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Editorial

Phage Therapy - a Hope for Future !

Prof. Dr. Parimal Chandra Sarker

Bacteriophages also known as phages are a form of viruses can infect bacterial cell. They attach to bacterial and inject a their (viral) genome into them. The bacterial cell getting infection and unable to reproduce, and instead produces additional phages.[1] Phages are very selective in the strains of bacteria they are effective against.[2]

During in the year 1896 Ernest Hanbury Hankin reported that something in the waters of the Ganges and Yamuna rivers in India had a marked antibacterial action against cholera . They also reported that these agents could pass through a very fine porcelain filter.[3] After that in 1915, British bacteriologist Frederick Twort, superintendent of the Brown Institution of London, discovered a small agent that infected and killed bacteria. He believed the agent must be one of the following: a stage in the life cycle of the bacteria ,an enzyme produced by the bacteria themselves, or a virus that grew on and destroyed the bacteria. Unfortunately Twort's research was interrupted by the onset of World War I, as well as a shortage of funding and the discoveries of antibiotics.[4]

Another researcher, French-Canadian microbiologist Félix d'Hérelle, working at the Pasteur Institute in Paris, announced on 3 September 1917, that he had discovered "an invisible, antagonistic microbe of the dysentery bacillus". For d'Hérelle, there was no question as to the nature of his discovery: "In a flash I had understood: what caused my clear spots was in fact an invisible microbe… a virus parasitic on bacteria. D'Hérelle called the virus a bacteriophage, a bacteria-eater (from the Greek phagein meaning "to devour"). He also recorded a dramatic account of a man suffering from dysentery who was restored to good health by the bacteriophages. It was D'Herelle who conducted much research into bacteriophages and introduced the concept of phage therapy.[5]

Later on Phages have been used since the late 20th century as an alternative to antibiotics in the former Soviet Union and Central Europe, as well as in France.[6] They are seen as a possible therapy against multi-drug-resistant strains of many bacteria. Phages are known to interact with the immune system both indirectly via bacterial expression of phage-encoded proteins and directly by influencing innate immunity and bacterial clearance.[7]

Phages are often compared to antibiotics.8 Phages tend to be more successful than antibiotics where there is a biofilm covered by a polysaccharide layer, which antibiotics typically cannot penetrate. Bacteriophages are much more specific than antibiotics. They are typically harmless not only to the host organism but also to other beneficial bacteria, such as the gut microbiota, reducing the chances of opportunistic infections.[8] They have a high

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therapeutic index, that is, phage therapy would be expected to give rise to few side effects, even at higher-than-therapeutic levels. Because phages replicate in vivo (in cells of living organism), a smaller effective dose can be used.[9]

The simplest method of phage treatment involves collecting local samples of water likely to contain high quantities of bacteria and bacteriophages, for example effluent outlets, sewage and other sources.[10] The samples are taken and applied to the bacteria that are to be destroyed which have been cultured on growth medium. If the bacteria die, as usually happens, the mixture is centrifuged; the phages collect on the top of the mixture and can be drawn off.The phage solutions are then tested to see which ones show growth suppression effects (lysogeny) or destruction (lysis) of the target bacteria. The phage showing lysis is then amplified on cultures of the target bacteria, passed through a filter to remove all but the phages, then distributed.[11]

Phages in practice are applied orally, topically on infected wounds or spread onto surfaces, or used during surgical procedures. Injection is rarely used, avoiding any risks of trace chemical contaminants that may be present from the bacteria amplification stage, and recognizing that the immune system naturally fights against viruses introduced into the bloodstream or lymphatic system.[12]

Individualised phage therapy was successfully used by Robert T. Schooley and others to treat a case of multi-drug-resistant Acinetobacter baumannii in the U.S. in 2015. Reviews of phage therapy indicate that more clinical and microbiological research is needed to meet current standards.[13]

Many clinical trials were completed since 2007 different bacterial agents like Psaudomonas aeruginosa , Staphylococcus aureus and Escherichia coli (E. coli). In July 2020, the FDA approved the first clinical trial of nebulized phage therapy in the United States. This double blind, placebo controlled study at Yale University will be focused on treating Pseudomonas aeruginosa infections in those with Cystic Fibrosis.[14]

Attention should taken to overcome of different obstacles to established an alternative option (Phage therapy) against different bacteria including MDR bacteria also. The need for banks of phages and regulatory testing for their quality and safety. Try to overcome the negative public perception of viruses may also play a role in the reluctance to embrace phage therapy.

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Original Article

Association between Thyroid Function and Metabolic Syndrome among Healthy Young Female.

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ABSTRACT:

