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Dr. Vandana Raphael
Editor

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From the Editor's desk

Dear Readers,

We are very proud to place before you this issue of NEIGRIHMS Journal .We are very glad that we received wide variety of articles from Faculty, postgraduate students and resident doctors and we are very thankful to them for choosing our Journal to publish their scientific work and clinical experiences which are unique to this region.

We are putting in a lot of efforts to bring recognition to this journal so that you will be very proud to publish your work in our journal. I thank all the contributors for their enthusiasm and overwhelming response. We are planning to introduce online version in near future and increase the number of issues.

I am indebted to the peer reviewers for timely reviewing the articles and thank all of them from the bottom of my heart. Their valuable inputs will definitely add to the quality of our publications.

Yours sincerely

Prof. Vandana Raphael

Editor

NEIGRIHMS Journal of Medical & Health Sciences

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Original Article

Aetiology, Burden of Disease and Clinical Profile of Chronic Kidney Disease in North East India

PK Bhattacharya[1], Md. Jamil[2], A Roy[3], B Barman[4], M Lyngdoh[4], KG Lynrah[5]

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Abstract

Introduction: Chronic Kidney Disease (CKD) is a leading cause of morbidity and mortality and its incidence is on the rise worldwide. Its aetiology is diverse and varies from region to region. Although CKD is common in this region, there is no comprehensive published data on the aetiology, demographic pattern and clinical profile of CKD from this region.

Aims & Objectives: To study the aetiology, disease burden and clinical course of CKD in the northeast India.
Methodology: An observational study was carried out in all adults (>18 years) with CKD, during a 1½ year period in a premier tertiary care hospital in northeast India, to determine the aetiology, hospital incidence (disease burden), clinical profile and outcome. CKD was diagnosed as per the criteria laid down by the "Kidney Disease: Improving Global Outcomes" (KDIGO) Work Group on Evaluation and Management of Chronic Kidney Disease, 2012. Patients with acute kidney injury (AKI), not progressing to CKD were excluded. Data on patient demographics, clinical profile and laboratory parameters were collected. Descriptive statistical analysis was computed using percentage, mean, median and frequency of occurrence of variables. Co-relation between comparable variables was done using Spearman's Rank Co-Relation Co-efficient by SPSS version 17.

Results : A total of 368 consecutive CKD patients, selected within a span of 18 months as per laid down criteria, were studied. The incidence of CKD was 14.10% with a male preponderance (54.9%). Males were also relatively younger than the females. The BMI, haemoglobin level, serum creatinine and eGFR were similar in both the sexes. In majority (39.40%) cause of CKD was unknown. Other aetiologies included diabetic nephropathy (23.36%), hypertension (14.68%), chronic glomerulonephritis (10.05%), infective causes (6.79%) and obstructive uropathy (5.72%). The most common infective cause was malaria. The eGFR had a significant negative co-relation with haemoglobin level ($r = -0.76$, $p<0.01$). Hemodialysis (HD) was the commonest form (88.3%) of renal replacement therapy (RRT), with the maximum patients (64.4%) receiving 1 HD/week. While 9.5% of patients were lost to follow-up, 53.5% of the patients expired and only 37% were alive at the end of the follow-up period.

Conclusion : The burden of CKD and the high mortality in the north eastern region of India poses a significant challenge to health care workers as well as policy makers. While diabetes and hypertension remain pre-eminent causes, CKD due to undetermined etiologies and infective causes poses substantial threat. Further prospective studies are needed to identify the true incidence and overall burden of the disease to formulate strategies for early detection of the disease and steps to reduce both the morbidity and mortality from CKD.

Key Words: *Chronic Kidney Disease, Renal Replacement Therapy, Hemodialysis, eGFR*

Introduction

The incidence of Chronic Kidney Disease (CKD), also known as End Stage Renal Disease (ESRD) has been steadily on the rise globally, both in the developed and developing countries. According to the 2010 Global Burden of Disease study CKD was ranked 18th in the list of causes of global death with an annual death rate 16.3 per 100 000.[1] One of the major reasons for this increase is due to the increase in the prevalence of hypertension and diabetes, both being major causes of CKD.[2,3]

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It is estimated that more than 80% of all patients receiving treatment for CKD are in the developed countries,while these figures are much lower in the developing countries mainly because CKD patients in these countries do not get access to renal replacement therapies (RRT).[4,5]

While diabetes and hypertension are the leading causes of CKD in all developed and many developing countries, the demographic characteristics of patients with CKD vary from region to region and among different sections of the population worldwide. In the USA, African Americans and Hispanics develop CKD at a younger age than Caucacians.[6] In sub-Saharan Africa CKD is common in the young adults due to hypertension and glomerulonephritis.[7] In India, CKD of unknown origin is more common in the younger population of economically poorer communities, who are more likely to present with more advanced CKD than people with CKD of known causes.[8] In the developing countries of Asia and Africa CKD due to unknown causes, infectious diseases, environmental pollution, pesticides, analgesic abuse, herbal medications, and use of unregulated food additives also constitute major etiological factors of CKD.[9,10]

In India, although there has been sporadic data on the overall magnitude and pattern of CKD there is no systematic study on the aetiology and demographic pattern of the disease across various parts of the country.[8] In a population based survey of approximately 570,000 individuals the age-adjusted ESRD incidence rate was 232 per million, while in another multi-centric hospital based study the prevalence of CKD was shown to be 17.2%.[11,12] In another study, 2.5% of 5300 subjects had dipstick positive proteinuria and 4.8% had GFR < 60 ml/min.[13] The first report of Indian CKD registry has shown the mean age of CKD as 50 years, with a male preponderance (70:30). Diabetic nephropathy was the commonest cause (31%), followed by CKD of undetermined etiology (16%), chronic glomerulonephritis (14%) and hypertensive nephrosclerosis (13%). Relatively younger population had CKD in the north zone compared to the east zone of the country. Patients in lower income groups had more advanced CKD at presentation. Patients presenting to public sector hospitals were poorer, younger, and more frequently had CKD of unknown etiology.[4]

Most of these studies on CKD carried out in India have failed to include patients from the north eastern region of the country.[4,10,11,14] However, it has been observed that the number of CKD patients treated at NEIGRIHMS, which caters to a large section of the northeast region, is considerably high. But no systematic study has been carried out in this region to determine the prevalence, aetiology, and clinical course and outcome of CKD in this part of the country. Hence it has been planned to carry out this hospital-based study in patients with CKD treated at NEIGRIHMS, so as to have an overview of the burden of the disease in this region of the country.

Objectives :

The present study was undertaken with the following objectives:

1. To study the incidence of CKD at NEIGRIHMS
2. To determine the aetiology, demographic pattern, as well as the biochemical profile and clinical course and outcome of these patients with CKD

Methodology :

This was an observational study carried out on all patients with CKD admitted to the Department of General Medicine, NEIGRIHMS, Shillong between January 2013 to June 2014.

Method of collection of data: All patients, aged above 18 years, diagnosed as CKD as per the criteria laid down by the "Kidney Disease: Improving Global Outcomes" (KDIGO) Work Group on Evaluation and Management of Chronic Kidney Disease, 2012 were included in the study.[15]

Inclusion Criteria:

Either of the following features present for >3months:

1. Marker of Kidney Damage: one or more of the following: Albuminuria (Albumin Excretion Rate ≥30mg/24hrs; ≥30; Albumin Creatinine Ratio mg/gm), Urine sediment abnormalities, Electrolyte and other abnormalities due to tubular disorders, Abnormalities detected by

histology, Structural abnormalities detected by imaging, History of kidney transplantation.

2. Decreased Glomerular Filtration Rate (GFR): GFR<60 ml/min/1.73 m^2.

Exclusion Criteria:

Patients with Acute Kidney Injury (AKI) not progressing to CKD.

Statistical Methods:

Descriptive statistical analysis was computed using percentage, mean, median and frequency of occurrence of variables. Co-relation between comparable variables was done using Spearman's Rank Co-Relation Co-efficient by SPSS version 17.

Results :

We studied a total of 368 patients with CKD over a span of 18 months out of a total admission of 2609, with an annual incidence of 14.1%. There was a slight male preponderance (54.9%) (Table 1), and males were also relatively younger than the females (Figure 1). While there were no differences in BMI, haemoglobin level, serum creatinine and eGFR between the sexes, the duration of CKD as well as RRT in the form of HD were longer in males compared to females (Table 2).

Our series of CKD patients had diverse etiologies (Table 3), but in the majority of cases (39.40%) the cause was unknown. Diabetic nephropathy and hypertension were the major causes. The most common infective cause was malaria. All the infective cases initially presented as AKI and then progressed into CKD.

Table 1: Age and Sex Distributions of the CKD patients

Age Group (In years)	Male		Female		Total patients	
	No of pts	%	No of pts	%	No of pts	%
18-29	50	13.59	26	7.06	76	20.65
30-39	34	9.24	27	7.33	61	16.57
40-49	26	7.07	28	7.61	54	14.68
50-59	47	12.77	46	12.50	93	25.27
60-69	30	8.15	20	5.43	50	13.58
70-79	10	2.72	14	3.80	24	6.52
80-89	5	1.36	5	1.36	10	2.72
Total	202	54.90	166	45.10	368	100.00

Table 2: Clinical Profile of Patients with CKD

Parameter	Gender	
	Male	Female
Mean Height (Metres)	1.57±0.11	1.46±.07
Mean Weight (Kg)	51.83±5.96	42±4.98
BMI (kg/m^2)	20.97±2.13	19.56±1.32
Mean Age (Years)	44.52±19.86	47.93±20.54
Median Age (Years)	45	46
Mean Creatinine (mg/dl)	10.06±5.02	9.44±5.46
Mean Haemoglobin (g/dl)	7.93±2.21	7.39±2.27
eGFR ($ml/min/1.73m^2$)	8.38±4.69	6.51±4.12
Duration of CKD (months)	46.83±17.85	42.46±27.54
Duration of RRT (HD) (months)	36.7 ±22.46	31.32±19.56
Average No of HD per week	1.33	1.79

BMI= Body Mass Index, eGFR= estimated Glomerular Filtration rate

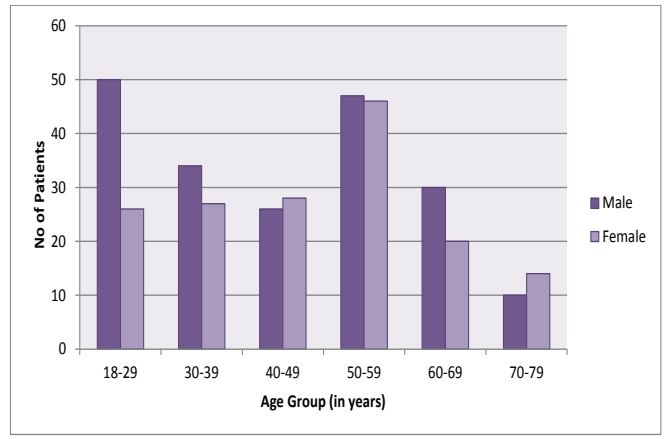


Fig 1 : Age and sex distribution of CKD patients

Table 3: Age and sex distribution in CKD of various aetiologies

Aetiology	Number of Patients					
	Males (n=202)		Females (n=166)		Total (n=368)	
	No.	%	No.	%	No.	%
Diabetic Nephropathy	41	11.14	45	12.22	86	23.36
Hypertensive Nephropathy	32	8.70	22	5.98	54	14.68
Chronic Glomerulonephritis	14	3.80	23	6.25	37	10.05
Obstructive Uropathy	17	4.63	4	1.09	21	5.72
Infective	19	5.16	6	1.63	25	6.79
Unknown	79	21.47	66	17.93	145	39.40

While the mean eGFR was7.15±4.386 ml/min/1.73m^2 about half of the patients had a eGFR between 2-5 ml/min/1.73m^2. The eGFR had a significant negative co-relation with haemoglobin level. However no significant co-relation could be ascertained of eGFR with age or BMI (Table 4).

Majority of the patients (64.40%) had HD once a week (Table 5). The overall mortality during the period of follow-up was 53.5% and 9.5% patients were lost to follow up (Table 6). The characteristics of various individual etiologies with respect to Chronic Kidney Disease have been demonstrated in Table 7. The average duration of disease was longest in those with hypertensive nephropathy and shortest in obstructive uropathy.

Table 4: Co-relation between e GFR with other parameters

Variable	Spearman's Co-relation Coefficient	p value
Age	-0.023	>0.05
Haemoglobin	-0.76	<0.01
Body Mass Index	-0.041	>0.05

Table 5: Frequency of Haemodialysis in Patients with Chronic Kidney Disease

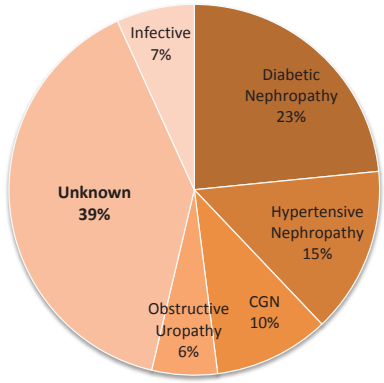
Frequency of Hemodialysis	Number of Patients (%)	
	No	%
Once Weekly	237	64.40
Twice Weekly	84	22.83
Irregular	4	1.09
Status Unknown	43	11.68

Table 6: Outcome of patients with Chronic Kidney Disease

Outcome	Number of Patients	Percentage (%)
Alive	136	37.0
Expired	197	53.5
Lost to follow-up	35	9.5

Table 7: Characteristic features in CKD of different aetiologies

Aetiology	Parameters				
	Incidence	Duration of disease	BMI	Age	eGFR
Diabetic Nephropathy	23.36%	6.8±3.6	21.08±1.76	48.52±19.72	5.5±2.46
Hypertensive Nephropathy	14.68%	7.2±2.8	20.32±1.97	46.73±20.16	5.1±2.81
Chronic Glomerulonephritis	10.05%	5.1±3.2	19.47±1.27	42.87±13.45	7.6±3.2
Obstructive Uropathy	5.72%	1.32±.09	20.88±2.12	37.22±11.24	9.2±2.4
Unknown	39.40%	4.6±2.1	19.32±1.34	45.54±18.23	5.6±3.3
Infective	6.79%	NA	20.97±2.46	26.33±5.65	8.2±2.6



CGN= Chronic Glomerulonephritis

Fig. 2 : Aetiology of Chronic Kidney Disease

Discussion :

The etiology of CKD in our study was found to be diverse. A majority of the study population had an unknown cause (39.40%). In the past clusters of cases of CKD of unknown origin have been reported in some areas of Sri Lanka and India and few studies from India have made a similar observation.[5,8] Diabetic Nephropathy and Hypertensive Nephropathy were also found to be a significant contributing factor towards the development of CKD. This trend is similar to that reported by Dash and Agarwal in the study conducted at the All India Institute of Medical Sciences, New Delhi.[16] Lysaght et al have also demonstrated similar trends in American populations.[17]

The mean age of the cumulative study population was 45.11 years. In the group wise age distribution it was found that the prevalence of Chronic Kidney Disease was maximum in the age group of 50-59 years (25.27%) closely followed by those in the age group of 20-29 years (20.65%). Previous studies have shown that the demographics of people with CKD vary widely worldwide. The mean age of 9614 patients presenting with CKD in India was 51±13.6 years, whereas in 1185 patients in China it was 63.6±14.7 years.[8,18] With the progression of age GFR decreases gradually and a decreased GFR in an elderly patient appears to be an independent predictor of adverse outcomes such as mortality and cardiovascular disease as reported in previous studies.[19] Similar findings are also reported by the National Kidney Foundations KVDOQI subgroup on children and adolescents study conducted by Fivush et al.[20]

There was a significant mortality associated with CKD in our study with 53.53% of the population under study having an adverse outcome. According to the 2010 Global Burden of Disease study, Chronic Kidney Disease stood 18th with an annual death rate 16.3 per 100 0001 and the burden of this disease is expected to be on the rise in years to come.

RRT in the form of HD, peritoneal dialysis or renal transplantation remain the primary therapeutic modalities with patients with CKD. In our study of HD was the primary modality of therapy for the patients. A majority (64.40%) of them were undergoing dialysis on a once-weekly basis while 22.83 % had an access to twice-weekly schedule. Studies have shown that over 60% of Stage V CKD patients were being managed with conservative treatment without dialysis at the time of presentation. A large proportion of these cases require emergency dialysis soon after presentation but are unable to continue it on a long-term basis because of financial reasons.[21] A shortage of manpower for delivery of RRT and the financial implications of lifelong therapy is a grave point of concern for health care providers in a developing nation like India and there needs to be well-concerted efforts to cope with such concerns.

In our study of the 368 patients 202 (54.90%) were males and 166 (45.10%) were females. Male gender has been recognized as an important factor in the development of CKD and similar results have been shown before by Silbiger SR, Neugarten J and our results are in concordance with those.[22] For males the mean age was found to be 44.52±19.86 whereas for females it was at 47.93±20.54.The BMI was low in both the sexes (males: 20.97±2.13; females: 19.56±1.32). In patients with CKD, and especially in those undergoing maintenance dialysis, have a low BMI. The so called 'uremic malnutrition' (also referred to as protein energy wasting [PEW]) is a strong risk factor for adverse outcomes and death.[23]

Creatinine levels were found to be high in both genders proportionately with eGFR of 8.38±4.69 and 6.51±4.12 for males and females respectively. Prevalence of anaemia was universal with mean haemoglobin levels being 7.93±2.21 in males and 7.39±2.27 in females. Similar observations have

been made previously with haemoglobin levels less than 10g/dl in more than 90% of the study population.[24] The duration of maintenance HD was more for males as compared to females which may be due to earlier age of presentation in males as well as other socio-economic considerations.

The mean age of presentation in CKD due to diabetic nephropathy, hypertension and those without any known cause was above 40 years. In contrast, patients with obstructive uropathy and infective causes presented with CKD at a much younger age. Previous studies have shown that patients with diabetic nephropathy and hypertensive nephropathy were significantly older and had more males, whereas those with undetermined etiology were younger and had a greater proportion of females.[8] The duration of disease for diabetic nephropathy and hypertensive nephropathy were found to be 6.8±3.6 and 7.2±2.8 respectively whereas for those with unknown etiology it was 4.6 ±2.1.The duration of disease of obstructive and infective causes was found to be lower. Thus we see that patients with diabetic and hypertensive nephropathy require RRT at an older age in comparison to those with undetermined or other acute causes. The eGFR was found to be lowest for those with diabetes, hypertension as well as unknown causes, reflecting a greater severity of kidney damage in these subsets of the study population. The BMI for different etiological subgroups were comparable with patients with diabetic nephropathy having a slightly higher index.

Conclusion :

The incidence of CKD is high among the adult hospital patients of NEIGRIHMS. While diabetes and hypertension were important causes of CKD, in a large percentage the aetiology remained unknown. A sizeable number of CKD patients had an infective aetiology, mainly severe malaria, which is basically preventable at the stage of AKI before it proceeds to CKD. CKD is more common in the young and middle-aged adults with a male preponderance, which further adds to the financial burden in the population. In the absence of renal transplantation, these patients were depended on HD for survival, majority requiring at least one sitting of HD per week. In spite of which the mortality was significantly high. Being a hospital based study the true incidence and mortality from the disease in the community has probably not been reflected, nevertheless, our study has been able to project the high incidence of the disease, its dependence on long-term HD and ultimate mortality. Hence further studies should be undertaken in this region to try to find out the cause(s) even in those cases which are labeled as of unknown etiology, as well as try to find out the true incidence of the disease in the community, and identify steps to delay the onset of end-stage disease

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Original Article

Effectiveness of Planned Health Education Program regarding Personal Hygiene on children studying in Class IV – VI

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Abstract

School health education services are an economical and powerful means of raising the standard of community health, especially for the future generations. School is considered as an ideal setting for positive health growth for the prevention of diseases and for awakening health consciousness in children. A pre-experimental study was conducted to assess the effectiveness of planned health education program on knowledge and express practice regarding personal hygiene among school children studying in class IV – VI in a selected rural school in Meghalaya. The school was selected by convenient method (most of the schools were still on winter vacation). The time period allotted for the study was one week and only 53 samples were present during the time of data collection. The study was conducted in Sharon Memorial Secondary School located in Mawdiangdiang. A pre-test was administered by using structured questionnaire for assessing the knowledge and a checklist for assessing the practice followed by planned health education program on the 3rd day after the pre-test. After 7 days of Health Education Program a post-test was conducted. The result of the post-test score revealed that the planned health education program had a good impact on improving the level of knowledge and practice regarding personal hygiene among school children studying in class IV – VI. The study finding implied that education had a vital role in improving the knowledge and practice among school children regarding personal hygiene.

