A separate subject enrolment code with details of the subjects' identification and contact information like address and telephone number was maintained. In the questionnaire, reports and all other documentation and communication relevant to the study were inducted. The subject was identified only by code number.

The data obtained was incorporated in Microsoft Excel version 2010 and was analysed by descriptive and inferential statistical methods. Categorical data were represented in the form of percentages and diagrams like pie charts, bar diagrams were prepared by Microsoft Excel. Regression equations were formed and the analyses were done using Minitab Version 18 to establish relationships between variables by link function logit.

Ethical considerations: The study protocol was approved by the Independent Ethics Committee of the institution for necessary approval. The informed consent form was prepared in Hindi, English, and Bengali for the patients. The information was maintained confidential and was solely utilized for academic and research purpose.

OBSERVATIONS

To determine the educational level, the study populations are divided into seven groups as follows:-

- Group- I No formal education
- Group- II Primary school not completed
- Group- III Primary school completed
- Group- IV Secondary school completed
- Group- V High school completed
- Group- VI Graduate and
- Group-VII Post – Graduate

From the Figure 1, it can be seen that majority of the population (32.34%) have completed primary school (Group- III). Majority of the study population (40.59%) has an annual family income of Rs 20000-100000. It has been found that majority of the patients (70.3%) live in a nuclear family. Majority of the patients (89.11%) do not own a glucometer. Of the 33 people who use glucometer, 16 had completed graduation and 17 had completed post graduation.

The study population divided into three groups depending into time spent for exercise. It was found that Majority of the study population (54.13%) does not exercise regularly. Regarding food habit it was observed that majority of the study population (51.16%) consumes fruits and vegetables for more than 5 days a week, in relation to meat (07.92%) and

sweetener (16.17%). The habit and timing of pill consumption was observed as it is very important for diabetic population. It was found that majority of the study population (89.11%) consume their pills regularly.

Table 1: Distribution of Study Population according to Education (n=303)

Educational Level	Cases in Percentage
No Formal Education	18.82
Primary School Not Completed	21.78
Primary School Completed	32.34
Secondary School Completed	2.64
High School Completed	2.64
Graduate	10.89
Post Graduate	10.89

Table 2: showing the number of patients using Glucometer (n=303)

Using Glucometer	Number of Patients
Yes	33
No	270

Table 3: showing the time spent by the study population on Exercise (n=303)

Time Spent on Exercise	Cases in Percentage
No Regular Exercise	54.13
<= 30 minutes	27.06
> 30 minutes	18.81

Table 4: Distribution of Study Population according to Complications of Diabetes Mellitus (n=303)*

Type of Complications	Cases in Percentage
Eye	45.95
Kidney	10.81
Feet	40.54

*Multiple complications possible

Majority of the patients have completed primary school (32.34%) (Table 1). Majority of the patients (270) do not use a glucometer (Table 2). Majority of the study population does not exercise regularly (54.13%) (Table 3).

Majority of the patients suffer from eye complications (45.95%), followed by complications in kidney (40.54%), followed by complications in feet (10.81%). On applying regression analysis, it was found that people who have lower educational level have a greater chance of developing complications than people with higher educational level. ($p=0.971$, which is significant). The probability of complications in patients with no formal education was the

highest (0.70792) and the lowest for patients who were post graduate (0.694058).

DISCUSSION

In the study, it was seen that the educational status is up to primary school (32.34%) in most of the patients. The annual family income lies between Rs 20000-100000 in most of the patients (40.59%). The patients mostly live in a nuclear family (70.3%). In a nuclear family, a person is subjected to greater financial and emotional burdens which might increase the prevalence of diabetes mellitus.

Most of the patients (89.11%) do not own a glucometer; hence they do not check their plasma glucose levels regularly. Many of the patients (54.13%) do not exercise regularly. The commonest diet pattern in the study group is- fruits and vegetables for > 5 days per week, they do not add extra salt in food. 89.11% of the patients take their pills regularly. On regression analyses, it was found that the probability of complications increases with low levels of education, low levels of exercise, family history of diabetes mellitus, irregular intake of pills, intake of sweeteners.

In a study conducted by Yusuf Kayar¹⁵ in Turkey in 2016, it was found that patients with lower educational level(not completing high school) have poorer glycaemic control ($HbA1c \geq 7$) than those who have higher educational level. It is in compliance with the current study which shows that lower educational level increases the probability of complications. It is because glycaemic control depends on multiple factors like proper diet, regular exercise, drug compliance, regular checkups, regular monitoring of plasma glucose by glucometer: and all these factors are related to the educational level of the patients.

Another study conducted by Dr. Ahmad Ali S. Al-Rasheedi¹⁶ conducted in Saudi Arabia in 2014, revealed that the educational level had no impact on glycaemic control, but the patients of high educational level had better awareness of the complications and a high rate of adherence to diet. Thus, it can be deduced from the current study that better awareness reduces the chances of complications.