BACKGROUND: *Thyroid hormone has been affects the many metabolic process. Thyroid dysfunction, metabolic syndrome and dyslipidemia are the high-risk factors for cardiovascular diseases.* ***OBJECTIVE:*** *To assess the association between thyroid function status and metabolic syndrome among healthy young female.* ***METHODS:*** *This cross-sectional study was carried out in the Department of Biochemistry at Bangabandhu Sheikh Mujib Medical University, Dhaka. All young female were selected as study population for these analysis after fulfil inclusion criteria. According to definition by the IDF panel, the diagnostic criteria for the metabolic syndrome include central obesity (defined as waist circumference ≥ 94 cm in men or ≥ 80 cm in female with 2 of the following: blood triglyceride (TG) ≥ 1.7 mmol/dl (150mg/dl) and blood HDL-C <50 mg/dl at (18-25) years of age were included for this study. Student's t test performed with the help of software-SPSS version 15.0 windows.* ***RESULT:*** *Total 200 participants among them 28% had metabolic syndrome and 72% had non-metabolic syndrome. Mean ± SD of BMI in metabolic syndrome group, is 29.40 ± 4.46 whereas in non-metabolic syndrome group, is 27.63 ±4.33 (p value = 0.011). Mean ± SD of waist circumference in metabolic syndrome group, is 93.18 ± 10.69 meanwhile in non-metabolic group, is 85.49 ± 9.39 (p value = <0.001). Mean ± SD of TSH in metabolic group, is 3.07 ± 2.24 on contrary in non-metabolic group, is 2.48 ± 1.33 (p value = 0.023). Serum TSH level is increased in metabolic syndrome than in non-metabolic syndrome group. In metabolic syndrome 73.2% had euthyroid followed by 7.1% overt hypothyroidism 16.1% had subclinical hypothyroidism and 3.6 % subclinical hyperthyroidism. In non-metabolic syndrome 96.5 % euthyroid followed by 2.8%subclical hypothyroidism and 0.7% subclinical hyperthyroidism.* ***CONCLUSION:*** *Our study showed significant associated thyroid disorder with metabolic syndrome among healthy young female.*

Key word: Thyroid function, Metabolic syndrome, Young female.

INTRODUCTION:

In clinical practice, frequently we observed patients with both thyroid dysfunction and metabolic syndrome. More than 20% of adult people fulfilled the criteria of metabolic syndrome in different study population.[1-4] In recent years worldwide increases the prevalence of obesity and metabolic syndrome.[5] Metabolic syndrome ,comprises a cluster of metabolic abnormalities that are characterized by central obesity, high triglycerides (TGs), low high density lipoprotein cholesterol (HDL-C) , hypertension and hyperglycemia ,has been used to identify individuals at high risk of cardiovascular disease (CVD).[6-7] Patients with metabolic syndrome have 12%-17% increased for cardiovascular disease, 6%-7% for all- cause mortality and 30%-52% diabetes.[8] In recent years,

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the incidence of rates of nutritional metabolic diseases such as obesity, hypertension , and diabetes increased due to development of social economy.[9] Economic development , improvement of living standards, dietary and lifestyle changes and decrease physical activities all are play key role in this process.[10] Thyroid hormone plays specific effects that influence the body adiposity ,glucose or lipid levels and blood pressure.[11-14] Thyroid dysfunction and metabolic syndrome both are associated with cardiovascular diseases.[15-17] some studies found that subjects with hypothyroidism and subclinical hypothyroidism had an increased risk of metabolic syndrome.[18,19] The upper limit of TSH (2.5-4.5 mU/L) had increased rates of obesity, increased TG levels, and increased metabolic syndrome.[20] TSH levels >2.5 mU/L should be assessed for the presence of metabolic syndrome in young healthy women[21] but other studies did not show any significant association between high TSH levels and metabolic syndrome.[22,23] Thyroid dysfunction affects lipid and glucose metabolism, body weight and blood pressure. These metabolic parameters are associated with components of metabolic syndrome.[24] This cross- sectional study investigated the association between thyroid dysfunction and metabolic syndrome in young healthy female.

METHODS:

This cross-sectional study was carried out in the Department of Biochemistry at Bangabandhu Sheikh Mujib Medical University, Dhaka. All young healthy female subjects (18-25) years were selected as study population. Written consents were obtained, and the institutional review board and ethic committee of Bangabandhu Sheikh Mujib Medical University Bangabandhu Sheikh Mujib Medical University approved this study.

MEASUREMENTS:

Anthropometric and biochemical parameters:
TSH, FT3 and FT4 were performed by using Micro particle enzyme immunoassay (Axsym system, Abbott Co.Ltd.) according to manufacturer's instructions.

Lipid profile:

Estimation of serum fasting TG by enzymatic (GPO-PAP) method (Bucolo & David 1973), TC by CHOL method (Siemens Healthcare Diagnostics Inc.2008) and serum HDL Cholesterol by Homogenous/Direct method (Lin et al 1998). For those low-density lipoprotein cholesterol (LDL-C) was calculated with Friedewald equation .[25]

Body mass index: This value was calculated as (Weight in kg/Height in m^2).

Statistical Analysis:

Data were collected using a preformed data collection sheet. Collected data were checked processed and analyzed with the help of software-SPSS (Statistical package for windows version 15.0.The result were expressed as mean ± SD (standard Deviation) and proportion. Probability value <0.05 was considered as level of significance. Student's t test has been performed to see the association between quantitative variables. The summarized data was interpreted accordingly and was then presented in the form of tables.

RESULTS:

A total of 200 subjects are classified into metabolic and non-metabolic group according to definition by the IDF panel, among them 56 (28%) had metabolic syndrome and 144 (72%) had non-metabolic syndrome (Table I).

Table I: Metabolic syndrome among study subjects (N=200)

Metabolic syndrome	Frequency (n)	Percentage (%)
Metabolic	56	28.0
Non-metabolic	144	72.0
Total	200	100.0

Table II: Age and clinical parameters of the patients with and without metabolic syndrome (N=200)

Metabolic status	Metabolic syndrome	Non metabolic syndrome	p-value
Age (years)	21.34 ± 1.89	21.06 ± 2.04	0.369
BMI (kg/m2)	29.40 ± 4.46	27.63 ± 4.33	0.011
Waist circumference (cm)	93.18 ± 10.69	85.49 ± 9.39	<0.001
Hip circumference (cm)	105.54 ± 11.84	98.91 ± 10.67	<0.001
SBP (mmHg)	112.05 ± 9.33	108.63 ± 8.98	0.017
DBP (mmHg)	59.55 ± 4.29	56.84 ± 5.08	0.001

Unpaired t test was done to see the level of conception.