Key Words: *Personal hygiene, Knowledge, Expressed Practice, Planned Health Education and Effectiveness.*

Introduction

In India, the concept of personal hygiene is intermixed with several ritual ideas and traditions. However, it needs to be practice properly by individuals alone who assume personal responsibility. There should be a motto to guide everyone to follow and practice that 'cleanliness is next to godliness', which is taught to a child even from primary school days.[1] Good personal hygiene usually means those measures a person takes to keep the skin and its appendages such as hair, finger nails, toe nails, teeth and mouth clean and in good condition.[2]

Hygiene behaviour among school children in rural area need the role of a school based hygiene promotion. Schools are most important places of learning & behaviour change for children and childhood is the best time for children to learn hygiene behaviour. Despite many efforts 11.5% of school children in rural population have poor personal hygiene.[3,4]

Childhood is the best time for children to learn hygiene behaviours as children are the agents for change in future. The promotion of positive health by teaching the children on maintenance of personal hygiene will in turn improve the health at the community especially of future generation.[5] Hence this present study has been undertaken to assess the effectiveness of planned health education regarding personal hygiene in children studying in class IV – VI in terms of knowledge and expressed practice in a selected school located in a rural area in Meghalaya.

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Objectives:

- To assess the knowledge of the children studying in class IV – VI regarding personal hygiene.
- To assess the expressed practice on personal hygiene of children studying in class IV – VI.
- To determine the effectiveness of planned health education program in terms of knowledge and expressed practice on personal hygiene.

Methodology:

A quantitative pre- experimental research design was adopted to assess the effectiveness of Plan Health teaching program regarding personal hygiene in children studying in class IV – VI. The school was selected by convenient method (most of the schools were still on winter vacation). The time period allotted for the study was one week and only 53 samples were present during the time of data collection. The study was conducted in Sharon Memorial Secondary school located in a rural area in Meghalaya, Mawdiangdiang. Ethical approval was taken from the Institute Ethical Committee, NEIGRIHMS and written informed consent was taken from the Principal of the Sharon Memorial Secondary School after explaining the purpose and procedure of the study. Confidentiality and anonymity was maintained throughout the study period. Structured questionnaire regarding personal hygiene for assessing knowledge and expressed practice check-list was developed & validated. The population comprised of both male and female students studying in class VI – VI in Sharon Memorial Secondary School, Mawdiangdiang. By using convenience sampling technique 53 samples were selected for the study. Pre-test was administered on 21st May, 2014, followed by health education on 23rd May 2014 and then on 30th May, 2014 post-test was conducted. Data was analyzed by using descriptive and inferential statistics.

Results :

Findings related to the socio demographic data

Most of the children (41.50%) were in the age

Table 1: Socio demographic characteristics of the respondents

N=53

Variables		F	%
1.	Class		
a)	IV	15	28.30
b)	V	22	41.50
c)	VI	16	30.19
2.	Age (in years)		
a)	8-9	06	11.32
b)	10-11	22	41.50
c)	12-13	21	39.62
d)	14-15	04	07.54
3.	Gender		
a)	Female	28	52.83
b)	Male	25	47.17
4.	Religion		
a)	Christianity	40	75.47
b)	Hinduism	01	01.89
c)	Islam	02	03.77
d)	Others	10	18.87
5.	Mothers educational status		
a)	Illiterate	07	13.21
b)	Class I-IV	18	33.96
c)	Class V-VII	09	16.98
d)	Class VIII-X	12	22.64
e)	Class IX -XII	06	11.32
f)	Graduate	01	01.89
6.	Fathers Educational status		
a)	Illiterate	08	15.09
b)	Class I-IV	15	28.30
c)	Class V-VII	07	13.21
d)	Class VIII-X	11	20.76
e)	Class IX -XII	05	09.43
f)	Graduate	07	13.21

group of 10 and 11 years and 41.50% were studying in class V. Maximum (52.83%) of the children were female and 75.47% were Christians. Majority of the parents of these children were educated till class IV, mother (33.96%) and father (28.30%)

Findings related to knowledge and expressed practice of children studying in class IV – VI

Table 2: Frequency and Percentage of the respondents in three categories of knowledge score of personal hygiene in pre-test and post-test

N=53

Knowledge category	Score	Pre-test		Post- test	
		f	%	f	%
Good	15-21	07	13.21	34	64.17
Average	8-14	31	58.49	17	32.08
Poor	1-7	15	28.30	02	03.77

Table 2 depicts that the knowledge category of the respondents in pre test and post test on personal hygiene. It reveals that the good knowledge increase from 07(13.21%) in pre test to 34 (64.17%) in post test, the average knowledge change from 31(58.49%) to 17 (32.08%) in post test while the poor knowledge decreased from 15 (28.30%) in pre- test to 02(03.77%) in post- test

Table 3: t test value showing the effectiveness of the planned health education on personal hygiene in terms of knowledge

N=53

Knowledge	Pre-test	Post- test	t-Value
Mean	9.6	15.66	8.59
SD	3.36	03.88	

Table 3 depicts that in pre- test knowledge the mean score was 9.6 with the S. D of 3.36, whereas in post- test the mean score was 15.66 with S. D of 3.88. The t-test value was 8.59 which is statistically significant at $p<0.05$ level of significance.

Table 4 reveals the expressed practice category of the respondents in pre test and post test. The good expressed category improved from 13(24.53%) in pre test to 34(64.15%) in post test, fair expressed practice category 35(66.04%) in pre test change to 18(33.96%) in post test and the poor decreased from 05(09.43%) to 01(01.89%) in post test

Table 4 : Frequency and Percentage of respondents in three categories of expressed practice score on personal hygiene in pre test and post- test

N=53

Expressed practice category	Score	Pre-test		Post- test	
		f	%	f	%
Good	15-20	13	24.53	34	64.15
Fair	8-14	35	66.04	18	33.96
Poor	1-7	05	09.43	01	01.89

Table 5: t- test value showing the effectiveness of health education on personal hygiene in terms of expressed practice

N=53

Expressed practice	Pre-test	Post- test	t-Value
Mean	11.45	15.16	05.15
SD	03.65	03.79	

Table 5 depicts that in pre-test expressed practice the mean score was 11.45 with the S. D. of 3.65, whereas, in the post- test, the mean score was 15.16 with S. D of 3.79. The t-test value was 5.15 which is statistically significant at $p<0.05$ level of significance.

Discussion:

Hygiene education programs in school promote personal hygiene of school children which contributes to better health and reduces the burden of communicable diseases which also improves academic performance of children.[6]

In the socio-demographic data ,the study revealed that out of 53 students 22(41.50%) of the children were in the age group of 10-11 years. According to the study conducted by Sarkar, M. on knowledge and practice of personal hygiene among school children in Chetla, Kolkata (2013) children were in the age group of 7-12 years.[7]

In the present study, the pre-test knowledge score of the school children revealed poor knowledge of 15 (28.30%), average knowledge of 31 (58.49%) and good knowledge of 34 (64.15%). In a study conducted by Shuza Uddin (2014) to assess the level of knowledge regarding personal hygiene among students in order to help formulate proper educational program in schools, it was found that out of 120 respondents 19.17% respondents had a good knowledge, 58.33% had fair knowledge and 22.5% had poor knowledge on personal hygiene.[8]

In the present study the post- test knowledge score 40(75.47%) on necessity of regular bath was found to be higher than the pre –test knowledge score 13(24.53%). The post- test knowledge score 20(37.74%) on frequency of washing face was improved from pre-test score 15(28.30%). According to study conducted by Behera, B.K. et al to assess the hygiene practices among school children in rural area of Pondicherry (2011) was 84.98% of children washed their face using soap and water ,68.22% children took bath daily.[9]

The present study revealed that 32(60.38%) of children in pre-test always practice covering mouth with handkerchief during coughing and sneezing which had improved to 42(79.25%) in post- test after administering health education programme. A survey conducted by social science research centre of the university Hongkong (2005) found that 85.70% of the subjects knew about covering mouth and nose while coughing and sneezing and 92.10% practice it.[10]

The present study revealed that the post- test knowledge score 50(94.34%) on hand washing with soap and water after toilet was found to be higher than pre-test knowledge score 41(77.36%) after administering health education. Knowledge on keeping nails short and clean was significantly improved from 10(18.87%) to 38(71.70%). Similarly the study conducted by Dongre, A.R. et al in Wardha district (2007) found that after health education the promotion of children having practice of hand washing using soap after visiting toilet was found to be significantly improved from 63.60% to 78% and clean and cut nails from 67.80% to 80%.[11]

Implications:

Implications for Nursing Practice

- Posters can be displayed on the importance of personal hygiene to increase the knowledge and improved the practice of children and the community as a whole.

Implications for Nursing Administration

- Nurse as an administrator can motivate health care providers such as auxiliary nurses and midwives, village health guides, nurses working in community centre to utilize any opportunity to give health education to school children on personal hygiene.

Implications for Nursing Education

- All the health care providers such as auxiliary nurses and midwives, village health guides, nurses working in community centre should provide in-service education regarding personal hygiene.

Implications for Nursing Research

- Mass survey can be conducted in the community to assess the knowledge regarding personal hygiene among school children in order to formulate self instructional modules in schools.

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Original Article

Awareness regarding HIV/AIDS among the Adolescents in terms of knowledge in a selected Higher Secondary School of Meghalaya.

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Abstract

Summary: Adolescents are exposed to the risk of being victims of HIV/AIDS, because of low level of awareness and inadequate access to its prevention and treatment services available. As school education has been described as a social vaccine which serves as a powerful preventive tool. A quantitative descriptive research approach was utilized to assess awareness of HIV/AIDS in terms of knowledge of adolescents. The selection of the school was done by convenient method. The time period allotted for the study was one week and only 80 samples were selected using non-probability convenience sampling of all the adolescents of the age group of 16-20 years. The study was conducted at the B.K Bajoria Higher Secondary School, Shillong. Data was collected using semi-structured questionnaire for assessing the knowledge of adolescents. Result revealed that 90% (n=72) of the adolescents have good knowledge and 10% (n=08) were of less knowledge regarding HIV/AIDS. There is a significant association between adolescents' knowledge on HIV/AIDS and gender the calculated chi-square value (5.77) is higher than the table value (3.84) with degree of freedom (1) at $p < 0.05$, in which females adolescents are more knowledgeable than the males

Key Words: *HIV/AIDS, knowledge, Adolescents*

Introduction

Globally an estimated 33 million people were found to be infected with HIV in 2009 with 2.6 million new infections and 1.8 million HIV related deaths nearly an estimated 5 million people infected with HIV lived in Asia in 2009 and about 380,000 people were newly infected.[1]

In India, estimated number of HIV infections as of 2009 is 22 million. The distribution of HIV infection and mode of transmission varies by state. Most HIV infections in India (86% of reported AIDS cases) are due to unprotected heterosexual transmission. The epidemic of HIV/AIDS is now progressing at a rapid pace among young people. Studies have reported that young people form a significant segment of those attending sexually transmitted infection (STI) clinics and those infected by HIV.[2]

The WHO states that youths are at the epicentre for preventing the progression of the HIV/AIDS pandemic. It is also estimated that youths ages 15 to 24 comprise 50% of all new HIV infections and consequently must be targeted for education in decreasing transmission and reducing the stigmatization of an HIV diagnosis.[3]

In India, young people in the age group 15-24 years comprise almost 25% of the country's population, however, they account for 31% of the AIDS burden in 2009. Well known factors such as peer pressure, increasing levels of social interaction

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with the opposite sex, and even household factors like broken families and poverty, contribute to increased sexual activity and promiscuity. In a conservative society where sex-related issues constitute a taboo for discussion, young people are hindered from actively seeking counselling regarding sexual health. Social ostracism and disease-associated stigma have created an attitude of negativity and shame in the minds of especially young people. This results in lack of knowledge about self-protection measures, leading to a silent spread of the disease. Despite these worrisome statistics, some Indian states have banned sex education in schools, following protests from legislators that it would have a negative impact on the vulnerable minds of school students. Widespread ignorance about the disease is still prevalent, even among youth belonging to the affluent sections of society.[4]

Adolescents are of interest in HIV/STD studies as they are a group whose behaviour places them at increased risk of HIV infection. Adolescents are a period characterised by the development and formation of sexuality, a process which frequently involves a high turn-over of sexual partners. According to WHO/UN definitions adolescent refers both gender in the age group of 10-19 years (2010).[5] A cross sectional studies on adolescence awareness: a better tool to combat HIV/AIDS in Uttar Pradesh among secondary school students by Srivastava Anurag et al had taken the adolescents age groups of 11-19 year, similar study conducted in Bangladesh by Mizanur Rahman M et al also took the adolescents age groups of 16-19 years. Teenage experimentation with drugs and alcohol frequently leads to the adoption of high risk behaviours or engagement in unplanned episodes of casual sex. In addition, adolescents are particularly vulnerable to the normative social influences of their peers. These influences among adolescents tend to discourage the adoption of safe sexual behaviour by encouraging negative associations to be attached to condoms and their use. While the intense influence of normative social values on adolescents makes them increasingly vulnerable to HIV infection, if HIV preventive behaviour can be made to seem the norm, teenagers may also be readily influenced by this.[6]

Finally, aspects of teenagers' lives are dominated by feelings of invulnerability which allow them to take the chances they see as developmentally important. While adolescents know about HIV, most have not personalised the threat of AIDS. The factors which place adolescents at risk of HIV tend to stereotype adolescence as a period of traumatic social behaviour. In conclusion the study had conducted among the adolescents group studying in higher secondary school to assess the awareness their knowledge regarding HIV/AIDS.

Objectives of the study:

1. To assess the knowledge regarding awareness of HIV/AIDS among the adolescents.
2. To find the association between the adolescents knowledge regarding HIV/AIDS with demographic variables.

Methodology :

A quantitative descriptive research approach was utilized to assess the awareness of HIV/AIDS among the adolescents in terms of knowledge. The study was conducted at the B.K Bajoria Higher Secondary School, Shillong. Ethical consideration was taken from the institute ethical committee, NEIGRIHMS and written consent was taken from the participants and parents. A semi-structured knowledge questionnaire tool was developed and validated. Population of the study comprises of all the adolescents age group of 16-20 years and by using non-probability convenience sampling 80 adolescents participated in the study. Data was collected from 21-23rd May 2014. Descriptive and inferential statistics were used to analyze the data.

Results:

Findings related to the Sample characteristics of the adolescents

Table 1: Frequency and percentage distribution of the sample characteristics

N=80

Variables		F	%
1.	Age		
a)	16-17	54	67.5
c)	18-19	26	32.5
d)	19-20	00	00
1.	Gender		
a)	Female	51	63.8
b)	Male	29	36.3
1.	Number of siblings		
a)	0-2	42	52.5
b)	3-5	25	31.3
c)	5 & above	13	16.3
1.	Religion	f	%
a)	Christianity	40	50.0
b)	Hinduism	29	36.3
c)	Islam	05	06.2
d)	Others	06	07.5
1.	Residence		
a)	Rural	11	13.8
b)	urban	69	86.3
2.	Mothers education level		
a)	illiterate	01	01.2
b)	primary	05	06.2
c)	secondary	08	10.0
d)	higher secondary	23	28.8
e)	graduate $ above	43	53.8
3.	Fathers education level		
a)	illiterate	01	01.2
b)	primary	02	02.5
c)	secondary	03	03.8
d)	higher secondary	16	20.0
e)	graduate $ above	58	72.5
4.	Type of family		
a)	nuclear	51	63.8
b)	joint	23	28.8
c)	extended	06	07.4
5.	Distance to nearest health facility		
a)	≥5km	60	75.0
b)	≤5km	20	25.0

Majority (67.5%) of the adolescents belongs to the age group 16-17 years, (32.5%) 18-19years. More the half (63.75%) of the adolescents were female and male (36.25%). Most (52.5%) of the adolescents have 0-2 siblings, 3-4 siblings (31.25%) and 5 and above siblings (16.25%). Most (50%) of the adolescents were Christian followed by Hindu (36.25%), Islam and others (13.75%). Majority (86.25%) of the adolescents were urban dwellers, and 13.75% were rural dwellers. 63.75% belongs to nuclear type of family, joint family (28.75%) and 7.5% belongs to extended family. Most of the adolescents fathers (72.5%) and mothers (53.75%) were graduate and above. Majority (75%) of the adolescents were residing of ≥5 km to nearest health facility and (25%) ≤5km. Majority (72.5%) of the adolescents had received information about HIV/AIDS from school, news paper (57.5%), television (67.5%) , radio (23.75%) and health personnel (27.5%).

Awareness regarding HIV/AIDS in terms of knowledge

Table 2(a) : Frequency and percentage distribution of the sample characteristics

N=80

Level of knowledge	f	%
Good (≥ 15)	72	90
Poor (≤ 15)	08	10

Table 2(b): Mean & SD of adolescents awareness regarding HIV/AIDS in terms of knowledge

N=80

Variables	Mean	SD
Knowledge	19.1	3.21

Table 2(a) and 2(b) Study reveals that majority (90%) of the adolescents has good knowledge and poor knowledge (10%). The mean knowledge score and SD of adolescents on awareness regarding HIV/AIDS in terms of knowledge is 19.1 and 3.024 respectively.

Association between adolescents knowledge regarding HIV/AIDS with sample characteristics

The study reveals that there is significant association between adolescents knowledge regarding HIV/AIDS with gender where the calculated chi-square value (5.77) is higher than the table value (3.84) with degree of freedom (1) at $p < 0.05$ level of significance.

Discussion

The school AIDS education is one of the important activities of NACP (National AIDS Control Programme) that focuses towards raising student- youths' awareness level and develop safe and responsible life-style.The knowledge is directly linked with the awareness of HIV/AIDS. The present study was undertaken to assess the knowledge regarding awareness of HIV/AIDS among the adolescent and to find the association between knowledge regarding HIV/AIDS with the selected demographic variables in a selected higher secondary school of Meghalaya.

The demographic variables of the present study revealed that 67.5% of the participants belong to the age group of 16-17 years. In a study conducted by P. Lal, et al, Anitha Nath et al and Gopal Kingle et al (2008) majority of the students (74.9%) belonged to the age group of 15-17 years. In the present study most (63.75%) of the adolescents were females and (36.25%) males. In a study conducted by Reddy, B.C. et al(2014); Rao, A.R. et al (2013); Reddy, Shanker et al(2013); Ravikumar, B.P. et al (2013), number of females were more (50.87%) than males (49.13%).[7-,9]

Majority of the adolescents (50%) were Christians, 36.25% Hindu, 7.5% belongs to others (Buddhist/ Sikh/ Indigenous) and 6.25% Muslim. In the study conducted by Li-Ping Wong et al (2008), Caroline-Kwong et al (2008) Leng Chin et al (2008), Wah-Yun Low et al (2008) and Nasruddin Jaafar et al majority (46.0%) of the participants were Muslims, (27.3%) Buddhists,) 19.8% (Christianity, (06.1%) Hindus and (0.8%) others.

Majority (86.25%) of the adolescents were urban dwellers and 13.75% rural dwellers. According to the study conducted by Sunder Arumugam et al; K.Selvarajan et al (2014), the analysis of area of domicile with the level of knowledge about AIDS showed that 61% of the respondents have rural background and 39% are from urban areas.[7-9]

Most of the adolescents fathers (72.5%) and mothers (53.75%) educational level were graduate and above. Majority of the adolescents (63.75%) belongs to nuclear type of family, 28.75% belongs to joint family and 7.5% belongs to extended type of family. A study conducted by M. Mizanur Rahmanl; M. Kabiret & M. Shahidullah et al; (2009) , most of the participants (56.4%) belongs to nuclear type of family and the other 43.6% belong to a joint family and none belong to the extended type.[9]

Majority of the respondents 72.5% got information from school, television (67.5%) newspaper (57.5%), health personnel (27.5%) and radio (23.75%). According to the study conducted by Anurag Srivastava, Syed Esam Mahmood et al, a higher proportion of students mentioned television (59.5%) and radio (46.9%) as the main sources of information. These observations show the strength and effectiveness of media as source of information and revealed the very poor effort by health personnel which needs to be strengthened.