It was found that knowledge about diabetes was significantly associated with the compliance to the pharmacological and non-pharmacological management in a study conducted by Vivek B Waghachavare¹⁷ in 2015 at a rural district of Sangli in Maharashtra, India. As a result knowledge which is related to educational level plays an important factor in good glycaemic control and reducing complications.

SUMMARY

Lack of education, inadequate family income, number of children, central or visceral obesity, addiction, association with other diseases, mental stress, irregular checking of plasma glucose, lack of exercise, unhealthy diet, increased salt intake, non-compliance, incorrect insulin administration techniques, irregular checkups, lack of awareness about complications.

The management of Diabetes Mellitus stands on 3 pillars- diet, exercise, medications¹¹. Other than these factors, diabetic care givers must not overlook the socioeconomic issues, and must properly counsel the patients, which can greatly reduce the cost burden of the family, improve the quality of life, reduce premature deaths. This approach can cause a monumental change in the pattern of diabetic care in India.

CONCLUSION

Patients suffering from Diabetes mellitus must be educated about the complications, importance of regular checkups, giving up addiction, regular checking of blood glucose, proper insulin administration techniques, and importance of compliance, healthy diet and exercise, relief of mental stress in leading a better quality of life¹². Education is a crucial factor in the management and control of Diabetes Mellitus^{13,14}. The purpose of the study is to establish a model for management of diabetes, based on the socioeconomic conditions of the patient, so that treatment can be individualized and quality of life can be improved. Treatment can be improvised by spreading awareness about the disease and its complications along with proper education (exercise, following diet plans and treatment regimens).

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ORIGINAL ARTICLE

Characteristics of Testicular Torsion in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia

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ABSTRACT

Background: Testicular torsion is an abnormality disease in the testicle because torsion of the spermatic cord resulting in occlusion and strangulation vascularization of the veins and arteries to the testes and epididymis. This study aimed at describing the characteristics of testicular torsion of urology patients based on age, clinical symptom, physical examination, supporting examination, duration and treatment.

Materials and methods: We reviewed medical records of urology patients testicular torsion in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia in 2011 - 2016. Statistical analysis of univariate was used. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

Results: There were 6 patients in this study in which testicular torsion was in 11-20 year old age group in 50% patients. The most frequent clinical symptom was scrotal pain in 83.3%. The physical examination of cremaster reflex was absent in 100% patients. The most frequent supporting examination was conventional scrotal ultrasonography in 66.6% patients. The duration of testicular torsion in > 12 hour was in 83.3%. The most frequent management was orchidectomy in 83.3% patients.

Conclusion : Testicular torsion in our hospital was characterized by mostly in young age, clinical symptom was scrotal pain, Cremaster reflex was negative in 100% in physical examination, supporting examination was conventional scrotal ultrasonography, duration symptom was in > 12 hours and managed by orchidectomy.

Keywords: Clinical symptom, Physical examination, Testicular torsion

INTRODUCTION

Testicular torsion is an abnormality in the testes because torsion of the spermatic cord resulting in occlusion and strangulation vascularisation of the veins arteries to the testes and epididymis. Testes can be infark and atrophy if more than 4-6 hours.¹ Testicular torsion is emergency in urology in young men with incidence rates 1:4000 people in < 25 year old. Study in America, patient of testicular torsion is 8.6/100.000 young age.² Testicular torsion are born with a higher risk for the condition although they may not know it. Normally, the testicles can't move freely inside the scrotum. The surrounding tissue is strong and supportive. Men and boys who experience torsion sometimes have weaker connective tissue in the scrotum. This is called a "bell clapper" deformity. If testicles have a bell clapper deformity, your testicles can move more freely in the scrotum⁴. This movement increases the risk of the spermatic cord becoming twisted. Testicular torsion can also occur after an injury to the groin. Rapid growth during puberty may also cause the condition. The condition can occur

anytime. Testicular torsion can occur when a man is sleeping or when he is engaging in physical activity. Sports injuries can cause torsion of the testes. As a preventive step, a man can wear sport. Testicular torsion usually occurs in only one testicle. Bilateral torsion, when both testes are simultaneously affected, is extremely rare⁵.

Pain and the swelling the scrotal sac are the main symptoms of testicular torsion. The onset of pain may be quite sudden, and the pain can be severe. Swelling may be limited to just one side, or it can occur in the entire scrotum. You may notice that one testicle is higher than the other. Some men also experience: dizziness, nausea and vomiting³.

Torsion of the testes is a medical emergency, but many adolescent males are hesitant to say they're hurting or seek treatment right away. You should never ignore sharp testicular pain. It's possible for some men to experience what's known as intermittent torsion. This causes a man to have a testicle twist and untwist. Because the condition is likely to

recur, it's important to seek treatment, even if the pain becomes sharp and then subsides⁷.