Table no II Central obesity (waist circumference) and hip circumference was significantly higher in metabolic syndrome than in non-metabolic syndrome (p value = < 0.001).

Table III: Association of thyroid hormone with metabolic syndrome and non-metabolic syndrome. (N=200)

Thyroid hormone	Metabolic syndrome	Non metabolic syndrome	p-value
TSH (mIU/L)	3.07 ± 2.24	2.48 ± 1.33	0.023
FT4 (pmol/L)	13.45 ± 2.73	14.24 ± 1.76	0.017
FT3 (pmol/L)	3.39 ± 1.14	3.66 ± 0.87	0.070

Unpaired t test was done

Table no III TSH is more in metabolic syndrome than non metabolic syndrome and (p value=0.023).

Table IV: Thyroid status of the patients with and without metabolic syndrome (N=200)

Thyroid status Euthyroid	Metabolic syndrome (n=56)	Non metabolic syndrome (n=144)	p-value
Overt hypothyroidism	41 (73.2)	139 (96.5)	<0.001
Sub clinical hypothyroidism	4 (7.1)	0 (0.0)	
Sub clinical hyperthyroidism	9 (16.1)	4 (2.8)	
	2 (3.6)	1 (0.7)	

Chi-Square test was done

Table no IV in metabolic syndrome group 41 (73.2%) euthyroid followed by 4 (7.1%) had overt hypothyroidism , 9 (16.1%) had subclinical and 2 (3.6%) had subclinical hyperthyroidism. In non-metabolic syndrome only 4 (2.8%) had subclinical hypothyroidism and 1(0.7%) had subclinical hyperthyroidism.

Table V: Correlation of TSH with waist circumference, BMI, serum fasting total cholesterol, serum fasting triglyceride, serum fasting LDL and serum fasting HDL (N=200)

Metabolic status	r	p-value
Waist circumference (cm)	0.113	0.111
BMI (kg/m2)	0.114	0.110
Serum fasting total cholesterol	0.143	0.043
Serum fasting triglyceride	0.218	0.002
Serum fasting LDL	0.104	0.145
Serum fasting HDL	-0.029	0.685

Table no V there are positive correlation with waist circumference, BMI, serum TC, TAG, and LDL but negative correlation with HDL cholesterol level.

DISCUSSION:

Thyroid hormone regulates various metabolic pathways which are relevant to energy expenditure and hypothyroidism associated with weight gain.[26,27] Low energy expenditure is a risk factor for obesity. Some studies have demonstrated a positive correlation TSH and BMI in obese participants, although the TSH levels were within normal range.[28-30]

We observed association between serum TSH and metabolic syndrome and this association was related to high level of TSH.[31, 32] It also found among euthyroid patients even in presence of normal TSH level.[31, 33] In our study ,among 56 metabolic participants, 41 (73%) had normal thyroid function, followed by 4 (7.1%) had overt hypothyroidism, 9 (16.1%) had subclinical hypothyroidism and 2(3.6%) had sub clinical hyperthyroidism whereas in non-metabolic syndrome only 4 (2.8%) had subclinical hypothyroidism and 1 (0.7%)had subclinical hyperthyroidism (Table no 4). Thyroid dysfunction affects lipid and glucose metabolism, blood pressure and body weight, that are associated with various metabolic parameters which may lead to development of components of metabolic syndrome.[34] The effects of hypothyroidism on the prevalence of metabolic syndrome in female was due to changes in lipid metabolism and increased risk of central obesity and hypertriglyceridemia. Women with hypothyroidism have higher risk of metabolic syndrome than men. Several studies found that increased serum TSH are associated with metabolic syndrome. Serum TSH level within normal reference were positively correlate with increase prevalence of metabolic syndrome in Korea.[35] Benesor Isabela M et al. found that high TSH was closely related to metabolic syndrome.[36]

Thyroid disorder more in metabolic syndrome than in non-metabolic syndrome. Also we found positive correlation between TSH and BMI, Waist circumference, serum TAG and negative correlation with HDL-C. In our study we found that TSH level was higher in metabolic syndrome than in non-metabolic (Table no 3), in accordance with result of previous study, which showed that serum TSH higher in metabolic syndrome than in non-metabolic syndrome among adults individuals.[37]

The prevalence of hypothyroidism has been found 8-15% in different population and the prevalence increases with age almost 20% in elder individual.[38] The knowledge that metabolic syndrome may not be a complication of thyroid dysfunction but also thyroid dysfunction may increase effect of metabolic syndrome.[39]

The prevalence of cardiovascular disease, stroke and risk of death 2-3 times more in Chinese patients with metabolic syndrome than in without metabolic syndrome.[40]

Our study did not show any significant association between thyroid function status and metabolic syndrome but TSH level is higher in metabolic syndrome group even in euthyroid state. Metabolic syndrome and high TSH is a risk factor for cardiovascular disease. This clinical awareness is helpful for early diagnosis of metabolic syndrome and thyroid dysfunction to reduce the mortality and morbidity.