Knowledge among the adolescents was good with a mean knowledge score of 19.1 out of 30 points. According to the study of Alexandra McManus et al (2008); Lipi Dhar et al (2008), knowledge among respondents was moderate ,with a mean knowledge score of 20.1 out of 32 points. There was a significant association with knowledge and gender, in which females adolescents are more knowledgeable than the males. According to the study conducted by Sonia Shirin and Shaila Ahmed et al (2007), although no statistical relationship could be established between the respondents' knowledge on AIDS and their socio- demographic attributes, some significance was seen with their branch of study, i.e. whether they were in the

Science, Arts or Commerce group. The students in the Science group seemed to be better informed than the others.

Nursing Implication:

Implications for Nursing practice:

Nurse is the most important member continuously in contact with the community peoples (adolescents). Nurses working in the health centre, schools, colleges should acquired adequate knowledge about HIV/AIDS to educate the adolescents regarding the same.

Implications for Nursing Administration:

In-service education programme, workshops, conferences and continuing nursing education programme can be organized to update the knowledge of the nurses and create awareness regarding any new findings and research studies done on HIV/AIDS so as best possible nursing care can be provided to the adolescents to to increase knowledge and skill concerning many aspects of adolescents cares.

Implications for Nursing Education:

Education is a powerful protective factor against HIV infection and therefore should be promoted. Education is the key to the development of excellence in nursing practice. Education faces tremendous challenge in keeping pace with the changes in nursing practice to maintain its high quality. Nurses with higher education and up to date knowledge will deliver cost effective and quality care. Education on HIV/AIDS is important to be incorporated in the nursing curriculum in order to provide knowledge to nursing students regarding HIV/AIDS which will help them to be more aware about HIV/AIDS and to facilitate imparting of the knowledge to the adolescents.

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Review Article

Therapeutic Interventions Of Peroxisome Proliferators-Activated Receptors In CNS Disorders

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Abstract

Peroxisome proliferators-activated receptors (PPARs) are ligand activated transcription factors belonging to the nuclear receptor superfamily. Activation of PPARα, both by natural ligands such as fatty acids, and eicosanoid derivates or by synthetic ligands regulates lipid and lipoprotein metabolism. These receptors play a key role in lipid metabolism as it regulates serum lipid profiles and fatty acid β-oxidation in muscle and adipose tissue. PPARs activation also helps regulate neuronal death in ischaemic, neurodegenerative and inflammatory cerebral diseases. Synthetic ligands of PPARs for neuroprotection in Alzheimers and Parkinsons disease are currently in preclinical phases of development.

Key Words: *Peroxisome proliferators-activated receptors, Neuroprotection, Alzheimers disease, Parkinsons disease.*

Introduction

Peroxisome proliferators-activated receptors (PPARs) are ligand activated transcription factors belonging to the nuclear receptor superfamily. Three isoforms of PPARs (α, β/ δ, and γ) have been identified which display distinct physiological and pharmacological functions depending on their target genes and their tissue distribution. PPARβ/δ also plays a key role in lipid metabolism as it regulates serum lipid profiles and fatty acid β-oxidation in muscle and adipose tissue.[1]

PPARs are able to regulate inflammatory pathways by transrepression of transcription factors nuclear factor-kappa B (NFkB) and thereby to regulate oxidative pathways. PPARα activation induces expression and activation of anti-oxidant enzymes such as superoxide dismutase or glutathione peroxidase. They also prevent the synthesis and release of cytokines and the induction of some inflammatory mediators such as cyclooxygenase-2 or adhesion proteins. In addition, PPARγ activation also reduces the expression of inducible nitric oxide synthase.[2,3]

Today, it is supposed that PPAR activation also helps regulate neuronal death in ischaemic, neurodegenerative and inflammatory cerebral diseases. In addition to expression in cerebral and spinal blood vessels, PPARs are also expressed in neurons and astrocytes; oligodendrocytes exclusively show PPARβ/δ expression. PPARβ/δ has been found in numerous brain regions while PPARα and PPARγ have been localized to more restricted brains areas. The transcription factor NFκB plays a key role in regulating inflammation and oxidative stress leading to neuronal death, which explains why PPARs have been suggested as possible targets for neuroprotection.[4]

In vitro studies have demonstrated that PPARγ agonists modulate inflammatory responses to bacterial endotoxin in brain and also prevent endotoxin induced neuronal death.[5] PPARα and

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PPARγ can inhibit macrophage and microglial activation which contributes to many degenerative, ischaemic, or inflammatory processes leading to neuronal death.[6] PPARγ agonists like Troglitazone and Ciglitazone inhibit both post-glutamate and low-potassium induced neurotoxicity in cerebellar granule neurons.[4] PPARs are also able to inhibit the entry of inflammatory cells into the CNS from the periphery by inhibition of chemokines, adhesion molecules, and metalloproteinases.

The mechanism of neuroprotection of Central Nervous System disorder by PPARs is being focused in this short review.

Targets Of PPARs As Neuroprotection In Central Nervous System Disorders

Alzheimers Disease:

Alzheimer's disease involve extracellular amyloid peptide (Aβ) deposition in neuritic plaques and intracellular deposits of hyperphosphorylated tau protein results in formation of neurofibrillary tangles and finally neuronal death, causing progressive memory loss and decline in cognitive functions. In vitro, it has been demonstrated that PPARα agonist inhibited Aβ stimulated expression of tumour necrosis factor α and interleukin-6 reporter genes in a dose dependent manner. PPARγ agonists were also shown to inhibit the β-amyloid stimulated expression of inflammatory cytokines and cyclooxygenase-2.[7,8] Recent data from in vivo studies also shows beneficial effect of PPARγ activation. It was evident by a 7 day oral treatment with the PPARγ agonist pioglitazone, which resulted in a reduction in glial activation as well as a reduction in the number of Aβ-positive plaque areas in the hippocampus and cortex of a murine transgenic model of the amyloid pathology of Alzheimer's disease.[9]

Parkinson's Disease:

Parkinson's disease is characterized by a progressive loss of dopaminergic neurons in the substantia nigra, which is experimentally mimicked by systemic administration of the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Oral administration of the PPARγ agonist pioglitazone attenuated MPTP induced glial activation and prevented dopaminergic cell loss in the substantia nigra pars compacta. Pioglitazone also prevented MPTP induced expression of inducible nitric oxide synthase.[10,11] This protective effect of pioglitazone is also associated with an increase in inhibitory protein-κ-Bα (IkBα) expression and inhibition of translocation of the NFκB subunit p65 to the nucleus in dopaminergic neurons, glial cells and astrocytes.[11] Recent evidence suggested that Indomethacin and Ibuprofen also functions as a micromolar ligand for the adipogenic transcription of PPARγ which delay or prevent Parkinsons disease making it a possibility that PPAR agonist may contribute to a therapeutic approach for this disease.[12]

Multiple Sclerosis:

Microglial activation and inflammation are keys to the pathophysiology of multiple sclerosis, which is why PPAR agonists have been tested in relation to this disease, in particular in the model of experimental autoimmune encephalomyelitis (EAE), which is characterized by CNS inflammation and demyelination together with remittent paralysis. Oral administration of the PPARγ agonist pioglitazone reduces motor symptom severity in monophasic EAE without delaying disease onset. In a relapsing model of EAE, pioglitazone reduces the severity of relapses and overall mortality without affecting onset and the severity of the initial attack.[13] The mechanisms of action of PPARγ agonists in EAE is complex. PPARγ activation inhibits production of nitric oxide, pro-inflammatory cytokines (tumour necrosis factor α, interleukin-1β, interleukin-6), and the chemokine MCP-1 by microglia and astrocytes. Prevention of phenotypical changes to the progenitor T cells is also probably involved and related to inhibition of interleukin-12 release. Moreover, PPARγ activators also modulate the maturation and differentiation of oligodendrocytes. From a clinical point of view, PPARγ activators suppressed T cell proliferation by

40–50% and secretion of interferon-γ and tumour necrosis factor α by 30–50%, supporting the potential use of PPAR-γ for immunomodulation in multiple sclerosis.[14] Oral administration of gemfibrozil and fenofibrate, the two PPARα agonists, also inhibits clinical signs of EAE by mechanisms involving secretion of interferon-γ and interleukin-4. Preferential localization of PPARβ/δ in oligodendrocytes and its role in oligodendrocyte differentiation suggest that PPARβ/δ could also be a pharmacological target for treatment of multiple sclerosis.[15]

Ischemic stroke:

Cerebral ischemia is the most common cerebrovascular disease and it is one of the leading causes of morbidity and mortality worldwide. The poor prognosis of cerebral ischemia is largely due to the lack of effective therapies. Inflammation plays a crucial role in the pathophysiology of cerebral ischemia by producing inflammatory mediators. Administration of the PPARγ agonists rosiglitazone or pioglitazone 24 or 72 hours before and at the time of cerebral infarction dramatically reduced infarction volume and improved neurological function following transient middle cerebral artery occlusion in rat.[16,17] Pretreatment with curcumin in rats decreased cerebral ischemia-induced IκB degradation. The neuroprotective effect of PPARγ agonists is related to inhibition of ischaemia induced inflammatory markers (interleukin-1β, cyclooxygenase-2, inducible nitric oxide synthase) and to an anti-oxidant effect (increase expression of superoxide dismutase 1). On the other hand, the inhibitory effects of PPARγ on NF-κB activation are increasingly being demonstrated in different cell systems. Inhibiting the activation of NF-κB leads to reduced infarcts in the acute stage of cerebral ischemia. PPARγ, suppresses proinflammatory gene expression at the transcriptional level through inhibiting NF-κB activation.[16,17]

Conclusion

Endogenous PPARγ activation plays an important role in promoting reparative mechanism in the injured CNS. Neuroprotection afforded by Thiozolidinedione derivatives as PPARγ against acute ischemic injury are clinically relevant. PPARs pathway remains largely unexplored, especially as a target for the treatment of multiple sclerosis. Thorough knowledge of the effectors of PPARs in the CNS especially in relation to ischemic injury and degenerative disorders and the development of new and efficacious PPAR activators will provide a pathway for treatment of disorders of the central nervous system.

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Review Article

A Review on Randomized Control Trial

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Abstract

Objective: To provide concise information to the health-care professionals about the structure, role, methodology and limitations of randomized control trials in medical & health research.

Data source: The literature has been searched online through the Pubmed, Medline and Cochrane data bases using the keywords 'Clinical Research', 'Clinical Trial', 'Randomized Control Trial' and 'Medical Ethics'.

Conclusion: Randomized control trials are the least biased of all clinical research and forms the cornerstone of evidence-based medicine, ranked only next to the systematic reviews in the heirarchy of evidence. Nevertheless, they have their limitations: the rigid selection criteria (internal validity/efficacy) compromises on their generalizability/effectiveness; they fail to answer certain clinical questions and they are time consuming and expensive.

***Key words**: 'Randomized Control Trial', 'Clinical Trial'.*

Introduction

Randomized Control Trial (RCT) is a type of clinical trial in which subjects (patients) are allocated at random to receive one of several clinical interventions. Although the term 'intervention' usually refers to treatment, it can include any clinical maneuver offered to the participants that may have an effect on their health status, including preventive strategies, screening programs, diagnostic tests, interventional procedures or educational and learning models.[1] The essence of an RCT is the process of randomization, thereby each subject (patient) has an equal chance of being put either in the interventional (experimental) or the control arm of the study. This prevents selection bias and increases the statistical power of the study.

Definition of terms:

Clinical research is research that directly involves human subjects or that uses materials from humans, such as their behavior or samples of their tissues.[2] It may range from ecological studies through observational epidemiological studies to RCT (Figure 1).

Clinical trial is one type of clinical research that follows a pre-defined plan or protocol to determine safety and effectiveness of specific health and medical products and practices, which can be either medications, medical devices, diagnostic tests or treatment regimens, intended for human use. Clinical trials can be used for the prevention, treatment, diagnosis or for relieving symptoms of a disease. They can be either randomized or non-randomized and can be with or without controls.

Randomized Controlled Trial, a type of clinical trial, is an experimental comparison study in which participants are allocated to treatment (intervention) or control (placebo) groups using a random mechanism (such as coin toss, random

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number table, or computer-generated random numbers). All participants have an equal chance of being allocated to an intervention or control group and therefore allocation (selection) bias is eliminated. It forms the Gold Standard of research designs and is the foundation for Evidence Based Medicine (EBM), if conducted according to principles and standards of Good Clinical Practice (Figure 1).

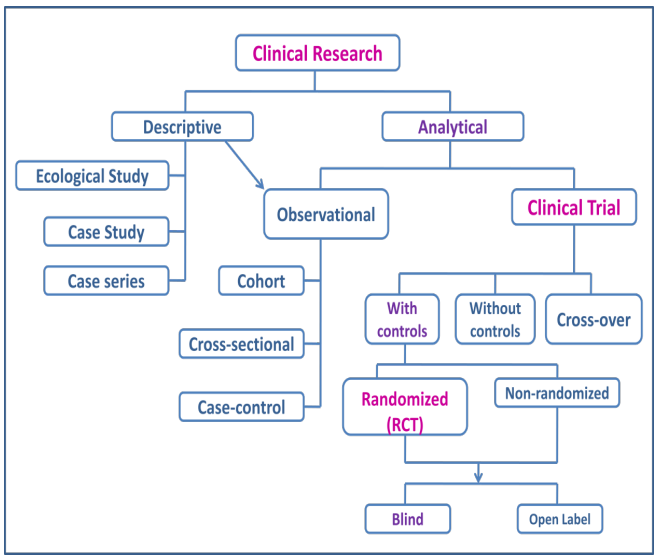


Fig. 1 : Clinical Research, Clinical Trial and Randomized Contolled Trials

History of Randomized Controlled Trials

The history of clinical trials dates back to approximately 600 B.C. when Daniel of Judah conducted what is probably the earliest recorded clinical trial.[2] He compared the health effects of the vegetarian diet with those of a royal Babylonian diet over a 10-day period. The trial had obvious deficiencies by contemporary medical standards e.g. allocation bias, ascertainment bias, and confounding by divine intervention, but the report has remained influential for more than two millennia

Credit for the modern randomized trial is usually given to Sir Austin Bradford Hill.[3] The Medical Research Council trials on streptomycin for pulmonary tuberculosis, carried out by Hill, are rightly regarded as a landmark that ushered in a new era of medicine. Since Hill's pioneering achievement, the methodology of the randomized controlled trial has been increasingly accepted and the number of randomized controlled trials reported has grown exponentially. The Cochrane Library already lists more than 724977 such trials and these are on the rise, and they have become the underlying basis for what is currently called "evidence-based medicine".[4]

Justification for Controlled Trials: Ideas of Treatment

Digoxin is used to treat heart failure, phenytoin is given in epilepsy, nitrates are given for angina pectoris …., the list is unending. There are also alternatives: beta blockers for heart failure, valproate or carbamazepine for epilepsy, or a Percutaneous Coronary intervention or CABG for angina pectoris. The idea to use some form of treatment or intervention for a disease or to search for better alternatives to the existing ones comes from different sources, like case reports, clinical observations, biological phenomena, scientific reasoning, epidemiological observations etc (Figure 2).

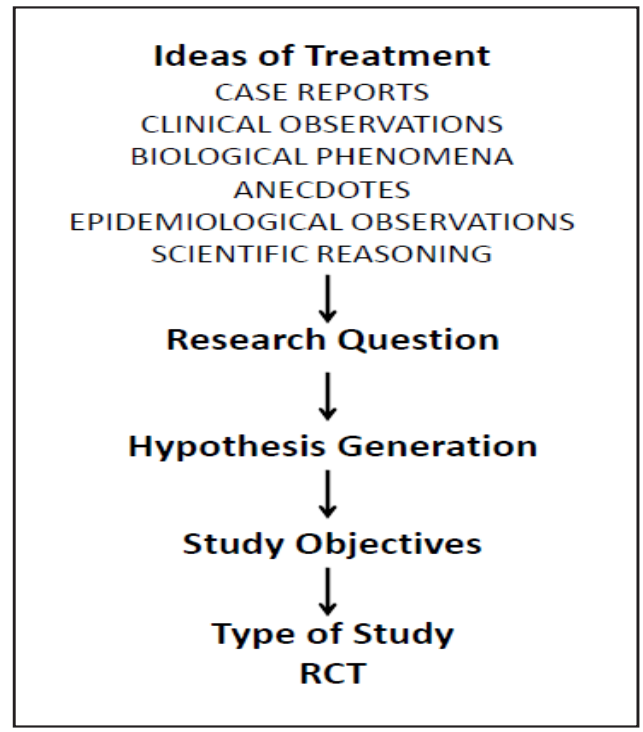


Fig 2 : Justification for Controlled Trails : Ideas of Treatment

These ideas lead to development of a research question which in turn leads to hypothesis generation and formation of study objectives. From the study objectives one can then decide the type of study to be undertaken. In case of questions relating to intervention the study design commonly adopted is the clinical trial to test that particular intervention. The best form of a clinical trial is the RCT. There are various examples of how ideas of treatment can lead to different clinical trials and their consequent outcomes.[5,6]

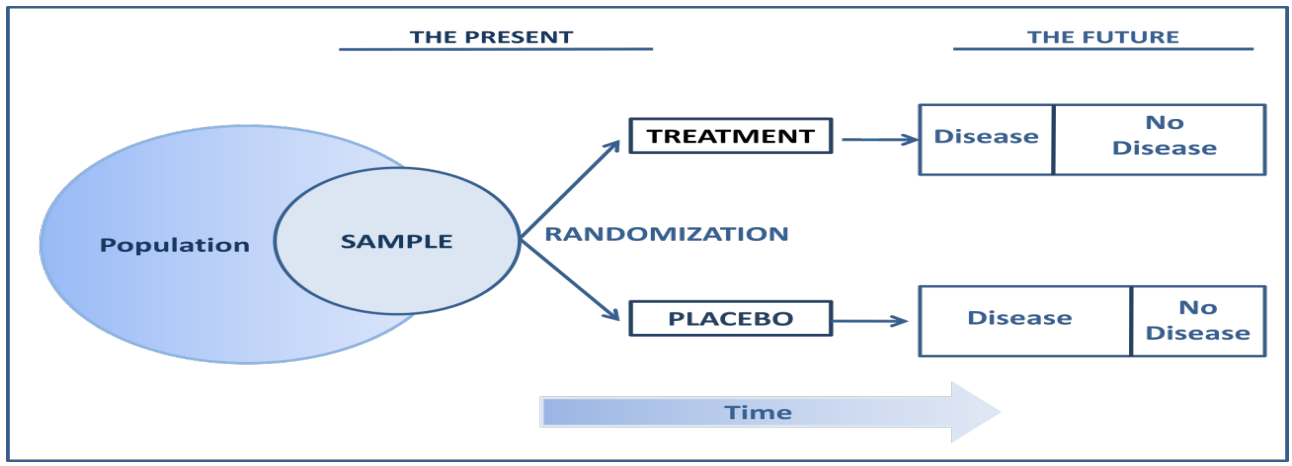
Amantadine was originally an antiviral drug used for influenza. It was incidentally found to reduce the symptoms of Parkinsonism in a woman who was taking this drug for influenza. This single case report led to many clinical trials and ultimately this established of this new class of drugs for Parkinsonism. This is an example of how idea of treatment can come from a single case report.

Minoxidil, a vasodilator originally used as an antihypertensive was discovered to have the side effect of hair growth and reversing baldness male pattern baldness. This led to clinical trials for the use of minoxidil as a topical solution for male pattern baldness and finally approved by FDA, an example of how clinical observations forms an idea for a clinical trial.