Surgical repair is usually required to treat testicular torsion. In rare cases, your doctor may be able to untwist the spermatic cord by hand. This procedure is called "manual detorsion." Surgery is performed as quickly as possible to restore blood flow to the testicles. If blood flow is cut off for more than six hours, testicular tissue can die. The affected testicle would then need to be removed. Surgical detorsion is performed under general anesthesia⁶. You will be asleep and unaware of the procedure. The doctor will make a small incision in your scrotum and untwist the cord. Tiny sutures will be used to keep the testicle in place in the scrotum. This prevents rotation from occurring again. The surgeon then closes the incision with stitches⁸.

METHOD

We reviewed medical records of testicular torsion patients in Arifin Achmad Regional General Hospital, Pekanbaru, Riau Province, Indonesia in 2011 – 2017. The research variable were age, clinical symptom. Phisycal Statistical analysis of univariate was used. Approval on the study was obtained from the Ethical Review Board for Medicine and Health Research, Medical Faculty, University of Riau.

RESULTS

There were 6 testicular torsion patients in this study.

Table 1: Frequency distribution of testicular torsion patient according to age

Age (year)	Cases (%)
1-10	1 (16.7)
11-20	3 (50)
21-30	1 (16.7)
31-40	1 (16.7)

Table 2: Phisycal examination of testicular torsion

Physical examination	Cases (%)
Reflex cremaster absent	6 (100)
Prehn sign	3 (50)
Angle sign	2 (3.4)
Tenderness	4 (66.6)

Table 3: Supporting examination in testicular torsion

Supporting examination	Cases (%)
Scrotal USG	
Convesional scrotal	6 (100)
Color Doppler USG	4 (66.6)
Nuclear scintigraphy	2 (33.4)

Table 4: Clinical symptom in testicular torsion patients

Clinical symptom	Cases (%)
Scrotal pain	5 (76.1)
Scrotal swelling	4 (15.2)
Nausea and vomitus	1 (8.7)
Total	92 (100)

Table 5: Physical examination in testicular torsion patient

Duration of testicular torsion	Cases (%)
< 4 jam	1 (16.7)
>4 jam	0 (0)
8-12 jam	0 (0)
>12 jam	5 (83.3)
Total	6 (100)

Table 6: Treatment of testicular torsion

The procedures	Cases (%)
Manual detorsion	1 (16.6)
Eksplorasi testis	6 (100)
Orchidectomy	5 (83.3)
Sinistra	3 (50)
Dextra	2 (33.4)
Orchidopexy	1 (16.6)

DISCUSSIONS

The study results showed the largest number of patients according to age was 11-20 year old age group in 33(50%) patients, and the least one was in the 1-10, 21-30, and 31-40 year old age. 10-20 year old age. Characteristics of patients by age in this study suited a study by Ashok Suryabhanji Gajbhiye (2016) showed that testicular torsion were mostly (56.7%) in 11-20 year age group¹⁸. This movement increases the risk of the spermatic cord becoming twisted. Testicular torsion can also occur after an injury to the groin. Rapid growth during puberty may also cause the condition. The condition can occur anytime. Testicular torsion can occur when a man is sleeping or when he is engaging in physical activity. Sports injuries can cause torsion of the testes. As a preventive step, a man can wear sport. Testicular torsion usually occurs in only one testicle.⁵

The study result showed the scrotal pain is the most clinical symptom in 5 (83,3%) patients. This study suited a study by CT Khartikeyan(2016) showed the most (95.1%) symptom of testicular torsion. Because occlusion and strangulation vascularization of the veins and arteries decrease to the testes and epididymis¹ and cause occlusion, ischemia-reperfusion injury and mediation from reactive oxygen²¹.

The study showed reflex cremaster were absent is the most physical examination in testicular torsion patient. This study suited a study by Suryabanji Gajbhiye (2016) showed the most (93,4%) phisycal

examination in testicular torsion. The cremasteric reflex, which is elicited by pinching the medial thigh, causes elevation of the testicle. Presence of the reflex suggests, but does not confirm, the absence of testicular torsion. Comparison of the affected and unaffected sides may help delineate abnormal clinical findings, although scrotal edema and patient discomfort may limit physical examination. Patients in whom the components of the spermatic cord can be distinctly appreciated, whose testes are normally oriented, who have minimal to no scrotal edema, and who have no systemic symptoms (particularly with examination) are unlikely to have acute testicular torsion^{28,29}.

This study result showed most supporting examination used conventional scrotal ultrasonography (66,6%) This study showed duration testicular torsion is > 12 hour. Because patient are late came to the hospital and more than 4 hour²⁴. This study result showed, the treatment of testicular torsion was mostly total orchidectomy 5 (83,3%) patient. This result suited study by Dr. Carlos Baeza Herrera (2008) in 43 (93,47%) patient. The treatment of testicular torsion is orchidectomy because testes can be infarcted and atrophy if more than 4-6 hours¹.

CONCLUSIONS

Testicular torsion in our hospital characterized by mostly in young age, clinical symptom was scrotal pain, physical examination of cremaster reflex was absent, supporting examination of conventional scrotal ultrasonography, duration of symptoms > 12 hours and the management by orchidectomy.

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