CONCLUSION:

We conclude that metabolic syndrome were not associated with thyroid disorder. But Serum TSH level higher in metabolic group than non-metabolic group. There were some limitations in this study. Some are mentioned below:

1. It was a single centered study.
2. Sample size was not reflecting the whole country scenario.
3. It was a purposive non-random sampling method.
4. This study was cross-sectional study rather than cohort study.

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Original Artical

Demographic Characteristics of ENT-OPD Patients at a Tertiary Care Hospital.

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ABSTRACT:

BACKGROUND: *Diseases related with ENT are one of the leading causes of major health problem in Bangladesh like other countries of Asia. It is influenced by environmental, economical, racial, social customs and various other factors.* ***OBJECTIVES:*** *To determine the prevalence of ENT diseases presenting at outpatient department, socio-demographic characteristics of these patients and to educate the people about different ENT diseases, their early treatment and prevention.* ***MATERIALS AND METHOD:*** *This is descriptive cross sectional study which included 2637 patients presenting with ENT problem in the Department of ENT OPD, East West Medical College and Hospital, Turag, Dhaka from July 2018 to December 2018.* ***RESULTS:*** *A total of 2637 patients were included Mean +SD age of the patients were 24 + 13 years. Male female ratio is 1:1.3. Majority of the patients (75%) were socio-economically poor. Throat problems were most commonly encountered. The common prevalent diseases were tonsillitis (17.54%), otitis media (16%), sinusitis (14.70%), pharyngitis (12.81%), thyroid gland related diseases (8.50%), allergic Rhinitis (7.68%) & others. Rare diseases mainly are atrophic rhinitis (0.65%) & parotid gland related disease (0.50%). It was observed that 30.29% of patients were under the age of 15 years.* ***CONCLUSION:*** *Among ENT diseases throat diseases are common then ear diseases, nose diseases and others. Approximately 37% of these diseases are preventable. They exist mainly in the poor socio-economic condition and most of them avail treatment. Appropriate control measures including health education and counselling should be taken to combat the diseases at community level.*

Keywords: Demographic characteristics, ENT-OPD patients

INTRODUCTION:

Geographically, historically Dhaka is the capital and largest populous part of the south Asia and Turag is one of the overcrowded, industrial area of Dhaka city. Diseases of ear 39.75% followed by throat diseases 33.71% and nasal diseases 26.51% in Bangladesh.[1] ENT diseases are most common public health problem world-wide.[2] The pattern of these diseases varies from one country to another country & in various regions within the same country. Morbidity of different age has several determining factors like basic education, socio-economic status, occupation, socio-cultural status and living environment etc.[3] This usual problems make a patient to visit health care person in rural area as well as urban areas are related to the ENT.[4,5]

According to World Health Organization (WHO), 42 million people (age >3 yrs) of the world having hearing loss.[6] Indeed, in the

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Iguelouane N et al series, ENT involvement was noted in 67.5% of the 200 patients followed in an Internal Medicine department for systemic diseases; this involvement was indicative of systemic disease and/or announcing her relapse in 37.5%of cases.[7] Diseases related to ENT affect 35-45% of the general population at any one time. There are lot of ENT diseases from minor problems to major problems like allergic rhinitis to malignancies. In India, A study was conducted on ENT diseases disorder in children, it was found that otitis media is the most common in male children (53.2%). Most of the children come from low socio-economic families, living in combined families and had uneducated mother.8 The present study was undertaken to describe prevalence of diseases related to ENT & the socio-demographic characteristics of the patients attending the ENT OPD.

MATERIALS & METHODS:

All new cases attending the outpatient in East West Medical College & Hospital, Dhaka during a period of six months from 1st July 2018 to 31st December 2018 were included in this study. Diagnosis was made on clinical grounds & confirmed by laboratory investigations wherever required. According to the monthly income of family in Bangladeshi currency (BDT) we divided the patients into four groups. The four groups are- very poor, poor, middle class & rich. A monthly earning by a family below 5000/- was categorized as very poor, between (5-10) thousand poor, (10-25) thousands middle class, and above 25000/- were designated as rich respectively. This income groups were made depending upon the existing salary & other earning patterns of our people and their average monthly expenditure to maintain their family. After clinically diagnosed by concerned medical officers at the out-door patient Department, the socio- demographic data were collected with the help of a carefully designed questionnaire. The socio-economic data of the patients and their different diseases were compared & correlated.

Inclusion criteria: Patients having ENT diseases.

Exclusion criteria: Patients having diseases other than ENT problems and hospital admitted patients.

RESULTS:

The total number of patients, who attended outpatient Department of ENT in East West medical college & Hospital during the study period, was 2637.

Table I: Age & Sex distribution of Patients.

Age in Years	No. of Patients		
	Male (%)	Female (%)	Total
0-5	234 (8.60%)	220 (8.20%)	(454 (16.80%)
6-15	212 (7.80%)	185 (6.64%)	397 (18.75%)
16-25	398 (14.63%)	357 (12.74%)	755 (27.80%)
26-35	448 (16.65%)	290 (11.20%)	738 (26.51%)
More than 35	226 (8.90%)	67 (2.80%)	293 (10.38%)
Total	1518 (56.84%)	1119 (44.25%)	2637 (100%)

(Figure in the Bracket indicate Percentage)

Table I shows that, from 2637 patients 1518 of them were male & 1119 were female. Male-Female ratio was 1:1.3 . It was observed that 30.29% of the patients were under 15 years of age.