Bed rest has been advocated as an adjunct therapy for many clinical conditions, like viral hepatitis, low back ache, myocardial infarction, following a lumbar puncture etc. This has led to many clinical trials on the benefits of bed rest on different clinical problems. A review of 39 such trials of bed rest for 15 different conditions found that outcome did not improve for any condition; and were worse with bed rest in 17 of these trials, including lumbar puncture, infective hepatitis, low back pain etc.

Steps in a Randomized Control Trial

Patients to be studied are first selected (sample) from a larger number of patients (population) with the condition of interest. They are divided, using randomization, into 2 (or more) groups of comparable prognosis. The group subjected to the intervention is called the treatment (or experimental) group and the other group receiving conventional therapy or placebo (i.e. no intervention) is called the control (or comparison) group. The treatment (or experimental) group is exposed to an intervention that is believed to be better than current alternatives. The control (or comparison) group is treated the same in all ways except not exposed to experimental intervention; and may receive placebo, usual care or current best available treatment. RCTs may have more than one control group. The course of disease is recorded in both the groups and the difference in outcome are attributed to the intervention (Figure 3).



[N.B. Treatment = Intervention/Experimental treatment; Placebo = Conventional treatment/Current best care/No treatment, as applicable and ethically permissible]

Fig-3: The structure of Randomized Control Trial

Why Randomized Control Trial is needed

The randomized controlled trial is one of the simplest but most powerful tools of research. In essence, the randomized controlled trial is a study in which people are allocated at random to receive one of several clinical interventions.[2] On most occasions, the term "intervention" refers to treatment, but it should be used in a much wider sense to include any clinical maneuver offered to study participants that may have an effect on their health status. Such clinical maneuvers include prevention strategies, screening programs, diagnostic tests, interventional procedures, the setting in which health care is provided, and educational models.

Randomized controlled trials are used to examine the effect of interventions on particular outcomes such as death or the recurrence of disease. Some consider randomized controlled trials to be the best of all research designs, or "the most powerful tool in modern clinical research", mainly because the act of randomizing patients to receive or not receive the intervention ensures that, on average, all other possible causes are equal between the two groups.[4,7] Thus, any significant differences between groups in the outcome event can be attributed to the intervention and not to some other unidentified factor.

Advantages of Randomized Control Trials over other clinical trials

The randomization procedure gives the randomized controlled trial its strength. Random allocation means that all participants have the same chance of being assigned to each of the study groups.[8] The allocation, therefore, is not determined by the investigators, the clinicians, or the study articipants.[2] The purpose of random allocation of participants is to assure that the characteristics of the participants are as likely to be similar as possible across groups at the start of the comparison (also called the baseline). If randomization is done properly, it reduces the risk of a serious imbalance in known and unknown factors that could influence the clinical course of the participants. No other study design allows investigators to balance these factors.

The main appeal of the randomized controlled trial in health care derives from its potential for reducing allocation (selection) bias.[2] No other study design allows researchers to balance unknown prognostic factors at baseline. Random allocation does not, however, protect randomized controlled trials against other types of bias.

Thus it can be said that RCTs are quantitative, comparative, controlled experiments in which a group of investigators studies two or more interventions by administering them to groups of individuals who have been randomly assigned to receive each intervention. Alternatively, each individual might receive a series of interventions in random order (crossover design) if the outcome can be uniquely associated with each intervention, through, for example, use of a "washout" period. This step ensures that the effects from one test are not carried over to the next one and subsequently affect the independent evaluation of the second test administered. Apart from random allocation to comparison groups, the elements of a RCT are no different from those of any other type of prospective, comparative, quantitative study.

Types of Randomized Control Trial

Various terms have been used to describe different types of RCTs. They can be classified as to the aspects of intervention that investigators want to explore, the way in which the participants are exposed to the intervention, the number of participants included in the study, whether the investigators and participants know which intervention is being assessed, and whether the preference of nonrandomized individuals and participants has been taken into account in the design of the study. We would make an attempt to briefly describe some of the important terminologies used in describing the RCTs.

a. RCT classified according to participants' exposure and response to the intervention:

I. Parallel design: in which each group of participants is exposed to only one of the

study interventions. This is the most common design for RCTs.

II. **Crossover design:** refers to a study in which each of the participants is given all of the study interventions in successive periods. The order in which the participants receive each of the study interventions is determined at random. This design, obviously, is appropriate only for chronic conditions that are fairly stable over time and for interventions that last a short time within the patient and that do not interfere with one another. Otherwise, is used in acute conditions, false conclusions about the effectiveness of an intervention could be drawn.[9]

III. **Factorial design:** A RCT has a factorial design when two or more experimental interventions are not only evaluated separately but also in combination and against a control.2 For example, a 2 × 2 factorial design generates four sets of data to analyze: data on patients who received none of the interventions, patients who received treatment A, patients who received treatment B, and patients who received both A and B. More complex factorial designs, involving multiple factors, are occasionally used. The strength of this design is that it provides more information than parallel designs. In addition to the effects of each treatment, factorial design allows evaluation of the interaction that may exist between two treatments. Because randomized controlled trials are generally expensive to conduct, the more answers that can be obtained, the better.

b. RCT classified according to the number of participants: RCT can be performed in one or many centers and can include from one to thousands of participants, and they can have fixed or variable (sequential) numbers of participants.

I. **"N-of-one trials":** RCT with only one participant are called "n-of-one trials" or "individual patient trials." RCT with a simple design that involve thousands of patients and limited data collection are called "megatrials" .[10,11] Usually, mega-trials require the participation of many investigators from multiple centers and from different countries.[2]

II. **Sequential trial:** A sequential trial is a study with parallel design in which the number of participants is not specified by the investigators beforehand. Instead, the investigators continue recruiting participants until a clear benefit of one of the interventions is observed or until they become convinced that there are no important differences between the interventions.[8] This element applies to the comparison of some diagnostic interventions and some procedures in interventional radiology. Strict rules govern when trials can be stopped on the basis of cumulative results, and important statistical considerations come into play.

III. **Fixed trials:** Alternatively, in a fixed trial, the investigators establish deductively the number of participants (sample size) that will be studied. This number can be decided arbitrarily or can be calculated using statistical methods. The latter is a more commonly used method. Even in a fixed trial, the design of the trial usually specifies whether there will be one or more interim analyses of data. If a clear benefit of one intervention over the other can be shown with statistical significance before all participants are recruited, it may not be ethical to pursue the trial, and it may be prematurely terminated.

c. RCT classified according to the different aspects of interventions evaluated:

I. **Explanatory or pragmatic trials:** Explanatory trials are designed to answer a simple question: Does the intervention work? If it does, then the trial attempts to establish how it works. Pragmatic trials, on the other hand, are designed not only to determine whether the intervention works but also to describe

all the consequences of the intervention and its use under circumstances corresponding to daily practice. Although both explanatory and pragmatic approaches are reasonable, and even complementary, it is important to understand that they represent extremes of a spectrum, and most randomized controlled trials combine elements of both.

II. **Efficacy or effectiveness trials:** RCT are also often described in terms of whether they evaluate the efficacy or effectiveness of an intervention. Efficacy refers to interventions carried out under ideal circumstances, whereas effectiveness evaluates the effects of an intervention under circumstances similar to those found in daily practice.

Special issues in Randomized Control Trial

1. **Blinding in RCT:** RCTs can be open-labelled or more commonly, blinded. Non-blinded (open or open label) denotes trials in which everyone involved knows who has received which interventions throughout the trial. The term blinding (masking) refers to keeping trial participants, investigators (usually healthcareproviders), or assessors (those collecting outcomedata) unaware of an assigned intervention, so that they are not influenced by that knowledge. Blinding of the study participants minimizes bias in patient responses; blinding of the investigators prevents those involved in the clinical study from knowing to which treatment groups the subjects have been assigned; and blinding of outcome assessors minimizes biasing of measurements.

Blinding can occur at the three possible levels, viz:

a. **Patient:** here the patients will not be aware whether they are put in the control group or in the treatment group.

b. **Investigator (usually Clinicians):** the clinicians actualy treating the patients will not know which of the patients are in the treatment group and which are in the control group of the trial.

c. **Measurement of outcome:** the observer who measures the outcome of the study, e.g. the clinician measuring the degree of regression of the liver enlargement by a experimental drug in a particular trial, the radiologist assessing the size of the pulmonary opacity, the cardiologist assessing the LV function in an echocardiograph, or the pathologist trying to measure the stageing of a tumour will not be aware whether his/her observation is in a patient from the treatment group or control group.

Single blind usually means that one of the three categories of individuals (normally participant rather than investigator) remains unaware of intervention assignments throughout the trial. In a double-blind trial, participants, investigators, and assessors usually all remain unaware of the intervention assignments throughout the trial. Triple blind usually means a double-blind trial that also maintains a blind data analysis. Some investigators, however, denote trials as triple-blind if investigators and assessors are distinct people and both, as well as participants, remain unaware of assignments. Considering the confusion over terminologies of blinding, investigators should clearly mention who are blinded in their trial, the participants, investigators or assessors, rather than only labeling their trial as single-blind, double-blind, or triple-blind.[12]

Blinding should be differentiated from alocation concealment. Blinding prevents ascertainment bias and protects the sequence after allocation. By contrast, researchers use methods of allocation concealment primarily to prevent selection bias and to protect an assignment sequence before and until allocation. Allocation concealment: is the process in which the person assigning the participant to either the treatment or control groups will himself/herself not be aware to which group he/she is assigning the participants.

2. **Implications of eligibility criteria in sampling:** When carrying out any clinical trial, investigators should try to select a sample (of participants) with rigorous inclusion and exclusion criteria for several reasons. It increases the homogeneity of patients selected, strengthens the internal validity of the study and it makes it easier to distinguish treatment effect from chance and bias. Sampling process should also follow strict exclusion criteria, and patients with co-morbidity, low life-expectancy, patients with contraindication to either treatment, or patients refusing participation in trial and those with poor compliance (adherence) are generally excluded from the study. However, after the study is over, there is a need to generalize the findings to a broad spectrum of patients who could potentially benefit from the superior treatment.

   These conflicting demands introduce an issue of balancing the inclusion/exclusion (eligibility criteria) such that the enrolled patients are as much alike as possible but, on the other hand, to be able to apply the results to the more general population (ie, generalizability). Figure 4 shows the balance between homogeniety and generalizability. There is always a trade-off between homogeneity and generalizability, and each study has to address this, given the availability of subjects, along with other considerations. This process of sampling represents one of the reasons that scientific inquiry requires reproducibility of results; that is, one study generally cannot be relied on to portray "truth."

3. **Efficacy and Effectiveness of a RCT:** In any RCT two questions come to the clinician's mind: (i) can this treatment work under ideal circumstances? And (ii) will this treatment work under ordinary circumstances. The first question will answer about the efficacy and the second one about the effectivenes of a trial. Efficacy trials are those in which treatment can work under ideal circumstances, having certain qualities like excellent patient adherence to treatment, best possible care has been provided, there is no extraneous effects from co-morbidities. These trials strengthen the internal validity of a trial. On the other hand, in effectiveness trial, treatment can work in day to day ordinary circumstances. Complete adherence to treatment by patients will not be met and there will be drop outs. Full compliance to take assigned medications will also be not present. These trials are usually analyzed

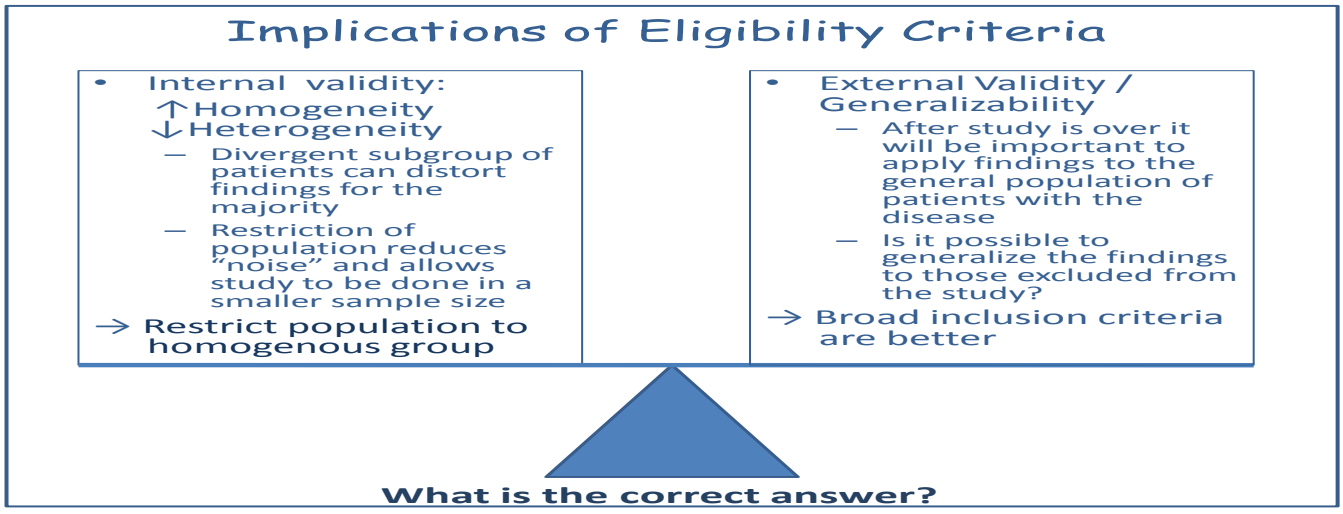


Fig. 4: Sampling in RCT: Implications of eligibility criteria
(Source: Glasser SP et al. J Clin Pharm 2006;46:1106-15)

'intention to treat'trials. These trials meet the criteria for external validity.

4. **Selection of interventional and comparison groups: Baseline characteristics:** For a RCT to be successful certain procedures are to be strictly followed. Allocation of treatment to either group should be done randomly. The patients assigned to either experimental or control treatment should be made by a disciplined procedure similar to flipping of a coin (randomization). This will ensure reduction of bias in the study. If strict randomization procedure is followed in treatment allocation, the baseline chaarcteristics (e.g. age, sex, habitation etc.) of patients in both the groups are likely to be similar and the groups would be comparable. But this is usually possible if the number of patients is sufficiently large enough. Hence to verify whether randomization has been effective it is essential to compare the baseline characteristics of the groups and find out if they are similar or not.

5. **Analytic method used:** In case of RCT and also other clinical trials, the actual number of patients assigned to the treatment (experimental/interventional) and control groups always do not rremain in the same groups upto the end of the trial. Some of them drop out of the study because of poor adherence, some will refuse the experimental treatment and opt for the conventional (control) one, hence migrate to the control group and vice versa. But the study designers will have to take some decisions as to the number of patients in either group at the end of the trial. This can be done by one of the several ways:

a. according to treatment to which the patients were randomized, i.e. analysis as randomized (also referred to as intention to treat analysis, or ITT)

b. compliers-only analysis (in which only those patients randomized to a treatment arm who completed the trial and complied with treatment are analyzed) and

c. as-treated analysis (in which only those who received a given treatment are counted, whether or not the patient was initially assigned to that treatment).

Of the three types of analyses, intention to treat analysis analysis is considered the gold standard of analytic methods because it is the only analysis that preserves randomization and thereby reduces confounding in the study process.

6. **Ethical Issues in Clinical trials:** although there are several ethical issues of concern in carying out a clinical trial it is beyond the scope of this discusssion to provide an elaborate discussion on the all the ethical issues related to clinical trials. However, the following two issues of importance are discussed in some details:

a. **Clinical Equipoise:** Although many researchers claim that RCTs are the ultimate in research methods, many important aspects of health care cannot be subjected to a randomized trial for practical and ethical reasons. A RCT is the best way of evaluating the effectiveness of an intervention, but before a RCT can be conducted, there must be equipoise, i.e. genuine doubt about whether one course of action is better than another13. It is not ethical to build a trial in which, before enrollment, evidence suggests that patients in one arm of the study are more likely to benefit from enrollment than patients in the other arm. Equipoise thus refers to the fine balance that exists between being hopeful a new treatment will improve a condition and having enough evidence to know that it does (or does not). RCTs can be planned only in areas of uncertainty and can be carried out only as long as the uncertainty remains.

b. **Protection of patient safety:** it is unethical to continue a clinical trial if there is compelling

evidence that one arm is safer or more efective than the other. Furthermore, it would be wrong to continue a trial that will not answer the research question because of less number of subjects enrolled, few outcome events, or high dropout rates. Therefore for any clinical trial there should be an independent Data Safety Monitoring Board (DSMB) which can decide whether study requires premature discontinuation.[14] Such interim analyses should be not be done by the researchers themselves, because unblinding (unmasking) the investigators to interim findings can lead to bias if the study continues. Procedures for examining interim data of the trial by the independent DSMB and subsequent premature termination of the trial (if necessary) should be specified in the data safety monitoring protocol (DSMP).

Phases in Clinical Trials

Clinical trials are conducted in various phases. At each phase the trials have a different purpose and help researchers answer different questions:

Phase I trials: Researchers test an experimental drug or treatment in a small group of people (10-50) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.Control group is not kept.

Phase II trials: The experimental study drug or treatment is given to a larger group of people (100-300) to provide preliminary information on whether the drug is efficacious and to further evaluate its safety and the relation between dose and efficacy

Phase III trial: These are randomized trials that provide definite evidence of efficacy and rates of common side effects. These trials include enough patients, usually several thousands, to detect clinically important treatment effects. But they are not large enough to detect uncommon side effects. The results are usually published in journals.

Phase IV trials (Post marketing surveillance): These trias are conducted after the drug is in general use. It is necessary to follow up very large number of patients for rare or uncommon side effects and their rates of occurrences and optimize the use of the drug.

Beyond Clinical Trials: Systematic reviews and Meta-analysis

Quite often it is found that several clinical trials attempt to answer similar questions about clinical effectiveness; e.g. does the new treatment confer significant benefits compared with the conventional treatment? Often many of the individual trials will fail to show a statistically significant difference between the two treatments. However, when the results from the individual studies are combined using appropriate techniques significant benefits of treatment may be shown. In the late eighties and early nineties several clinical trials were carried out to prove the effectiveness of thrombolytic therapy for the prevention of myocardial infarction, but none could conclusively demonstrate such effectiveness. A systematic review and meta-analysis of pooled results of these individual studies conclusively demonstrated the effectiveness of thrombolytic therapy in acute myocardial infarction. Had meta-analysis been conducted at an early stage, it would have demonstrated the benefits of thrombolytic therapy. Instead, experts remained unaware of its benefits for many years and patients were not given an effective therapy. A systematic review thus aims to provide an exhaustive summary of current literature relevant to a research question through a process of literature search for relevant papers that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question. The use of statistical techniques to combine the results of these eligible studies is called meta-analysis.

Conclusion

RCTs are the gold standards of any type of clinical intervention studies, and are the least bised of all research studies. They are ranked only next to the systematic reviews in the heirarchy of evidence. Although they are of very high standards, certain clinical questions cannot be resolved even after many RCTs, e.g. Is screening

mammography a really effective tool? There are also some practical limitations of RCTs . These trials are done in a limited number of patients at a time or in one place with strict selection criteria to enhance the internal validity but are also expected to have generalizability in applying to the general population. They are very expensive to carry out and takes a long time for any results to be published.

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Review Article

Low Tidal Volume Ventilation in the Operation Theatre – should it be the current trend

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Abstract

Mechanical ventilation is often mandatory for patients who are undergoing surgery under General Anesthesia. Though it is a life-saving necessity, mechanical ventilation adds mechanical stress to lung parenchyma and thus may cause injury on a cellular level. With the increment of our understanding on ventilator associated lung injury especially among critically ill patients and patients with diseased lung, lung protective ventilatory strategy has become well prevalent among critical care physicians. This has been extrapolated to the operating room where usually normal lungs of non critical patients are ventilated for relatively shorter duration. Though low volume ventilation has been suggested to cause less volutrauma and barotraumas, chances of atelectrauma is high in such patients. Here we review the advantages, disadvantages and evidences in the literature for low tidal volume ventilation in operation theatre.