Table II: Distribution of Patients by Education.

Education Level	No. of Patients	Percentage
Illiterate	220	7.7%
Primary	750	27.50%
Secondary	890	32.38%
Higher Secondary	408	18.10%
Degree & above	367	16.25%
Total	2637	100%

(Figure in the Bracket indicate Percentage)

The educational qualification of the 2637 respondents has been shown in table-2. A total of 220 (7.70%) respondents have no formal education, 750 (27.50%) had primary 890 (32.38%) had secondary level of education.

Table III: Socio-Economic status of the Patients.

Socio-economic Status	No of Patients	Percentage
Very poor	120	4.20%
Poor	1900	73.10%
Middle	450	17.90%
Rich	167	4.80%
Total	2637	100%

(Figure in the Bracket indicate Percentage)

The majority of the patient 1900 (73.10%) came from poor family & 450 (17.90%) came from middle class family, 167 (4.80 %) came from rich family and only 120 (4.20%) came from very poor family, out of 2637.

Table IV: Distribution of diseases according to Age in yrs.

Name of Diseases	0-5	6-15	16-25	26-35	Above 35	Total
Tonsillitis	94 (22.61)	36 (24.04)	104(24.20)	80 (20.18)	36 (9.59)	410 (17)
Asom (Acute suppurative Otitis Media)	63 (60.45)	43 (38.74)	6 (5.12)	8 (7.86)	6 (5.12)	126 (16)
Csom (Chronic Suppurative Otitis Media)	82 (23.30)	46 (13.07)	84 (23.86)	70 (19.89)	70 (19.89)	352 (16.8)
Furunculosis	71 (17.62)	84 (20.84)	66 (16.38)	121 (30.02)	61 (15.14)	403 (15.92)
Sinusitis	144(32.88)	80 (18.26)	70 (15.98)	74 (16.89)	70 (15.89)	438(14.70)
Pharyngitis	46 (20.54)	54 (24.11)	38 (16.96)	65 (29.02)	21 (9.38)	224(12.81)
Laryngitis	0	34 (16.90)	124(59.05)	43 (20.48)	9 (4.29)	215 (7.68)
Thyroiditis	0	0	28 (35.90)	35 (44.87)	15 (19.23)	78 (8.50)
Allergic rhinitis	32 (34.04)	22 (23.40)	8 (8.51)	18 (19.15)	14(14.89)	94 (7.68)
Otosclerosis	8 (13.79)	14 (24.14)	8 (13.79)	16 (27.15)	12 (20.69)	58 (2.10)
Arthritis	0	8 (14.29)	12 (21.43)	10 (17.89)	26 (46.43)	56 (2.6)
Parotid disease	40 (12.86)	20 (23.0)	20 (23.00)	15 (27.59)	5 (3.29)	100 (15.00)
Atrophic rhinitis	0	0	20 (23.00)	18 (38.43)	10 (6.5)	48 (1.12)
others	5 (10.92)	0	20 (23.00)	10 (6.5)	0	35 (30)
Total	585(21.45)	521(18.54)	608(24.01)	583(21.40)	355 (14.60)	2637 (100%)

(Figure in the Bracket indicate Percentage)

Table V: Distribution of respondents by disease pattern & Socio-economic status.

Disease	Very poor	poor	middle	Rich	Total
Tonsillitis	105 (21.40%)	215 (42.60%)	50 (15.40%)	40 (10.60%)	410 (100%)
ASOM	63(50.4%)	38(30.16%)	19(15.08 %)	6(4.76%)	126 (100%)
CSOM	120 (40%)	70 (15%)	90 (30%)	72 (15%)	352 (100%)
Furunculosis	145 (39.60%)	(105) (30.40)	80 (16%)	73 (14%)	403 (100%)
Sinusitis	95 (20%)	85 (15%)	135 (34.60%)	120 (30.40%)	438 (100%)
Pharyngitis	85 (41%)	55 (25%)	30 (16%)	54 (19%)	224 (100%)
Laryngitis	45 (20.80%)	60 (29.20%)	40 (16%)	70 (34%)	215 (100%)
Thyroid disease	13 (12%)	15 (18%)	20 (29%)	30 (41%)	78 (100%)
Allergic Rhinitis	18 (7.5%)	40 (49.5%)	20 (17.8%)	16 (15.2%)	94 (100%)
Otosclerosis	8 (10%)	12 (15%)	18 (35%)	20 (40%)	58 (100%)
Joint arthritis	8 (10%)	12 (15%)	18 (35%)	18 (35%)	56 (100%)
Parotid disease	25 (25.5%)	30 (29.5%)	30 (29.5%)	15 (16.5%)	100 (100%)
Atrophic rhinitis	5 (12%)	10 (15%)	15 (33%)	18 (40%)	48 (100%)
other	5 (15%)	8 (20%)	2 (5%)	20 (60%)	35 (100%)
Total	742 (30%)	597 (20%)	621 (22%)	676 (28%)	2637 (100%)

(Figure in the Bracket indicate Percentage)

Table-V shown that socio-economic status of the patients of the various diseases, tonsillitis emerged as the commonest group of disorders followed by otitis media, sinusitis & pharyngitis. Among the total 410 patient suffering from tonsillitis, 130 (31.70%) were under 15 years of age & a much higher proportion of tonsillitis is in chronic state. On the other hand 320 (78.19%) out of 410 tonsillitis patients were reported to come from poor family.

DISCUSSION

Bangladesh is a densely populated developing country. The climate is mostly hot & humid. Both of these factors are favorable for development of variety of diseases. Many of the diseases are directly associated to hygiene & healthy life practice. This healthy living is again related mainly on two factors: awareness & financial solvency. In this study, we tried to investigate different types of ENT diseases in different income group of patients. We didn't find a well defined patient of income group distribution among our citizens.

In the present study, tonsillitis (acute & chronic both) emerged as the single largest group of disorders affecting 17.54% of the total disease pattern. In our study tonsillitis under 15 years of age is most common disorder which was 130 (31.70%) patients out of total 410 patients. In another study in Nigeria found similar findings where 15.8% of under five years had pharyngotonsillitis and another similar finding from Scotland found tonsillitis to be common in children as compared to adult.[9,10] Poverty sticker people with poor hygienic habit are the usual victims of various diseases. Nutritional deficiency, lack of health education & lack of maintenance of general hygiene are the probable causes of high prevalence of diseases. All these factors are directly related to economic status. ASOM, CSOM & Furunculosis were the 2nd, 3rd & 4th largest group of disorder. The warm & highly humid climate of the country may account for the high incidence of diseases. This also observed in our study. Improvement in earnings is the vital for improvement of quality of life of the people. Strengthening of health education programmed especially school health education, for creation of public awareness, and motivation is of utmost importance for control & prevention of these diseases.

CONCLUSION:

In conclusion, Diseases related with ENT (Ear, Nose & Throat) are most common among young age group (16-25years) having secondary level of education with poor socio-economic status. Approximately 67% of these diseases are preventable. Appropriate control of measures including health education taking into account the above facts have to be taken to combat the diseases at community level.

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Original Artical

Study of Electrolyte disturbances in patients with Dengue Fever

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ABSTRACT:

BACKGROUND: *Dengue is the most common arboviral disease worldwide and is usually endemic, but several epidemics have been recorded. Dengue fever is associated with electrolyte disturbances.* ***OBJECTIVES:*** *To determine the pattern of electrolyte disturbances in patients of dengue fever, dengue hemorrhagic fever and dengue shock syndrome.* ***METHOD:*** *In this cross sectional study 120 serologically confirmed cases of dengue infection with available electrolyte profile, admitted to Bangladesh medical college hospital in the period of June 2019 to October 2020 were analysed. Serum electrolytes levels were measured at fifth and sixth day of fever irrespective of stage of dengue infection (DF/DHF/DSS). Dengue was confirmed by NS1 or IgM/IgG positivity. DHF was labeled as per WHO criteria of Dengue hemorrhagic fever.* ***RESULTS:*** *The majority of the patients (57.5%) were males while (42.5%) were females. The mean age was 36.61±14.55 years. The majority of patients 64.1 % were with Dengue fever, 24.1% with dengue haemorrhagic fever (DHF) and 11.6% patients were with dengue shock syndrome (DSS). Hyponatremia and hypokalemia was the frequent electrolyte disturbances found in dengue patients. The mean value of serum sodium was 132.65± 6.01mEq/L and of serum potassium was 3.64±0.67 mEq/L. The results were statistically significant between difference in serum sodium and potassium levels with Dengue clinical syndrome (DF, DHF, and DSS) which implies that as the difference between the levels increases, greater are chances of the Dengue fever towards DHF or DSS.* ***CONCLUSION:*** *Hyponatremia was the most frequent electrolyte disturbance and hyperkalemia was least common observed in patients with Dengue viral infection. Mild hyponatremia and mild hypokalemia were more common among patients of Dengue fever whereas moderate and severe hyponatremia and hypokalemia were more common among Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS).*

Keywords: Electrolyte disturbances, Dengue fever (DF), Dengue haemorrhagic fever (DHF), Dengue shock syndrome (DSS).

INTRODUCTION:

Dengue is a viral hemorrhagic fever caused by Flaviviridae. It is a mosquito-borne infection transmitted by Aedes aegypti and Aedes albopictus, it has 4 serotypes DENV 1, DENV 2, DENV 3 and DENV 4. It is the most common cause of arboviral disease globally.[1] The number of cases reported increased from 2.2 million in 2010 to over 3.34 million in 2016.[2] Dengue has been identified as a disease of the future owing to trends toward increased urbanization, scarce water supplies and possibly environmental change.[3]

Clinical spectrum of dengue infection in humans include, 1) mild flu like illness comprising fever, headache, nausea, vomiting, abdominal pain, arthralgia, and myalgia, rashes,

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2) dengue fever with warning signs like abdomen pain, persistent vomiting, clinical fluid accumulation, mucosal bleeds, lethargy, restlessness, hepatomegaly and raising haematocrit which was previously known as dengue haemorrhagic fever (DHF) and 3) severe dengue which comprises of severe organ impairment ,shock and severe plasma leakage leading to dengue shock syndrome (DSS). Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) are severe forms of dengue infection, characterized by evidence of plasma leakage.[1,4,5]

Dengue viral infection has been shown to be associated with electrolyte abnormalities and renal dysfunction due to several proposed mechanisms, one among which is direct action of immune complexes on glomeruli leading to AKI and deranged electrolytes.[6,7]