***Key words**: Low tidal volume ventilation, Operation theatre, Mechanical ventilation, Ventilator induced lung injury, Positive end-expiratory pressure, Acute lung injury& anesthesia*

Introduction

Since the discovery of harmful effects of mechanical ventilation (MV) on lung tissue and function, a number of elements responsible for these changes have been identified. Many investigations into the mechanisms of so-called ventilator induced lung injury (VILI) have been performed in animal models or intensive care unit (ICU) patients presenting with acute lung injury or acute respiratory distress syndrome (ARDS). The degree of VILI is determined by the interaction of the ventilator settings and patient related factors, particularly the condition of the ventilated lung.[1] High tidal volumes (Vt), increase inflation pressures, as well as low or zero positive end-expiratory pressure (PEEP) levels were found to be associated with more severe forms of VILI. In contrast to MV in lungs with acute diseases such as Acute Lung Injury (ALI) and ARDS, ventilation of normal and healthy lungs during anesthesia may cause less tissue injury and distant organ dysfunction. The occurrence, risk factors, and determinants of lung damage of the VILI type are less well examined in such patients. Although animal experiments in ex vivo isolated normal lungs and in vivo situations have shown similar types of damage to the parenchyma by MV and a preventive effect of PEEP, much remains to be clarified.[2,3,4] Clinical studies performed in patients undergoing MV for anesthesia and a surgical procedure have yielded conflicting results with regard to the effects of Vt on lung inflammation, protective effect and other signs of VILI.[5,6]

Positive Pressure Ventilation : Effects

Normal breathing is a process of negative pressure ventilation. When positive pressure is applied to the respiratory system, a host of physiologic changes occur. The pulmonary effects are redistribution of extra vascular water that leads to improved oxygenation, lung compliance

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and ventilation-perfusion matching and increase in the functional residual capacity leading to alveolar recruitment which decreases shunt. Cardiac effects are decrease in cardiac output which ultimately leads to decreased venous return, right ventricular dysfunction and alteration of left ventricular distensibility.[7]

Volume Targeted Mechanical Ventilation

In volume-targeted modes of ventilation, the controlled variable is the tidal volume, which is a function of inspiratory flow and time. The goal is to guarantee preset minimal minute ventilation, which is usually a function of set tidal volume and set respiratory rate. Because pressure will vary in volume-targeted modes of ventilation, careful monitoring and assessment of respiratory system, compliance and resistance is necessary.[8]

Adverse Effects of Mechanical Ventilation

Mechanical ventilation is associated with adverse effects, including atelectasis and VILI. Atelectasis occurs in 90% of patients undergoing general anaesthesia.[9] The result is decreased compliance, impaired oxygenation and lung injury. Acute extreme lung stretching and high airway pressures have been found to contribute to severe parenchyma changes increasing permeability of the alveolar-capillary barrier, resulting in pulmonary edema, parenchyma damage, increased inflammation and ultimately VILI.[10]

Predicted Lung Volumes

Normal lung volumes can be predicted on basis of sex and height.[11, 12] The predicted body weight (PBW) of male patients is calculated as 50±0.91(centimeters of height-152.4), that of female patients is calculated as 45.5±0.91(centimeters of height-152.4).[13] Unfortunately, many textbooks of medicine state 10ml/kg actual body weight as initial ventilator settings, exposing women and shorter patients to higher and potentially injurious Vt .[14]

Low Tidal Volume Ventilation

Mechanical ventilation practice has changed over past few decades, with tidal volume decreasing significantly, specially with ALI and ARDS. The main objectives of lung protective mechanical ventilation strategies are to minimize regional end- inspiratory stretch, thereby decreasing alveolar damage as well as alveolar inflammation. Few studies addressed the effects of mechanical ventilation using a high Vt strategy on pulmonary inflammatory response in patients without lung disease, mostly during major surgery.[15,16,17,18] The use of low tidal volume did not affect the sedation needs or vasopressor use and was not associated with altered requirements of higher PEEP and additional FiO2. Moreover by decreasing the need for fluids this beneficial hemodynamic effect could contribute to the reduced incidence of ALI/ARDS. The higher ventilatory rates in the lower Vt group keep PaCO2 and pH stable. Hypercapnia may have beneficial physiological and anti-inflammatory effects. Using a Vt of not more than 6ml/kg PBW has been shown to result in reduction of systemic inflammatory markers, increased ventilatory free days, and reduction in mortality when compared with Vt of 12ml/kg PBW in patients with ALI and ARDS.[13]

In the low Vt group, Vt was reduced further to 5 or 4 ml/kg of PBW if necessary to maintain plateau pressure (Pplat) at less than 30cm H_2O. A secondary analysis of the ARDS Network database showed a beneficial effect of Vt reduction from 12ml/kg to 6ml/kg PBW even in patients with low Pplat ranging between 16 and 26cm H_2O before tidal volume reduction. Schultz et al. suggest the use of low Vt ventilation with PEEP levels above 5 cm H_2O in patients without ALI or ARDS in absence of large scale prospective randomized trials.[19] He argued that in critically ill patients requiring MV for pulmonary edema, chronic obstructive pulmonary disease, congestive heart failure, aspiration, pneumonia and trauma after surgery not fulfilling ARDS criteria, mortality is associated with application of high Vt and Pplat. Two retrospective analysis identified high airway pressure and Vt are independent risk factors for development of ALI and ARDS in patients requiring MV for acute

respiratory failure. It is of importance that this analysis included patients who were critically ill and had obviously either cardiopulmonary disease or ventilatory dysfunction and had thus per se a certain risk to develop ALI or ARDS. Recent survey demonstrated that Vt in critically ill patients is on average approximately 7-8 ml/kg BW but still Vt between 12 and 18 ml/kg BW are used with low or no PEEP.[20] Based on this data, it seems justified to request protective ventilator strategies in risk patients routinely and not to wait until the ALI or ARDS criteria are fulfilled, although, we do not have evidence that the ventilator settings suggested by Schultz et al., which are essentially based on ARDS Network protocol, are the best way to ventilate patients at risk for ALI or ARDS.

Hong et al. recently presented interesting experimental work on this topic.[21] They applied different PEEP and Vt levels to normal anesthetized pigs and then looked for changes typical for VILI. The experimental protocol was MV for 8 hrs using a Vt of 6 or 15ml/kg BW and PEEP of 3 or 10cm H_2O. The authors observed that a low Vt / high PEEP resulted in significantly more severe parenchymal alteration and more pronounced lung inflammatory changes than a high Vt/low PEEP combination. At first glance, and looking at the mainstream literature coming from intensive care, the result reported seems surprising. Taking into account the quite different situation regarding pulmonary volume and mechanics of the normal lung compared with ALI, ARDS and ex vivo animal models, the observations by Hong et.al. may well have a strictly physiologic explanation.

Low Tidal Volume Ventilation in the operation theatre

It may be important to distinguish between mechanical ventilation in the operating room and in the intensive care unit (ICU). Patients in the operating room are mechanically ventilated for a much shorter time than those in the ICU. Both surgical patients and critically ill patients are at risk for several causes of lung injury. However they may not be the same for both patients group and each challenge may have different effects in both the groups. Nevertheless, while waiting for further results it is better to avoid high plateau pressure and high TV in patients who do not have ALI/ARDS at the onset of mechanical ventilation.

Apart from ventilator settings, a variety of cofactors such as positioning, systemic inflammatory response depending, for example, on the amount of surgical trauma, transfusion of blood products, prolonged (injurious) mechanical ventilation, aspiration and shock or sepsis are important for generation or prevention of VILI.[22-25] Recently, Wolthuis et al. have shown in patients scheduled to undergo an elective surgical procedure (lasting>5h) that MV with Vt of 12ml/kg and no PEEP increased myeloperoxidase and elastase in the broncoalveolar lavage fluid (BALF) when compared to a Vt of 6 ml/kg and PEEP but not in plasma inflammatory mediators.[26] In contrast, Michelet et al have shown that protective ventilation reduced the systemic pro-inflammatory response after esophagectomy.[27] Their results indicate that MV without PEEP and during one lung ventilation is more aggressive to the lungs and can promote a more intense VILI even after a short time. Moreover, in high Vt/PEEP it seems to promote fibrin depositions within the airways by increased procoagulant activity. These changes in pulmonary homeostasis are similar as those previously described in patients with pneumonia or ARDS and in human volunteers with endotoxin induced pulmonary inflammation, whereas low Vt /PEEP largely attenuates these changes in procoagulant activity.[28,29,30] As highlighted by Schultz et.al, smaller randomized trials of perioperative ventilatory strategies during major surgery revealed non uniform results. The impression is that ventilatory strategy is more relevant during surgery that triggers a higher inflammatory response, such as esophagectomy or cardiac surgery. However, these studies were not designed or powered to draw clinically relevant conclusions on clinical outcome measures, but studied inflammatory markers that

are likely to but not proven to be surrogate markers of clinical outcome.

Postoperative decrease in lung function is common after major upper abdominal surgery and usually prolong. Recently conducted randomized control trials of effect of low tidal volume ventilation or lung protective ventilation as compared to high or conventional ventilator strategy to compare lung function and clinical outcome is also not showing uniform results.[31,32] Though Futier et. al, have found that use of a lung-protective ventilation strategy in intermediate-risk and high-risk patients undergoing major abdominal surgery was associated with improved clinical outcomes and reduced health care utilization; the study conducted by Treschan et. al has failed to demonstrate amelioration of prolonged impaired lung function after major abdominal surgery by low tidal volume ventilation.[31,32] However Meta analysis combining randomized trials and observational studies showed a strong trend toward reduced mortality, lung infections, and ARDS in more than 2,000 people treated with low tidal volumes with a diverse spectrum of illness both in ICU and operation theatre.[33] Another Meta analysis conducted by Sutherasan et. al., have found nearly similar findings except mortality benefit.[34] They have found that implementation of protective ventilator strategies, consisting of Vt of 6 ml/kg, PEEP of 6–12 cm H_2O and recruitment maneuvers can decrease the development of ARDS, pulmonary infection and atelectasis but not mortality in previously non-injured lungs in the perioperative period and the ICU.[34]

Limitations of Low Tidal Volume Ventilation

Though low Vt ventilation has given a paradigm shift towards lung protective ventilation strategies, potential adverse effects of this should also be considered in all patients. Low Vt leads to low alveolar ventilation leading to accumulation of carbon-di-oxide leading to use of the concept "permissive hypercapnia".[35] Hypercapnia may cause respiratory acidosis, increased intracranial pressure, pulmonary hypertension, decreased myocardial contractility, decreased renal blood flow, and release of endogenous catecholamines.[36] Moreover, MV with low Vt and Pplat may promote atelectasis formation and therefore increased requirements of higher FiO2 and PEEP to maintain oxygenation.[5] To prevent hypercapnia, higher rates of breaths may be used which in turn will lead to auto PEEP generation.[37] To counteract cardiovascular depression caused by higher PEEP levels, fluid loading frequently associated with positive fluid balance and/or catecholamine infusion may be required. Therefore, all these variables must be carefully considered and balanced when reducing Vt in individual patients.

Should Low Vt be the current trend ?

After considering all these, question arises whether protective ventilation is beneficial in patients with healthy lungs requiring short-term MV during General Anesthesia? Multiple factors like airway closure, reduced lung volumes in the supine position, distortion of lung and rib cage, cephalic shift of the diaphragm, surfactant alteration, blood shift from abdomen to thorax, or a combination of these contribute to atelectasis formation in 90% of the patients during anesthesia.[38,39] Individual factors such as obesity, pneumoperitoneum, pre-existing disease, and some surgical interventions may also aggravate atelectasis formation in surgical patients. In the 1960s, use of Vt as large as of 15ml/kg body weight was advocated to reopen collapsed lung tissue and to prevent impaired oxygenation during anesthesia.[40] Cyclic opening and closing caused by recruitment and derecruitment of small airways or lung units may lead to increased local shear stress (atelectrauma), which has been suggested to contribute to lung damage even in the absence of high Pplat.[41] However, it has been shown that, for identical Vt and PEEP, reducing respiratory rate attenuates or delays lung damage, provided that tidal ventilatory stress is sufficiently low.[42] A ventilator cycles more than 900 per hour are probably not commonly applied during anesthesia whereas 20,000-40,000 cycles per day for few days to weeks in critically ill patients. This indicates that tidal ventilatory stresses in the operation theater

patients are very low as compared to ICU patients. PEEP levels of up to 10cm H_2O are necessary in healthy patients during anesthesia to keep open those alveolar units that are most likely close. However, any lung protective benefit of PEEP is expected to be unimpressive when Pplat is modest or when lung contains few recruitable units.[43] So, if we want to answer this question, the editorial conclusion by Putensen et al.[43] appears to be still justified. They concluded that, "it is essential to tailor ventilator settings during anaesthesia to the specific physiologic changes caused by surgery and preexisting disease of the patient, while treating the lungs gently".

Conclusion

To what extent postoperative complications are caused by respiratory dysfunction and ventilator settings during anesthesia is still not clear. Therefore, although not conclusive, most data and few randomized control trials suggest that low tidal volumes can be beneficial (or that high tidal volumes can be harmful) in patients without evidence of ARDS or acute lung injury and can be applied as ventilatory trend in operating room especially in high risk patients.

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Babinski Sign - From a student's desk for student's desk

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Joseph Babinski (1857-1932), a French neurologist of Polish descent, was the first one to describe extension of the big toe following stimulation of the sole of the foot on February 22, 1896. He referred to the sign as "phénomène des orteils" (toes phenomenon) which now is usually referred as the "Babinski sign" or descriptively as the extensor plantar response.[1] Babinski became a pioneer of modern neurology when he broke with the tradition of his former mentor, Jean-Martin Charcot, to develop and promulgate the neurologic examination. Charcot, unquestionably the leading neurologist of the mid-19th century, had relied primarily on medical history taking and astute observation to formulate clinical assessments. The information that may be deduced from scratching a patient's sole, is as important as a diagnostic sign as it is simple to elicit. When the great toe moves upward (sign of Babinski), this signifies, as everybody knows, a disturbance of the pyramidal tract. Some authors refer to the Babinski sign as the most important in neurology. It is basically a polysynaptic superficial reflex, designed to withdraw the stimulated part, i.e., the foot from a potentially dangerous stimulus. Babinski's sign (extensor plantar response) characterised by dorsiflexion of the great toe and variable fanning of the lateral four toes, is the prototype sign of upper motor neuron-type lesion. The reflex arc for the plantar reflex comprises of the afferent and efferent fibres in the tibial nerve and the L4-5 to S1-2 cord segments.

The muscles taking part in a fully developed response include extensor hallucis longus, tibialis anterior, extensor digitorum longus, hamstring group of muscles and tensor faciae latae.[2] The characteristic response is dorsiflexion (extension) of the big toe, which precedes all other movements. It is followed by fanning out and extension of the other toes, dorsiflexion of the ankle and flexion of the hip and knee joint. This complete response represents 'positive' Babinski sign. There is no such thing as a 'negative' Babinski sign.

Pyramidal Tract

There seems to be a close association between occurrence of the Babinski sign and impairment of voluntary foot movement. A Babinski sign can appear only if the intraspinal pathways of the flexion reflex synergy are operative, however, severe the motor deficit in the foot. The function of the pyramidal tract may not only be disturbed by structural lesions of myelin sheaths, axons, or both, but also by metabolic factors, for example, hypoglycaemia or an epileptic seizure.[3] In these cases the flexion reflex may become brisker, by disinhibition. The sign of Babinski emerges when the dysfunction involves those pyramidal fibres that project upon motoneurones of foot muscles; the great toe may again be recruited into the flexion synergy in the leg. Not all disturbances of the pyramidal system are associated with a Babinski sign, even in cases where the descending fibres to the foot muscles are clearly involved. The explanation for the lack of a Babinski reflex should be sought in

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a dysfunction of the segmental reflex pathways, the simplest being a pressure palsy of the peroneal nerve. In some cases there is temporary inexcitability of spinal motoneurones, most often by a transverse lesion of the cord (as in spinal shock), but sometimes after acute brain lesions. The muscle responsible for the up-going toe sign is located in the leg, the musculus extensor hallucis longus.[4]

Performing the manouevre

To start with, all leg muscles should be visible and in a relaxed state. This implies that the entire leg should be uncovered (removing socks is not enough), and that the patient should be supine, on a couch or in a bed (hoisting up the leg of a seated patient is asking for trouble).The patient should be warned that the sole is going to be scratched, and that it is important that the limbs remain as floppy as possible. It is the site of stimulation, intensity of inflammation, and even the object used for stimulation (from inverted patella hammer to shark's tooth or Bentley key) that has received by far the most attention in relation to difficulties in interpreting the plantar response.[5] Any instrument will do provided it is not too sharp and has not been used on other patients. Any part of the leg can be stimulated, but the chance of producing an up-going toe response in the presence of pyramidal tract dysfunction is greatest if the lateral plantar border is chosen, rather than the medial side, which overlies the flexor hallucis brevis muscle. Stimulation at that site is therefore more likely to make the toe go down. Ideally the stimulus should continue along the lateral border of the sole, and should be rather slow.

Judging the response

The normal and pathological responses to plantar stimulation are succinctly described by Babinski in his original communication (1896). "On the healthy side pricking of the sole provokes... flexion of the thigh on the pelvis, of the leg on the thigh, of the foot on the leg and of the toes upon the metartasus. On the paralysed side a similar excitation also results in flexion of the thigh on the pelvis, of the leg on the thigh, of the foot on the leg, but the toes, instead of flexing, execute a movement of extension upon the metatarsus".[6]

Types of Babinski Sign

a) Minimal Babinski Sign- Contraction of hamstring muscles and tensor faciae latae without recognizable toe movement.

b) Pseudo Babinski sign- This type of response may be encountered in sensitive individuals, plantar hyperaesthesia, choreo-athetosis due to hyperkinesis. True babinski can be clinically distinguished from the false babinski by the contraction of hamstring muscles in the former, and failure to inhibit the extensor response by pressure over the base of the great toe.

c) True Babinski sign- Fully developed extensor plantar response.

d) Inversion of plantar reflex- If the flexors tendons are severed accidentally or if the short flexors of the toe are paralysed, an extensor response may be obtained.

e) Exaggerated Babinski sign- Can be either in the form of 'flexor spasm' or extensor spasm depending upon the muscles involved i,e. whether flexors or extensors. Flexor spasms occur in spinal cord disease, multiple sclerosis and SCD of the cord, , bilateral UMN lesion at a supraspinal level, 'extensor spasm' occurs in patients with corticospinal tract lesion when the posterior column function is normal.[7]

f) Crossed extensor response/Bilateral babinski - Unilateral stimulation produces bilateral babinski in patients. Eg. Seen in bilateral cerebral disease and spinal cord disease.

g) Spontaneous Babinski - Seen in infants and children following manipulation of the foot. It is also seen in patients with extensive pyramidal tract diseases, passive extension of the knee or passive flexion of the hip and the knee, may produce a positive Babinski sign.

g) Tonic Babinski reflex - It is characterised by slow prolonged contraction of extensors of toe. It is seen in frontal lobe lesions and extrapyramidal involvement.

Interpretation of Plantar response

Three rules to interpretation of Babinski sign:

1) Upward movement of the great toe is pathological only if caused by contraction of the extensor hallucis longus muscle.

2) Contraction of the extensor hallucis longus muscle is pathological only if it occurs synchronously with reflex activity in other flexor muscles.

3) A true up-going toe sign is reproducible, unlike voluntary withdrawal of the toes.

Whilst as many as thirty other techniques for eliciting the same response have been described in the literature, none have been shown to be superior. However it is worth mentioning three variants that have endured may be encountered on neurology rounds:

1) Oppenheimer sign demonstrated by firmly stroking the medial tibial surface, 2) Gordon sign i,e. firm compression of the lower calf muscle 3) Chaddock sign which is stroking the skin beneath the lateral malleolus and observing the movement of toe simultaneously.[8]

Causes of an incorrectly interpreted positive Babinski sing

1) Isolated fanning of the toes- Although suggested by some to be an important feature of the Babinski sign, however, may be seen in healthy subjects and may not be seen in Babinski sign,so is of limited use.

2) Contraction of tibialis anterior -This causes the toes to go up passively due to ankle movement without contraction of EHL.

3) Very active flexion synergy- Following a brisk normal flexion synergy reflex including usual flexion of the toes, the observer sees the big toe return to its neutral position by going up, but this is caused by relaxation of the toe flexors rather than EHL contraction

4) Relative movement - The smaller toes go down, whilst the big toe remains immobile creating the illusion of an up-going toe.