Hyponatemia and hypokalemia are the commonest electrolyte disturbances seen in dengue fever. Sodium is an essential nutrient in humans; regulates blood volume, blood pressure, osmotic equilibrium and pH. Hyponatremia is frequent in dengue, which can cause central nervous system dysfunction.[8] Other mechanisms proposed for hyponatremia include it occurs as a consequence of salt depletion, excess water from increased metabolism, transient inappropriate antidiuretic hormone or the influx of sodium in the cells as a result of dysfunction of sodium potassium pump.[9]

Dengue infection also leads to mild hypokalemia due to poor intake and an increase in renal excretion due to activation of renin angiotensin and aldosterone system secondary to volume depletion.[10] Hypokalaemia is also common in Dengue which can lead to acute neuromuscular weakness including respiratory muscle paralysis.[11]

The purpose of the present study was to determine the pattern and prevalence of electrolyte disturbances in dengue infected patients and to compare whether there is significant differences in electrolyte abnormalities in patients with DF to complication of Dengue fever.

MATERAIL AND METHODS:

This cross-sectional descriptive study was carried in Bangladesh medical college hospital in the period of June 2019 to October 2020. All patients admitted in dengue ward with age between 25 to 70 years , with confirmed dengue infection (either NS1, IgM or IgG positive) were included in this study. Patients who were dengue serology negative or case of any other febrile illness were excluded. Total 120 patients were included in study. Serum electrolytes levels were measured at fifth and sixth day of fever irrespective of stage of dengue infection (DF/DHF/DSS). DHF was labeled as per WHO criteria of Dengue Hemorrhagic fever. Sodium and potassium were estimated by electrolyte kit method by ion selective electrode by full auto analyser.

Hyponatremia was defined as serum sodium level <135 meq/L; Mild Hyponatremia-between 125-135 meq/L; Moderate Hyponatremia- between 120-125 meq/L; Severe Hyponatremia- less than 120 meq/L; Hypokalemia was serum potassium levels < 3.50 meq/L; Mild Hypokalemia-between 3.00 to 3.50meq/L; Moderate Hypokalemia: between 2.50 to 3.0 meq/L; Severe Hypokalemia- less than 2.50 meq/l and Hyperkalemia: Serum potassium level more than 5.0 meq/L.[12-14] Descriptive statistics were used to describe the results. Chi-square test was used to compare the frequency of electrolyte disturbances between patients with DF, DHF and DSS. A p-value <0.05 was considered statistically significant.

RESULTS:

In the present study majority of the patients 69 (57.5%) were males while 51(42.5%) were female patients. The mean age of male patients was 38.96 ± 15.86 years and of female patients was 33.43 ± 12.01 years.

The majority of patients 77(64.1%) were with dengue fever, 29 (24.1%) patients were with dengue hemorrhagic fever and 14 (11.6%) patients were with dengue shock syndrome. Out of total 91(75.8%) patients had NS1 +ve,

Table I: Comparison of age, serum Sodium and Potassium levels in male and female

Characteristics	Male	Female	Total	p-value
Age (years)	38.96 ± 15.86	33.43 ± 12.01	36.61 ± 14.55	0.039
Sodium	133.04 ± 5.73	132.12 ± 6.39	132.65 ± 6.01	0.406
Potassium	3.69 ± 0.69	3.58 ± 0.66	3.64 ± 0.67	0.403

In the present study, the mean value of serum sodium was 132.65±6.01 mEq/L and of serum potassium was 3.64±0.67 mEq/L. In our study of the 120 patients studied majority of them 70 (58.3%) have serum sodium levels within normal limits, 38(31.7%) had reported mild hyponatremia, 6(5%) patients moderate hyponatremia and 6 (5%) patients reported severe hyponatremia. The mean sodium levels observed in each category of dengue fever was 135.07±3.14, 131.93±5.04 and 120.78 ±5.52 respectively.

In our study majority had potassium level within normal range i.e. 72(60%), 28 (23.3%) had mild hypokalemia, 6 patients (5%) had moderate hypokalemia, 6 patients (5%) had severe hypokalemia and 8 (6.7%) patients had hyperkalemia. The mean potassium levels of various category of dengue fever observed in our study was 3.72±0.40, 3.65±0.82 and 3.17±1.19 respectively.

Table II: Frequency of serum sodium and potassium levels among patients with DF, DHF and DSS

Serum sodium and potassium levels	Number of cases			Total
	DF (n=77)	DHF (n=29)	DSS (n=14)	
Normal	58	12	0	70 (58.3)
Mild hyponatremia	19	14	5	38 (31.7)
Moderate hyponatremia	0	2	4	6 (5.0)
Severe Hyponatremia	0	1	5	6 (5.0)
Mean± SD	135.07 ± 3.14	131.93 ± 5.04	120.78 ± 5.52	132.65 ± 6.00
Normal	58	14	0	72 (60.0)
Mild hypokalemia	15	9	4	28 (23.3)
Moderate hypokalemia	2	1	3	6 (5.0)
Severe hypokalemia	0	2	4	6 (5.0)
Hyperkalemia	2	3	3	8 (6.7)
Mean ± SD	3.72 ± 0.40	3.65 ± 0.82	3.17 ± 1.19	3.64 ± 0.67