Potentially Misleading Negative Babinski

1) Lower motor neuron lesions - Any cause of lower motor neuron dysfunction may mask a Babinski sign which would otherwise be present. For example pressure palsy of the common peroneal nerve which can occur in chronic parplegia can mask a Babinski sign.

2) Spinal shock -In acute spinal shock no response might be seen from plantar stimulation due to depressed activity of the segmental pathways which mediate the flexor synergy.

3) Joint deformity - Quite common, especially hallux valgus such that the joint can't go up, although EHL activation may be shown on EMG of these patients.

4) Incomplete pyramidal syndrome - If the fibres which innervate dorsiflexor muscles of the foot are not involved.

Myths Dispelled

1) The stimulus should be painful- This is incorrect, as the necessary intensity depends on the degree of disinhibition of the flexion reflex. In some patients a mere touch anywhere on the leg is sufficient.

2) In doubtful cases one should apply variants of the Babinski sign- Indeed the up-going toe sign can be elicited from many different sites at the foot or even the leg, but the physician (or student) should not be deterred by the variety of eponyms.

3) The movement should occur at the metatarsophalangealjoint- A more sensitive method than inspecting the joint is to concentrate on the tendon of the extensor

hallucis longus muscle,from which the movement originates. This tendon has its insertion at the terminal phalanx; it may tighten even without any visible displacement of the toe.

4) In doubtful cases the 'fan sign' is a useful measure- Fanning of the toes is of historical interest only. Babinski described this sign a few years after his discovery of the up-going toe sign, but he added that it may also occur in normal subjects.

Conclusion

In case of babinski sign the method of observation is much more important than the method of elicitation. Most important and vital question in interpreting the plantar response is not, whether the plantar goes up or not, but it is whether an upgoing toe is pathological or not.

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Duties of Doctors in Poisoning Cases

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Abstract

The article deals with the duties of a Registered Medical Practitioner in poisoning cases as to make the profession efficient as well as legal. One should have knowledge in offering immediate first aid i.e. having priority in life saving and thereafter the procedural criminal law should be allowed to operate in order to avoid negligent death. The doctor attending the patient has to fulfil his duties, first as a medical professional then as a medicolegal professional. The Attending Doctor cannot solely rely on the statement given by the patient or patient party regarding manner of poisoning. Hence, by going through mandatory medicolegal formalities, the doctor can, not only help himself but also the patient and the state.

Keywords: *Duty, Doctor, Poisoning, Criminal law, Medicolegal.*

Introduction

Poisoning, both accidental and intentional, is a significant contributor to mortality and morbidity throughout the world. Acute poisoning forms one of the commonest causes of emergency hospital admissions. According to World Health Organisation (WHO), 3 million acute poisoning cases with 220,000 deaths occur annually.[1] Of these 90% of fatal poisoning occur in developing countries particularly among agricultural workers. The exact incidence of poisoning in India is uncertain due to lack of data at central level as most cases are not reported and moreover mortality data is a poor indicator of incidence of poisoning. It has been estimated that about 5-6 people per lakh population die due to wrath of poisoning every year.[1] According to National Crime Record Bureau (2013), poisoning accounted for 27.9 % of all cases of suicidal deaths in India, out of which more than 50% of the cases are due to consumption of insecticides[2].

Pattern of poisoning in a region depends upon variety of factors such as availability of poisons, socio economic status, religious and cultural influences and availability of drugs. The commonest cause of poisoning in India and other developing countries is pesticides; the reasons being agriculture based economy, easy availability of highly toxic pesticides, unsafe practices, illiteracy, ignorance, lack of protective clothing etc. [1]

Role of Doctor (both clinical and legal)

As these cases of poisoning are brought to the nearest available hospital, so the doctors on duty should equip himself with the proper infrastructure and management skill in saving the life of these patients or after stabilizing them by giving them first aid.

A doctor attending a poisoning case has a dual role to play:–

1. Medical and

2. Medicolegal.

Though medical treatment in such cases is important but the legal duties cannot be undermined. In all such cases of poisoning what

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a registered medical practitioner should do both empirically as well as legally in managing such cases and following points must be kept in mind while treating these cases at clinic level or hospital.

1. Medical duty:

- The first and the foremost duty is the care and treatment of the patient. Without wasting any time the doctor should try to save the life of the patient by efficiently treating him.
- In emergencies, resuscitation and stabilization of the patient will be carried out first and medicolegal formalities may be completed subsequently. The consent for treatment is implied in all emergencies.
- Stoppage of further poisoning by isolating the patient to the hospital.
- A medical practitioner must be very cautious in giving his opinion about poisoning .On mere suspicion; he should never give a verbal or a written opinion until and unless he is sure about the case from
  - o Symptomatology
  - o The history of the patient
  - o Toxicological analysis and other investigation reports.[3]
- The attending doctor should always consult a senior physician in strict confidence for second opinion in all matters regarding diagnosis and treatment of a case. Use of Poison information services may also be made.[4]

2. Medicolegal duty:

- Doctors working in government hospitals are required to report every case of poisoning regardless of the nature, to the police.[3]
- If a case of poisoning is accidental or suicidal in nature, the attending doctor is under no legal obligation to notify the police in case he is working in a private hospital. But if the patient dies, the police have to be informed. Death certificate must not be issued. However, if a medical practitioner in private practice is convinced that the patient upon whom he is attending is suffering from homicidal poisoning he is bound under section 39 Criminal Procedure Code (CrPC) to communicate it to the nearest police officer or Magistrate. Non compliance is punishable under section 176 Indian Penal Code (IPC).[3]
- If the police require information on any case of poisoning which is either suicidal or homicidal in nature, the attending doctor has to divulge it. There is no scope for professional secrecy in such matters (175 CrPC).

  If information is withheld or wrong information is provided, the doctor becomes culpable under section 202 and 193 IPC respectively.[4]
- Every effort must be made by the attending doctor to collect and preserve evidence suggestive of poisoning. Deliberate omission to do so can attract punishment under section 201 IPC.[4]
- To collect vomitus, faeces, stomach washings, contaminated foods etc. and despatch the same for chemical analysis to the nearest Forensic science laboratory. Non compliance is punishable under section 201IPC.
- Each specimen when obtained from patient should be properly packed, sealed and labelled. The samples thus obtained by the doctor should directly be handed over to no other than the escorting police personal. Chain of custody of evidence should be maintained at any cost and it should not be damaged, contaminated or altered in any significant way.[4]
- Regarding sampling of specimen for toxicological analysis, the following should be done,[5]

1. Blood: - 5-10 ml to be collected from the vein using vacuum sampling tube containing

EDTA or Citrate as anticoagulant and Sodium fluoride as a preservative. If situation permit multiple samplings at different interval are desirable.

2. Urine: - Larger amount are preferable to be sampled with preservative such as sodium azide or sodium fluoride, at a concentration of 1 mg/ml.

3. Vomitus and Gastric lavage fluid: - It should be stored in amounts as large as possible with preservative such as sodium azide or sodium fluoride. The volume should be strictly recorded.

- The treating doctor/authorized nursing staff will only be permitted to administer food and medicines to the patient.[4]
- Any case of alleged snakebite to be observed for at least 24 hours before discharging. During the observation time the patient should be kept under electronic vitals monitoring.[6]
- If a poisoned patient is conscious but on the verge of death, it is mandatory to record a dying declaration relating to the circumstances. It is preferable to call a magistrate for the purpose, but if death appears imminent, or if there is likelihood of delay in the arrival of the magistrate, the attending doctor must himself record the declaration as per section 32, clause1 of the Indian Evidence Act (IEA). Even when a magistrate is available to note down the declaration, the presence of a doctor is desirable to certify that the dying victim was in compos mentis as clouding of judgement may be sometimes encountered in the victim in the final moments before death.[6]
- If a patient dies before the exact diagnosis could be made about, or he was brought dead to the hospital, the duty doctor must notify the police who will in all probability order an autopsy to be done. Death certificate should not be issued.[6]
- In suspected homicidal poisoning cases, the body should never be released for cremation without police intimation and postmortem examination.
- In case of autopsy, Death certificate should be issued only after obtaining chemical analysis report from Directorate of Forensic Sciences or Forensic Science Laboratory. But if it is deemed necessary to issue the death certificate prior to receipt of the chemical analysis report for any reason then in that case it should be given as "Opinion regarding cause of death is kept pending till receipt of chemical analysis report".
- It is compulsory to maintain written record of the case in meticulous detail as it is useful if the case is petitioned in the court of law for documentary evidence.[6]
- The indoor patient's record should be made and preserved for upto 3 yrs. If relative of patient seek record, it should be provided within 72 hrs.[7]
- In case of food poisoning originating from public eatery (canteen, cafe, hotel etc.), public health authorities must be notified without delay.[8]

Social Responsibility

One of the important rights of a Registered Medical Practitioner is the right to possess and dispense dangerous medicine or drugs. However, in this regard the doctor has the moral duty to handle the poison carefully. He should keep those drugs or poisons in a separate bottle, properly labelled preferably with red ink and kept in a separate shelf

If a doctor comes to know about suicidal tendency of a patient during treatment of the patient and suspects that the person may again try to commit suicide by

Poison or by any means then he should disclose the condition to the patient's guardians or relatives.

He can also involve actively in any public awareness campaign regarding any poison and its preventive measures.

Conclusion

The doctor in cases of poisoning should not refuse to treat the patient due to fear of legality. He should treat the patient efficiently and adhere to the other legal duties to avoid medicolegal complications. The way by which medicolegal issues are handled by a doctor has a profound impact on the public image .The administrative authorities must also help in maintaining goodwill and avoiding legal complications. By performing his duties, both clinical and legal, the doctor not only helps the patient but also helps himself by not omitting his duties and society at large.

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Short Communications

Attidues Scales - Made Easy

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Abstract

Attitude denotes the inner feeling or belief of a person towards a particular phenomenon. Attitude measurement becomes integral part of human research as it directly influences other measurement variables. The best possible approach to measure attitude is using well constructed and tested scales. The researchers are often facing difficulties in constructing good attitude scales. The following article discusses the types, construction and scoring of attitude scales in an attempt to facilitate the reader to construct an attitude scale with least difficulty.

Keywords: *Attitude scales, Likert Scale, Semantic Differential Scale, Thurstone scale*

Introduction

In medical, nursing and health care research, there is usually interest in measuring cognition, affect, and psychomotor skills and/or physical functioning. Affective measures seek to determine interests, values, and attitudes.

Self-report measures are the most direct approach to the determination of affect. In this type of measure subjects are asked directly what their attitudes, interests, or values are. For example, subjects might be given a list of favorable and unfavorable statements regarding particular issue and asked to agree or disagree with each. Such a self-report inventory is referred to as an attitude scale.

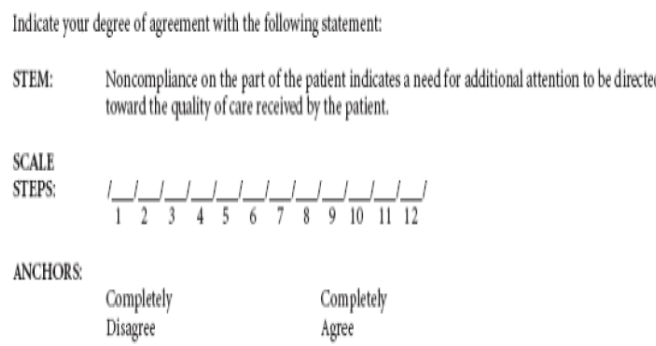
The researchers are often facing difficulties in constructing good attitude scales. The following article discusses the types, construction and scoring of attitude scales in an attempt to facilitate the reader to construct an attitude scale with least difficulty.

Methods of assessing attitude:

1. Direct Method: It is the best way to assess the attitude of the individual. It involves assessing the behaviour in natural setting and real life situation. This method is commonly applied in qualitative research.
2. Indirect Method: It is the method commonly adopted in research to assess attitude. It involves asking the individual directly how he feels about a subject through the use of questionnaire or interview. In this method, he is also asked to indicate his agreement or disagreement with a series of statements about a controversial subject.

General components of Attitude Scales:

1. A stem, which is a statement relating to attitudes or an attitudinal object to be rated by the respondent.
2. A series of scale steps.
3. Anchors that define the scale steps.


Indicate your degree of agreement with the following statement:

STEM: Noncompliance on the part of the patient indicates a need for additional attention to be directed toward the quality of care received by the patient.

SCALE STEPS: /__/__/__/__/__/__/__/__/__/__/__/__/
1 2 3 4 5 6 7 8 9 10 11 12

ANCHORS:
Completely Disagree — Completely Agree

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There are different types of anchors that can be employed: numbers, percentages, degrees of agreement/disagreement, adjectives (e.g., worthless / valuable), actual behavior, and products (e.g.,samples of nursing care plans to be rated 1 to 6). Usually numerical anchors are preferred.

Types of attitude scales:

A scale is an instrument which measures subjective variables. Each of these important scale types provides the means to gather subjective data objectively.

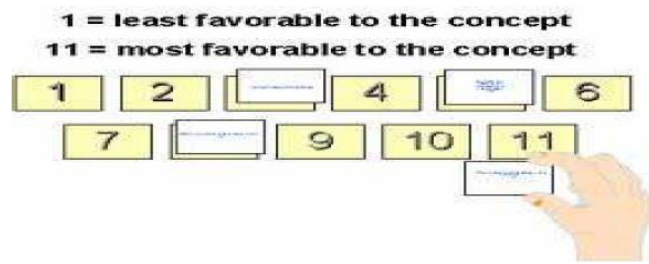
1. Differential scale-Thurstone scale.
2. Summated scales-Likert scale.
3. Cumulative scales-Guttman's scale.
4. Factor scales-Semantic Differential Scale and Multi Dimensional Scales.

Thurstone Scale

- Selection of items is made by a panel of judges who evaluate the items of relevancy and unambiguous in implication.
- Researcher collects a large number of statements usually twenty or more.
- The statements will be evaluated by panel of judges, each of whom asked to arrange the statements in 11 piles from most favourable to least favourable.
- The items which bring out a marked disagreement between the judges in assigning a position are discarded.
- Median value calculated, and any one statement is computed as median by all judges.
- All the items arranged in random order, and respondents are to state whether they agree or disagree to the item.
- The respondent is to give his reaction to each statement by endorsing or rejecting it. Median value of the statements that he endorses establishes the score.
- This scale is considered as most appropriate and reliable when used for measuring single attitude.

Limitation

Values assigned to the various statements by the judges may reflect their own attitude.



Summated scales (Likert type of scales)

A Likert scale consists of several declarative items that express a view point on a topic. Respondents are asked to indicate the degree to which they agree or disagree with the opinion expressed by the statement. Likert scales are developed using item analysis approach.

A particular item is evaluated on the basis of how well it discriminates between those whose total score is high and whose score is low.

Steps of construction of Likert scale

1. Collects a large number of statements about the topic based on representative of opinion held by a substantial number of people and referring adequate literature.
2. The statements express definite favourableness or unfavourableness to a particular point of view is retained. Neutral statements and the statements that everyone will agree or disagree will be discarded.
3. Determine the number of degrees (responses). The Likert scale usually contains five degrees (but at times 3 - 7 may also be used). i.e SA-

A-NEUTRAL -DA-SDA {I recommend that you use four or six levels of response. Many Likert scales have 5 levels, with a "no opinion" center. This neutral middle option allows subjects an easy way to avoid considering the statement.)

4. Trial test should be administered to a number of subjects (small group of people) to refine statement selected.

5. Select equal number of favourable and unfavourable statements are selected and arranged in random order.

6. Good Likert scale contains 5-20 items.

Administration of Likert scale:

1. Proper instruction should be given to the respondent. Respondent are asked to indicate the degree to which they agree or disagree with the opinions expressed.

Instructions :

Individuals may have difference of opinion in regard to sex education to adolescents. The following tool contains opinions of various people in the form of statements. These statements are neither right nor wrong. Kindly indicate your degree of agreement or disagreement after carefully reading the each statement below. Circle the letter which best describes your response to the statement. If you strongly disagree with the statement, circle SD. If you DISAGREE, circle D, AGREE, A, or STRONGLY AGREE, SA.

2. Never give any approval to the responses if interview method is adopted. Do not summarize the responses given by the respondents. Respondent may change his degree of agreement due to influence of the one item over another.

3. Strictly follow the order and wording of the questions.

4. Use response show card if you use more than 5 degrees during interview.

5. If neutral or undecided responses expressed, repeat the statement after all the statements are responded.

Scoring of Likert scale:

1. All favourable statements are scored from maximum to minimum as

SA	A	N	DA	SDA
5	4	3	2	1

2. All unfavourable statements are scored from minimum to maximum as

SA	A	N	DA	SDA
1	2	3	4	5

The total scores obtained on all the items measure a respondent's favourableness towards the subject in question.

Scoring :

Interpretation:

$$\frac{(\text{Maximum score} \times \text{Total No.of Items}) + (\text{Minimum score} \times \text{Total No.of Items})}{2}$$

For e.g..if 5 degree(SA-A-N-DA-SDA) Likert scale contains 20 items

$$\frac{(5 \times 20) + (1 \times 20)}{2} = 60$$

The total score is above 60= Positive/desirable/ favourable attitude

The total score is below 60 = Negative/undesirable/ unfavorable attitude

The total score is exactly 60=Neutral attitude

Hence the Likert type scales are summated scale, the score of individual item should not be taken in to account to decide the opinion/attitude.

Advantages of Likert Scale

1. It is relatively easy to construct in comparision of thurstone type of scale.

2. It is more reliable because the items included in the scale are the statements expressed by substantial number of people in their own words.

3. Likert scale is having good discriminating power.

4. Very easy to administer and assign scoring. It facilitates to have individual comparison.

Limitations of Likert scales

1. There is no basis for the belief that the five positions indicated on the scale are equally placed.

2. They answer to the items based on what they should feel rather than how they feel!

3. Responses may be inaccurate; the attitude will differ in the real life situations.

Semantic Differential Scales

Semantic Differential Scale consists of two opposite adjectives with a 7-point scale between them. Respondent is asked to rate a given concept by selecting one point on the scale that best describes his or her point of view. The adjectives commonly used such as effective/ineffective,good/ bad, or important/unimportant. The semantic differential is a method for measuring the meaning of concepts that was developed by Osgood, Suci, and Tannenbaum (1957).

Components:

The semantic differential has three components: (1) the concept to be rated in terms of its attitudinal properties, (2) bipolar adjectives that anchor the scale, and (3) a series of 5 to 9 scale steps(7 is the optimal number of steps suggested).

Logic underlying the semantic differential stems from the recognition that, in spoken and written language, characteristics of ideas and objects are communicated largely by adjectives. It is reasonable on this basis to assume that meaning often can be and usually is communicated by adjectives; it is also reasonable to assume that adjectives can be used to measure various facets of meaning.

Indicate your degree of agreement with each of the following statements:

a. Antagonistic behavior on the part of the patient indicates a need for additional attention and time from the nurse.

/_____/_____/_____/_____/_____/_____/
1 2 3 4 5 6

Completely Disagree — Completely Agree

b. Antagonistic patients receive more than their share of staff time and attention.

/_____/_____/_____/_____/_____/_____/
1 2 3 4 5 6

Completely Disagree — Completely Agree

Factor analytic studies of semantic differential scales have suggested that there are three major factors of meaning assessed by such scales: (1) evaluation, (2) potency, and (3) activity.

Scoring of Semantic differential Scale:

Scoring pattern similarly like Likert scale. Scores 1-7 are assigned to each bipolar scale response, which higher scores generally associated with positively worded adjective.

	Factor		
	Evaluation	Potency	Activity
BIPOLAR ADJECTIVES	good ..... bad fair ..... unfair positive ..... negative honest ..... dishonest successful ..... unsuccessful valuable ..... worthless	strong ..... weak large ..... small severe ..... lenient hard ..... soft	active ..... passive quick ..... slow tense ..... relaxed sharp ..... dull

Advantages:

1. Highly flexible and easy to construct.

2. It is very useful in evaluating several concepts such as person, place, situation, abstract idea, controversial issue and so forth.

Example of Semantic Differential Scale:

(Ph.D thesis submitted by Elizabeth Noela Emmanuel -reproduced with permission)

Instructions:

The purpose of this questionnaire is to measure what certain things mean to you. I am interested in what these ideas mean to you. There is no right or wrong answers. The page that follows has a different idea printed at the top followed by pairs of opposite words below it to describe each idea.

Each pair of opposite words is separated by seven spaces. We call these spaces scales. For your better understanding, please read the following example.. My home.

My Home

You are requested to respond to what the idea means to you on each of the scales below it. For example, taking the idea, "My Home", if to you its meaning is very closely related to 'neat' you would mark it this way :

Neat	X							Messy

Conclusion:

Attitude denotes the inner feeling or belief of a person towards a particular phenomenon. Attitude measurement becomes integral part of human research as it directly influences other measurement variables. The best possible approach to measure attitude is using well constructed and tested scales. Attitude scale measures subjective inner view or feeling in more objective way.

Neat	X							Messy

Myself as Mother

Successful								Unsuccessful
Unvilling								Willing
Tough								Fragile
Vigorous								Feeble
Dangerous								Safe
Complete								Incomplete

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'Competency Based Medical Education' – What's there to know about this?

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Of course we know all about (or at least quite a bit) about competencies! So where does this fit in among all the other jargon of Medical Education ?

Let us think about it for a minute. How is our MBBS course at present? We have four and a half years of 'studies' and one year of internship, at the end of which we expect our graduates to be a 'competent' doctor. But we all know that the time taken to achieve competence in any task varies from individual to individual, because people learn in different ways and at different speeds. Like any biologic variable only half of a group of 'normally distributed' medical students will achieve a level of competence within a given time frame. Consider on the other hand if we had a mechanism wherein a student has to demonstrate competence in specified tasks no matter what the time taken. With this objective in mind medical education can be tailored such that each student needs to be certified as competent in various tasks before they are perceived as being fit to advance to the next level of training and ultimately obtain the license to practice. So the duration of the course will be flexible (with a minimum defined duration) according to the time taken to achieve the specified competencies.

But what exactly is a competency? It could be defined as an ability that is observable. This ability could integrate multiple components like knowledge, skills, values and attitudes. Competence involves more than the mere possession of knowledge, skills and attitudes – it requires one to apply these abilities in the clinical setting, so as to achieve optimal results.

A clear definition of the expected competency is required. This is what is called a 'milestone'. A milestone is a significant point in the professional development of a medical trainee. A milestone would be the minimum competence required and acquisition of various competencies will enable both the trainee and the institution to know the trajectory of progress. The Dreyfus model, (Fig 1) is useful to assess the progress of the trainee. What is required for any patient is competence on the part of the treating doctor and a student has to necessarily demonstrate this before being licensed to practice.

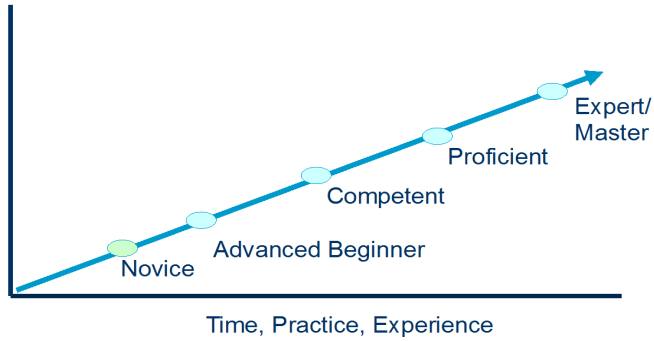

Fig 1 : The Dreyfus model

Competencies require enabling characteristics or descriptors to describe the components of the learning process necessary to achieve competence.

A competency-based curriculum is learner centered, because it requires the trainee to be an active learner and use whatever method of learning

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he/she prefers in order to achieve competence in the task. It is also more flexible and accountable. The focus is clearly on outcomes rather than content unlike traditional curricula. How to define competencies; identify the meaningful ones and how to ensure the performances are the critical issues involved. In the West competency based training is rather well established in many Residency (postgraduate) training programs. At an undergraduate level it is still not very commonly employed however. Yet another aspect to be kept in mind is that a gradual transition to a competency based medical education is likely to be successful rather than an abrupt change in the curriculum. It is important to involve the stakeholders' viz. the students and the faculty in a process of dialogue before implementation of a competency based medical education.

This also means that the teaching learning processes have to be restructured. Apart from the cognitive elements the student has to learn various skills. Large classroom teaching will play only a minor role and there will be greater emphasis on small group discussions and problem solving exercises, which facilitate active learning. At the end of all this, imagine that the faculty are told, "Don't tell us what you taught them" instead "Show us that you know what they can do!" In a nutshell this is what competence based education is all about.

My appeal to each one of you is to identify core competencies in your departments required by an undergraduate. Thereafter frame these competencies with adequate descriptors and choose the best teaching learning methods and assessment techniques. The required time frame for an average student to achieve competence should also be stated. Subsequently try to incorporate these competencies within our own curriculum at your Institute and assess the results of such a programme. Let us hope that we can take the initial step in this direction soon!

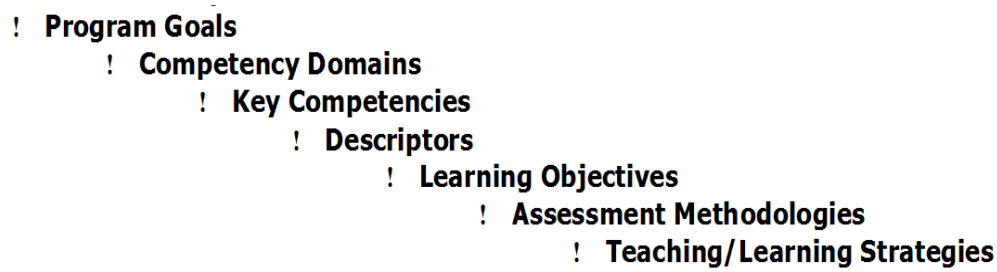

Fig 2 : Outline to develop a Competency Based Curriculum

Case Report

A Case of Gout Nodulosis: An Unusual Presentation of Gout

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Abstract

Gout is a common inflammatory arthritis associated with monosodium urate (MSU) crystal deposition in articular or periarticular tissues and renal tract. Gouty tophi are usually seen in chronic disease but may also present as the first sign of the disorder. Here, we report a patient with normal blood uric acid level who presented with an isolated tophi, at an unusual site, prior to any other manifestation of gout. We also emphasise the importance of fine needle aspiration cytology (FNAC) in the diagnosis of such presentation.

Keywords: *Gout nodulosis, FNAC*

Introduction

Gout is an inflammatory arthritis that results from deposition of MSU crystals in the synovial fluid and other tissues. It follows a typical clinical course and can be described in 4 stages: asymptomatic hyperuricemia, intermittent acute gout, intercritical gout, and advanced or chronic tophaceous gout.[1] Chronic tophaceous gout results in chronic arthritis with the formation of tophi.[2] Although gouty tophi are usually seen in chronic disease, it may occasionally occur as the initial manifestation of gout, in the absence of arthritis. This unusual presentation is referred to as gout nodulosis.[3] We report a case of thirty-year- old man who presented with tophi without any other manifestation of gout.

Case report:

A 30-year-old male presented to the OPD with a gradually increasing painless subcutaneous swelling in the left cheek of 3 months duration. There was no history of joint pain. The nodule measured 1cm in diameter, was firm, mobile, non-tender and the over lying skin appeared unremarkable (Figure 1). On laboratory examination, his serum uric acid level was 5 mg/dl. Random blood sugar level was 74 mg/dl. Serum levels of calcium, phosphate, albumin, electrolytes, urea, creatinine, lipid profile, thyroid profile were within normal limit. Radiographs of both the feet and the hands showed soft tissue swellings with no involvement of bones and ultrasound examination of the abdomen did not reveal any abnormality.

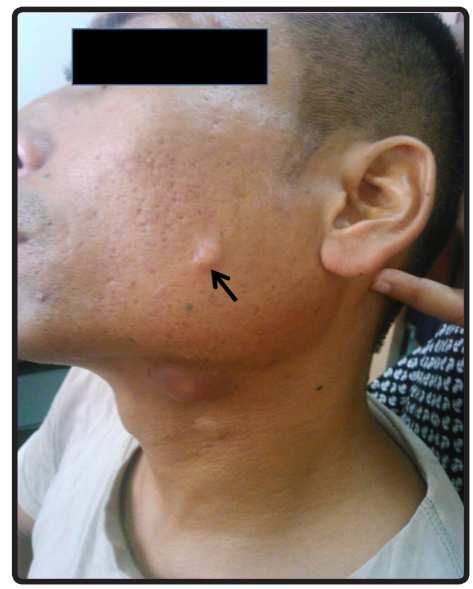

Figure 1 : Clinical Image of the nodule over the left cheek

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Fine needle aspiration was performed from the swelling using a 23 gauge needle. Gritty sensation was felt on needling and the procedure yielded whitish chalky material. Light microscopy of the May-Grunwald Giemsa stained smears demonstrated abundant granular amorphous material with scattered slender needle shaped crystals, along with chronic inflammatory infiltrate (Figure 2). Polarizing microscopic examination of the smear revealed negative birefringence needle shaped crystals, confirming the presence of MSU (Figure 3).

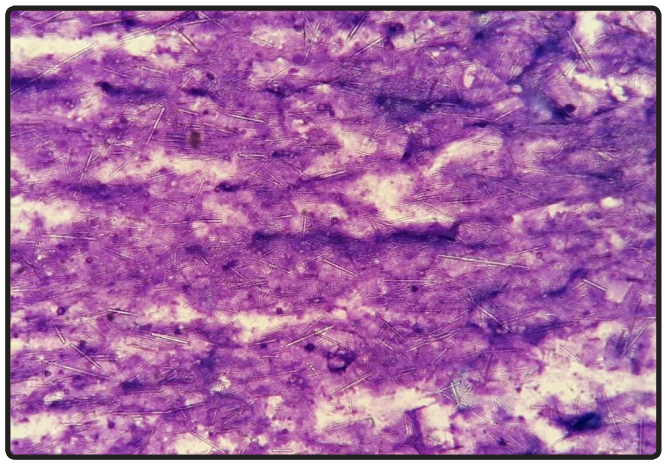

Figure 2 : Light microscopy microphotograph showing granular amorphous materials with scattered slender needle shaped crystals. (May Grunwald Giemsa stain, 10x)

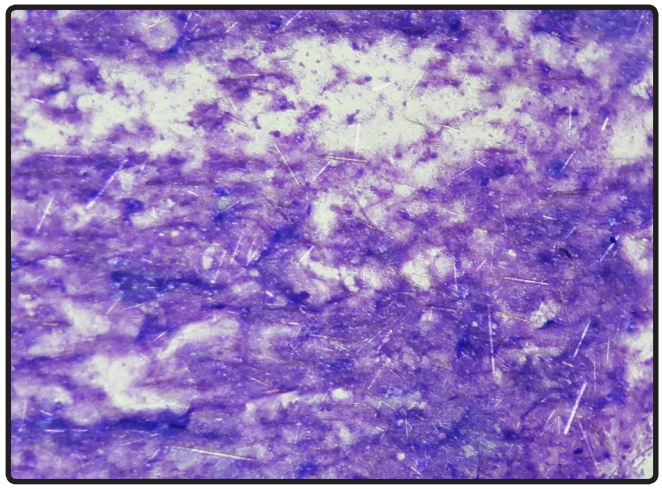

Figure 3: Polarising microscopic picture showing negatively birefringent needle shapped crystals suggestive of monosodium urate (May Grunwald Giemsa stain, 10x)

Discussion:

Gout is an increasingly common condition in both primary care and specialist practice. It is the most common inflammatory joint disease in men and the most common inflammatory arthritis in older women.[4] It is classically characterized by chronic hyperuricemia, recurrent attacks of acute arthritis provoked by the release of MSU into synovial spaces, and eventual development of tophi.[5] However, nearly half of the time, gout presents without hyperuricemia, and most people with raised uric acid levels never develop gout, limiting the diagnostic utility of measuring serum uric acid level.[6] Our patient had normal serum uric acid level at the time of diagnosis, and since the patient did not have any clinical feature suggestive of gout, the uric acid level was never estimated before.

Gout has traditionally been regarded as primary or secondary. Primary gout is caused by inborn defects of purine metabolism or by inherited defects of the renal tubular secretion of urate. Secondary gout is caused by acquired disorders that result in increased turnover of nucleic acids, by defects in renal excretion of uric acid salts, and by the effects of some drugs.[7]In 90% cases of primary gout, hyperuricemia results mostly from relative renal urate under-excretion, while in about 10% of subjects, hyperuricemia is due to endogenous overproduction of uric acid. Gout is also influenced significantly by dietary factors that include overeating, obesity, alcohol abuse, dyslipidemia, insulin resistance syndrome and widespread prescriptions of thiazide and loop diuretics.[8,9]

The diagnosis of gout can be made according to the American College of Rheumatology (ACR)/ Wallace criteria proposed in 1977 (Table 1). Demonstration of MSU crystals in the joint or tophi is considered as the gold standard for the diagnosis of gout. Pertaining to the changing spectrum of gout, this might often be difficult. The recent European League Against Rheumatism (EULAR) recommendations, emphasises that classic podagra and presence of tophi have the highest clinical diagnostic value.[8]

Table 1: American College of Rheumatology (ACR)/ Wallace criteria for diagnosis of gout

A	The presence of characteristic urate crystals in the joint fluid
	Or
B	A tophus proved to contain urate crystals by chemical means or polarized light microscopy
	Or
C	Six of the following 12 clinical criteria: a. Maximum inflammation within the first day b. More than one attack of acute arthritis c. Monoarticular arthritis d. Redness observed over joints e. First metatarsophalangeal joint pain attack f. Unilateral metatarsophalangeal joint attack g. Unilateral tarsal joint attack h. Suspected tophus i. Hyperuricaemia j. Asymmetric swelling within a joint on x-ray k. Subcortical cysts with no erosions on x-ray l. Negative bacterial culture of joint fluid

Gout follows a typical clinical course and can be described in 4 stages: asymptomatic hyperuricemia, intermittent acute gout, intercritical gout, and advanced or chronic tophaceous gout. It begins with years of asymptomatic hyperuricemia, followed by acute intermittent attacks which correlates with the degree of hyperuricemia. At serum urate level greater than approximately 6.8 mg/dl, the saturation point of urate in biological fluid is attained, resulting in the deposition of MSU crystals into the joints. Gouty attacks are thought to occur by the abrupt release of these crystals into the joint space, where they may initiate an acute inflammatory reaction.[10] The initial attacks are usually monoarticular, most commonly involving the metatarsophalangeal joint of the great toes(podagra), but may eventually become polyarticular. After each attack, long asymptomatic intervals may occur, which are referred to as the intercritical period. Eventually, the attacks becomes more frequent and results in chronic arthritis with the formation of tophi, or collections of MSU crystals that have served as the nidus of a granulomatous reaction. Tophi generally form in or close to joints or the pinna. However, several atypical locations of tophi have been described in literature including cutaneous tissue, head and neck including eye, and some visceral locations including pancreas and cardiac valves.[2]

Tophi may also occasionally occur as the initial and only manifestation of gout, in the absence of other features.[3] Referred to as gout nodulosis, patients with such presentation may have normal uric acid level. Our patient presented with an isolated tophi in the left cheek without any other manifestation of gout. In such cases, FNAC is an indispensable tool for diagnosis.[11] FNAC is a rapid, simple and cost effective technique. The demonstration of MSU crystal in FNAC smear under polarised microscope is superior to histopathology, in which the crystals may be lost during tissue processing.

We report this case to emphasise that gout nodulosis might be a warning sign for development of symptomatic gout in future, and the patient might require follow up for early diagnosis of the same. Notwithstanding the simplicity of the procedure, FNAC is an indispensable and a gold standard diagnostic tool in evaluation of such patients. To our knowledge, this is the second case of gout nodulosis, reported in India.

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Case Report

Delayed Hemolytic Transfusion Reaction (DHTR) due to Anti c (small) & Anti N: A case report

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Abstract

Delayed hemolytic transfusion reactions (DHTRs) may occur after alloimmunization to red blood cells (RBC) antigen(s) where there is an antigen mismatch between transfused RBCs and recipient RBC antibodies where sensitized RBCs are cleared by macrophages or complement activation leading to immunoglobulin G (IgG) mediated hemolysis. This usually occurs within few days to two weeks after administration of donor red cells although they were shown to be compatible in cross match tests by the antiglobulin technique. Delayed Hemolytic Transfusion Reaction is a condition which goes unnoticed resulting in significant morbidity and mortality if not managed promptly and properly.

KEY WORDS:

Delayed Hemolytic Transfusion Reaction, Pre transfusion testing, Irregular antibody, Packed Red Cells.

Introduction

Delayed Hemolytic Transfusion Reaction (DHTR) is most often the result of an anamnestic response in a patient who has previously been sensitized by transfusion, pregnancy, or transplant and in whom antibody is not detectable by standard pre-transfusion methods. Unexpected or unexplained decreases in hemoglobin or hematocrit values following transfusion should be investigated as a possible DHTR.[1] Many clinicians are aware of the immediate or acute transfusion reactions but frequently delayed reactions go unnoticed or may be misdiagnosed which could lead to inappropriate treatment.

Case Report:

A 42-year-old multiparous female patient who was diagnosed as a case of auto-immune hemolytic anemia (AIHA) in heart failure was referred to our Blood Bank from a private hospital in the city of Shillong with a request for Packed Red Cells (PRBC). There was history of transfusion of three units of Whole Blood two and a half months prior to the present referral. After this, the patient received three more units of Whole Blood and the patient was discharged with hemoglobin of 9.0 gm% fifteen days prior to the present referral. Following this the patient's hemoglobin deteriorated further to 3.2 gm% and no more compatible units could be found and thus was referred to our Blood Bank. In the pre-transfusion work up, antibody screening with inhouse prepared panel of 3 cells was performed which showed the presence of some irregular antibody. As the antibody screening was positive, antibody identification along with auto-control was performed with inhouse prepared 11 cell panel, which indicated the presence of multiple allo-antibodies with probability of anti c(small) & anti N. To confirm the identity of these allo-antibodies, PEG adsorption was performed using two sets of cells, (i) c(small) antigen positive, N antigen negative (c+N-) & (ii) c(small) antigen negative, N antigen positive (c-N+). This was followed by Cold Acid elution of the adsorbed cells. Antibody identification was further performed with inhouse

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prepared 11cell panel on the elutes of the two treated sets of cells. This indicated the presence of anti c(small) & anti N. Extended phenotyping using anti c (small) & anti N showed the patient's red cells did not possess the antigens c (small) & N. Thus, from the adsorption-elution tests & extended phenotyping, the presence of allo-antibodies anti c(small) & anti N are confirmed.

As the patient's red cells did not possess the antigens c (small) & N, either because of sensitization by (c+N+) fetal cells during her previous pregnancies or by the transfusion of (c+N+) red cells from amongst the first three units she received, allo-antibodies anti c(small) & anti N were formed. The allo-antibodies thus formed led to the destruction of (c+N+) red cells in the subsequent transfusions which she received two months later further reducing her hemoglobin level from 9 gm% to 3.2 gm% with rise in bilirubin, inspite of the transfusion of 6 units of whole blood. The diagnosis of AIHA (Auto Immune Hemolytic Anemia) made in the hospital where she was admitted could have been concluded because of positivity of DAT (Direct Antiglobulin Test). They could not find any further compatible unit and was referred to our Blood Bank. As she received 3 units of whole blood at the time of second admission where her Hb had dropped to 3.2 gm%, there was probably volume overload which caused her to go into failure. Three units of c(small) & N negative Packed Red Cells (PRBC) were issued to this patient from our Blood Bank. The hemoglobin level measured 72 hours after the third unit was 9.2 gm%. Thus, correctly phenotype matched PRBC helped in improving the condition of the patient.

Discussion:

Blood is considered a drug and a Blood Bank functions as per the guidelines laid down by the Drugs & Cosmetics Act 1946. When used judiciously it is a life saving intervention but if used inappropriately, can be a hazard.[1] There are many adverse effects associated with transfusion of Blood & Blood Components of which Delayed Hemolytic Transfusion Reactions (DHTR) is one challenge we are often facing. Two different types of DHTR have been identified - Primary allo-immunization & Secondary (anamnestic) response to transfused RBCs. In DHTR caused by primary allo-immunization, the patient has no past history of pregnancy, transfusion, or transplant. In DHTR caused by a secondary response, about 3 to 7 days from time of transfusion are needed for enough antibody to be produced by the patient to cause clinical signs and symptoms of extra vascular RBC hemolysis.[2]

Many clinicians are well aware of the Immediate Transfusion Reactions like allergic reactions, Immediate Hemolytic Transfusion Reactions (IHTR) due to ABO mismatches, Febrile Non-Hemolytic Transfusion Reaction (FNHTR), etc. but DHTR usually go unnoticed or are misdiagnosed and the line of treatment of such a condition goes in a different direction.[3] Thus, it is very important for the Blood Bank & the clinicians to coordinate and establish the diagnosis of DHTR so that only phenotype matched blood is transfused.

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Case Report

Hypothyroid with IgA Nephropathy: A Rare Association

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Abstract

Varieties of renal dysfunction may coexist with thyroid disorders. Association of hypothyroid with different glomerular diseases although well documented is rare. Most frequently reported glomerular disease with hypothyroid is membranous glomerulopathy with nephrotic syndrome followed by IgA nephropathy and membranoproliferative glomerulonephritis. Coexistence of the two pathologic conditions could be explained by a common autoimmune pathogenesis.

KEY WORDS: *Hypothyroid, IgA nephropathy, Nephrotic syndrome*

Introduction

Disturbance of renal function is known to occur in hypothyroidism. The most common renal manifestations of thyroid diseases are: rise of serum creatinine, reduction in glomerular filtration rate (GFR) and renal plasma flow (RPF), disruption of capacity to excrete free water and hyponatremia.[1] Association of different immune mediated glomerular diseases with different thyroid diseases like hypothyroid, Hashimoto's thyroiditis, and Graves' disease are very well documented in a few case series in literature. Membranous glomerulonephritis is the most common form of glomerulonephritis encountered with thyroid disease followed by sporadic case reports of IgA nephropathy, minimal change disease and membranoproliferative glomerulonephritis.[2, 3] We are reporting a case of hypothyroid with biopsy proven IgA nephropathy that was treated successfully with medical management.

Case report:

A 22- year- young girl presented to us with the complaints of generalised swelling of the body for one month followed by easy fatigability, weakness and palpitation. The swelling started in the legs with early morning puffiness and then gradually involved the whole body over the time period. At presentation, patient had mild periorbital swelling with peripheral pitting oedema with pulse rate of 62/minute and blood pressure of 160/100 mmHg. Systemic examination was normal. There were no bruits and thyroid examination was normal. Blood tests revealed Hb 11gm/dl, WBC 7400/mm3, ESR 38 mm at 1 hr, blood glucose 110 mg/dl, blood urea 38 mg/dl, serum creatinine 1.0 mg/dl, normal liver function tests and serum electrolytes. Urine analysis showed specific gravity of 1.012, PH 6.5, protein 4+, RBC nil and WBC 2-3/high power field. Subsequently, 24 hours urine showed 3341.6 mg of protein. Her viral serology including HIV test and anti-nuclear antibody (ANA) tests were negative. ASO titre was negative and coagulation profile was normal. Thyroid function test showed free T3 of 2.69 (2.5-3.9 pg/ml), free T4 of 1.04 (0.61-1.12 ng/ml) and TSH of 11.89 µIU/ml. Ultrasonography

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abdomen revealed two kidneys of normal size. Fasting lipid profile showed mixed lipidemia with total cholesterol 227 mg/dl, triglyceride 216 mg/dl, HDL 42 mg/dl and LDL 146 mg/dl. Electrocardiography, 2D Echocardiography, Chest X-Ray and ultrasound thyroid gland showed normal study.

Subsequently, a renal biopsy was performed that showed sclerosed glomeruli with increased mesangial matrix and thickening of the capillary basement membrane. Tubules showed evidence of protein resorption along with areas of atrophy. Interstitium is widened due to fibrosis and chronic inflammatory cell infiltrates consisting of lymphocytes and foamy histiocytes(Figure 1). Vessels showed medial wall hypertrophy. Immunofluorescence microscopy showed IgA (3+), IgM (1+), IgG (negative), C3 (negative), Kappa (1+) and Lambda (2+).

A diagnosis of IgA nephropathy with nephrotic syndrome associated with hypothyroidism was made and she was started with prednisolone, thyroxine, diuretics, ACE-I and atorvastatin. Patient responded to treatment very well without any side effects. On follow up visits she had clinical response as there was decrease in oedema with normalisation of her blood pressure. Her 24 hours urinary protein excretion was reduced to 713.1 mg and TSH to 0.48 at the end of 6 months.

Discussion:

42 million people are suffering from thyroid disorders in India and the majority of cases belong to hypothyroid, affecting one in ten adults.[4] Thyroid hormone affects nearly every organ system in the body. Hypothyroid is associated with different autoimmune diseases. Renal involvement in hypothyroid is multifactorial, varies from rise in serum creatinine, reduction in GFR, hyponatremia

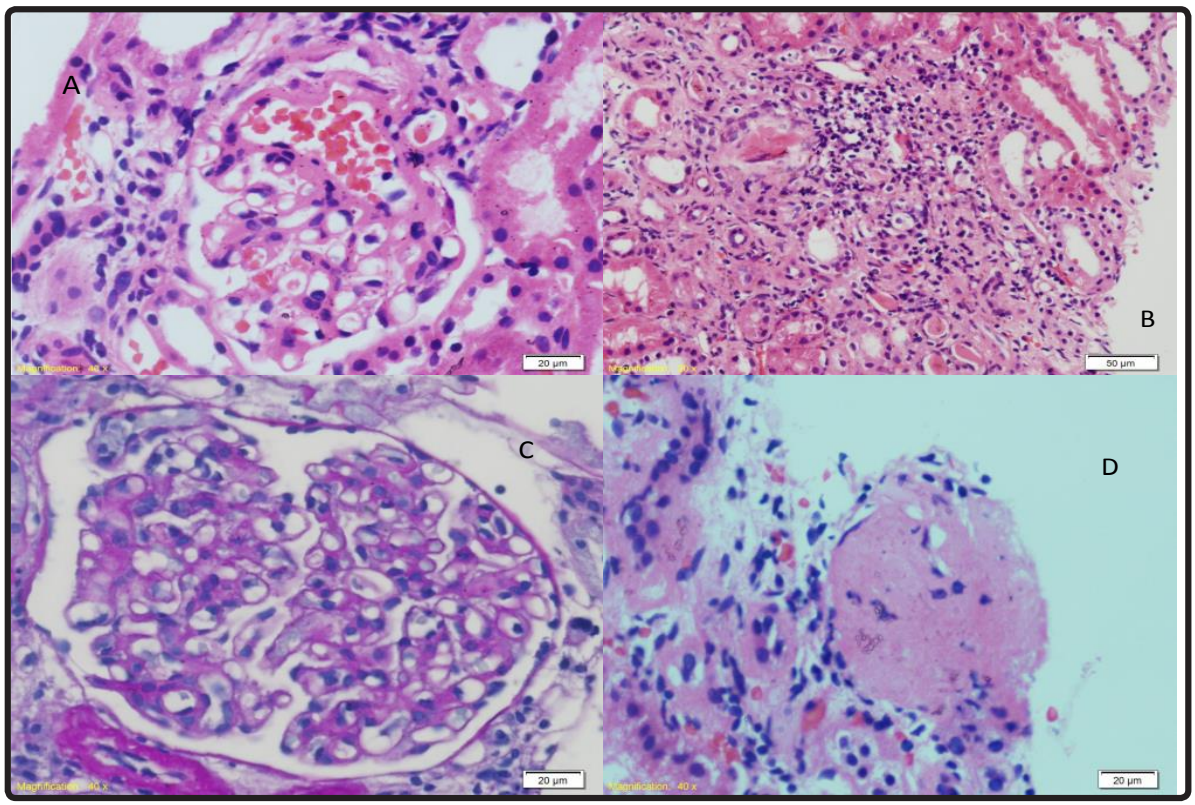

Figure 1 : IgA Nephropathy showing **A** endocapillary thickening of the basement membrance (H&E) ; **B** Interstitial inflammatory cells infiltration with atrophied tubules (H&E) ; **C** PAS stain showing basement membrance thickening; **D** Sclerosed glomerulie (H&E)

to glomerulonephritis and chronic kidney disease. Association of different types of glomerulonephriris with hypothyroidism is although very well documented in literature but is rare. Membranous glomerulonephritis with nephrotic syndrome is the most frequently encountered glomerulonephrities with thyroid disorders.[5] However there are sporadic cases of IgA nephropathy, minimal change disease and membranoproliferative glomerulonephritis associated with thyroid disease.[6] The presentation may vary from proteinuria with nephrotic syndrome to severe uraemia or pulmonary edema. Different mechanisms have been hypothesized for the association of thyroid and renal involvement. The mostly accepted theory is autoimmune for the following reasons: 1) the association of kidney and thyroid diseases of autoimmune origin, 2) its association with other autoimmune diseases like type I Diabetes Mellitus, and 3) the presence of deposits of immunoglobulins and thyroglobulin in the glomeruli of some patients. Patients with nephrotic syndrome have urinary losses of thyroid hormone binding proteins such as thyroxin binding globulin, transthyretin or prealbumin and albumin. This can result in a reduction in serum total thyroxin (T4) and sometimes, in total T3 levels. However, patients often remain euthyroid, because free T4 and T3 levels are usually normal. This suggests that thyroid is able to compensate for hormonal urinary losses, although some of them may develop clinical hypothyroidism specially those who are having low thyroid reserve. Similarly, patients with nephrotic syndrome who are on exogenous thyroid hormone replacement may need an increase dose to maintain euthyroid status.

Conclusion:

In conclusion, hypothyroid may be associated with different types of nephrotic syndrome. In a patient with nephrotic syndrome or with thyroid dysfunction, a thorough history taking, laboratory examinations and even pathological studies are necessary to resolve another coexisting disease as potential aggravating factor.

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Case Report

Synchronous tumors of prostate and urinary bladder: An uncommon entity

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Abstract

Synchronous tumors are neoplasms appearing at the same time and are not a common occurrence. Most of the synchronous urothelial tumors described has been prostatic and kidney cancers. Here we describe a case of synchronous tumors of adenocarcinoma prostate and urothelial carcinoma urinary bladder in a 50 –year-old male. The patient in the study was a decade younger than average age of presentation and already had metastasis of the tumor to lungs. Chronic smoking and beetle nut chewing may have been the causative etiology. Only a conservative management could be provided as patient already had metastasis.

KEY WORDS: *Synchronous tumors, neoplasm, metastasis, urothelial carcinoma, adenocarcinoma prostate*.

Introduction

Synchronous tumors are not a frequent presentation of malignancies. Koyama et al reported that among synchronous urological tumors, prostate and kidney cancer have more common association as compared to other synchronous urothelial malignancies.[1] We report a case of synchronous tumors of adenocarcinoma prostate and urothelial carcinoma urinary bladder in a 50-year-old male

Case report:

A 50- year-old male presented with pain in the lower abdomen along with intermittent burning micturition, progressive difficulty in passing urine,increased frequency of micturition, urgency to pass urine and passage of narrow urine flow since 4 months.The symptoms progressed and following acute retention of urine,patient was admitted in a private hospital where a supra-pubic cystostomy was done to relieve the retention, before being referred to our hospital.In personal history,patient was a chronic smoker and regularly chewed beetle nut.

On general examination, patient had pallor. Contrast Enhanced Computed Tomography(CECT) of the kidney-ureter-bladder showed an enhancing intraluminal mass lesion arising from the postero-lateral aspect of the bladder measuring 3.2x2.5 cm along with irregular and thickened wall. Prostate was mildly enlarged with foci of calcification. Radiological examination of the lungs showed multiple nodules on the right side along with pleural effusion. On cystoscopic examination, a mass in prostatic urethra was seen measuring 1.8x1.5cm which almost had occluded the lumen. A solid looking erythematous mass was seen in the lateral aspect of the urinary bladder measuring 5x7cm. The serum prostatic specific antigen(PSA) of the patient was found to be 18.46ng/dl. Biopsy from the urinary bladder showed features consistent with high grade urothelial carcinoma. A trans-urethral ultra-sound guided biopsy of the prostate was done which yielded multiple linear cores measuring 1cm each.

Histopathological examination of the specimen showed features consistent with high

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grade adenocarcinoma of prostate (Gleason score=4+4=8). In order to confirm that the tumors were synchronous tumors, Immunohistochemistry using anti- PSA antibody was done on both the specimens. Tumor from the prostate was positive whereas the bladder tumor was not, confirming that the tumors were synchronous. As the patient already had metastatic foci, he was managed conservatively with prophylactic bilateral orchidectomy. (Fig. 1 - 4)

Discussions :

The word synchronous tumors refer to neoplasms appearing at the same time and are synonymous to the word simultaneous tumors. In western male population, prostate cancer is the most prevalent cancer and the second leading cause of death.[2] Adenocarcinomas constitutes over 90% of prostate cancers.[3] Bladder cancer on the other hand is fourth most prevalent tumor in western population.[4] Urothelial or transitional carcinomas

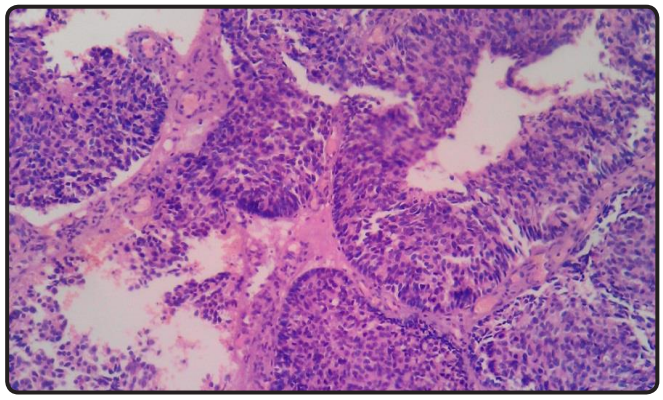

Fig. 1:Microscopic examination shows multiple fragments consisting of transitional cell carcinoma forming papillary projections

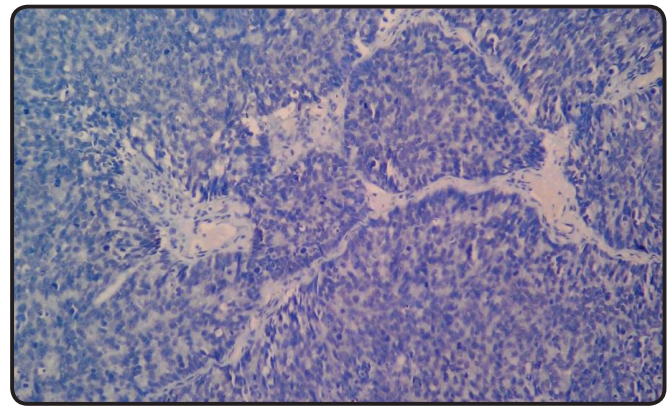

Fig. 2: Negative PSA study of Fig No. 1

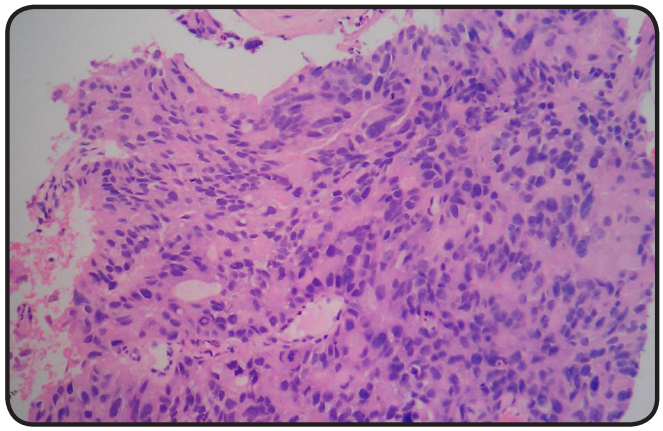

Fig. 3 : Microscopic examination shows malignant cells with few interspersed glands

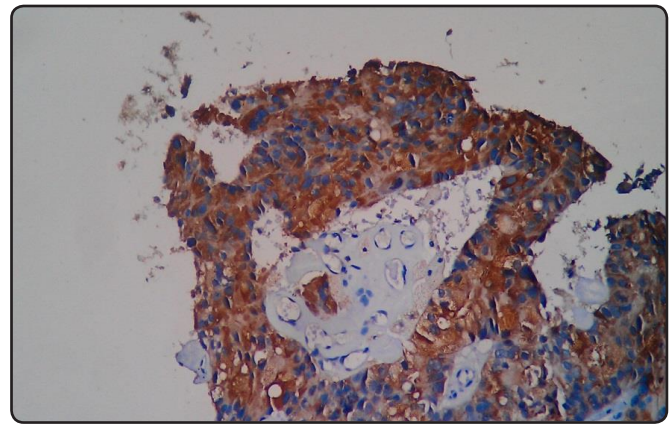

Fig. 4: PSA positivity in Fig No. 3

constitute 90% of the bladder tumors.[5] Various etiopathogenesis has been hypothesized about synchronous urothelial tumors. One hypothesizes that synchronous urothelial tumors occur as the genitourinary region is under the influence of the same carcinogenic stimuli. Yet another hypothesizes that the first malignant tumor affects the adjacent environment, predisposing to the development of second malignancies.[6]

The mean age of prostate cancer is 65-years and its incidence increases exponentially with each decade of age.[7] Senility may play a role in its pathogenesis. Most bladder cancers occur after 50 years of age. The factors favoring the aetiopathogensis present in this case were smoking and beetle nut chewing. As cigarette smoke is known to cause changes in genome, perhaps it had initiated carcinogenesis in the transitional epithelium. Bladder cancer is a disease recognized for molecular alterations.[5] In this case it was important to establish the primary nature of both tumors and to exclude invasion of the prostate with poorly differentiated urothelial carcinoma. Differentiation of two types of malignant tumors is imperative, as therapy for these two conditions differ. In a synchronous tumor with both prostate and bladder location, in the absence of glandular differentiation in the prostate, immunohistochemistry is recommended.8 One of the markers useful in highlighting prostatic origin of poorly differentiated tumor is PSA.[7, 8]

A study done by Abbas F et al to find the incidence of prostatic adenocarcinoma in patients undergoing radical cysto-prostatectomy for bladder cancer, had reported a prevalence of 27–46% whereas a much lower prevalence,10 of 248 bladder cancer patients (4.03%), was reported by Lee S H et al.[9,10]

Lee S H et al found one adenocarcinoma to have seminal vesicle invasion and another showed seminal vesicle with bladder invasion with a high Gleason pattern,serum PSA values of which were 1.55ng/mL and 2.09ng/mLrespectively. The rest of 8 cases were confined to the organ.10 But no significant correlation between preoperative prostate-specific antigen level and the presence of adenocarcinoma was found by Saad et al.[11] Lee S H et al also found cystoprostatectomy procedure to be an entirely adequate treatment modality for almost all patients in their study, with only 2 of them (0.8%) requiring further treatment for their prostate cancer.10 Most prostate cancer patients were beyond 60 years of age in the respective studies done by Lee S H et al and Hiros M et al.[10,12]

In our case, the patient was younger than 60 years and associated with high serum PSA level. Unfortunately the tumor already had metastasized, so the patient was managed only conservatively.

Conclusion :

We recommend digital rectal examination (DRE) and serum PSA assessment to be undertaken as part of the routine procedure for male bladder cancer patients aged 60 years and older. Bladder cancer patients presenting with an abnormal DRE, elevated serum PSA or a free PSA less than 15% should under go a prostate needle biopsy to rule out prostate cancer. If organ-confined prostate cancer is found and if the prostate is completely excised at cystoprostatectomy, perhaps no additional therapy would be required and that it should merely be specified that such patients should be followed with periodic PSA. Further studies with large sample sizes and long follow-up periods are needed to be carried out to establish more extensive and definitive guidelines for the management of these synchronous tumor patients.

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