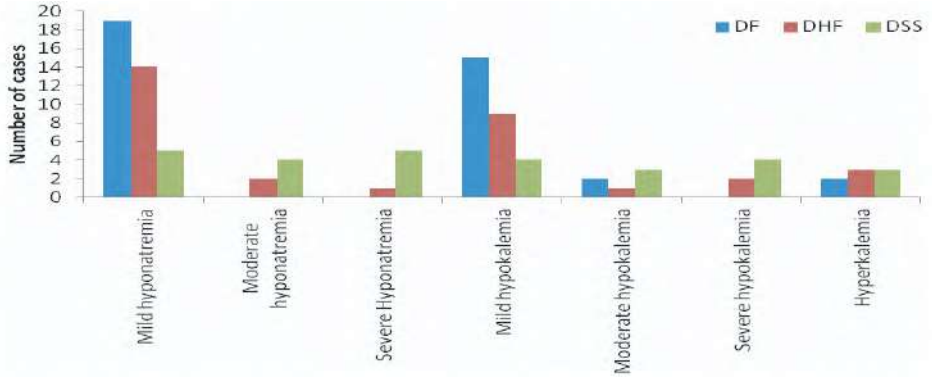

Figure 1: Distribution of cases according to classification of hyponatremia and hypokalemia

Mild hyponatremia and mild hypokalemia were more common amongst DF compared to DHF and DSS where as moderate and severe hyponatremia and hypokalemia were common amongst DHF and DSS (Table: II & III and figure:1). Significant association was observed in moderate and severe hyponatremia and hypokalemia among patients with DHF and DSS as compared to DF. Similarly insignificant association of serum sodium and potassium levels in male and female dengue patients was observed (Table: I)

Table III: Comparison of electrolyte derangements in patients with DF, DHF and DSS

		DF (n=77)	DHF (n=29)	p-value	DSS (n=14)	p-value
Sodium (mg/dl)	**Mean±SE**	135.08 ± 0.36	131.93 ± 0.94	<0.001	120.79 ± 1.48	0.001
	No (%) of patients with <LLN	19/58 (24.7)	17/12 (58.6)	0.001	14/0 (100.0)	<0.001
Potassium (mg/dl)	**Mean±SE**	3.72 ± 0.05	3.66 ± 0.15	0.604	3.18 ± 0.32	0.002
	No (%) of patients with <LLN	17/60 (22.1)	12/17 (41.4)	0.047	11/3 (78.6)	<0.001

DISCUSSION:

Majority of the patients 69 (57.5%) were males while 51 (42.5%) were female patients. The mean age of male patients was 38.96 ± 15.86 years and of female patients was 33.43 ±12.01 years. Rahul Unnikrishnan et al cited that the mean age of the cases was 66.1 ± 4.7 years, of which 87% belonged to the age group of 60-70 years, 11% were in the age group 70-80 and 2% of the patients were 80+ years old.[15] Muhammad AM et al cited that two-thirds (70.9%) were male. The mean age was 35.2 ± 14.7 years (range 15-85 years).[16]

In our study, the mean value of serum sodium observed was 132.65±6.01 mEq/L this is similar to the study done by Mekmullica et al (2005) which had a mean of 132 mEq/L.[8] Lumpaopong et al, (2010) found that serum sodium level in dengue patients in Thailand was 133mEq/L.[7] Sarfraz in 2018 found mean value of Na in the population 134 mEq/L.[17] Another studies done by Khandelwal et al and Shankar et al in 2019 found the mean value of serum sodium 133.92 and 133.69 mEq/L respectively.[2,10] Rahul Unnikrishnan et al quoted that the incidence of hyponatremia (serum sodium <135 mEq/L) was higher 50.9% mean values of sodium in each category done by Khandelwal was 134.66±3.57, 130.55±8.05(mean 129.8 with SD of 14.66) with seven patients (13.2%) of the patients developing significant hyponatremia (<125 mEq/L).58% of the hyponatremic patients were found to be symptomatic.[15] Bandaru A et al started that the mean serum sodium level was 136.6±5.4 in Dengue fever cases.[18]

The mean sodium levels observed in each category of dengue fever was 135.07±3.14, 131.93±5.04 and 120.78±5.52 respectively. This is similar to the study done by Shankar et al found sodium levels observed in each category was 134.66±2.48, 129.55±6.05 and 117.66±9.89 respectively.[2] In another study the and 118.66±10.39 respectively.[10] Mekmullica J et al cited that hyponatremia was 9.7 times more common in dengue patients, the mean serum sodium level was significantly lower in shock patients compared to non-shock patients (p- value=0.003).[8]

In the present study, serum electrolyte levels of Dengue patients were studied on the day of fifth and sixth day of admission, 70 (58.3%) patients were having serum sodium levels within normal limits, whereas 38 (31.7%) patients had reported mild hyponatremia, 6 (5%) patients reported moderate and severe hyponatremia.

In our study majority of patients had potassium levels within normal range. i.e. 72 (60%), 28 (23.3%) had mild hypokalemia, 6 patients (5%) had moderate and severe hypokalemia and 8(6.7%) patients had hyperkalemia. This is similar to study by Khandelwal Vinay et al, studying electrolyte disturbances in dengue fever in adults where 55.44% patients had normal serum potassium levels, 33.16% patients had mild hypokalemia, 5.94% patients reported moderate hypokalemia and 2.97% patients reported severe hypokalemia while 2.47% patients also reported hyperkalemia .[10] The mean potassium levels of various category of dengue fever observed in our study was 3.72±0.40, 3.65±0.82 and 3.17±1.19 respectively. Shankar et al found potassium levels observed in each category was 3.54±0.42, 3.19±0.72 and 2.62±0.18 respectively. He found mean value of potassium 3.58 mEq/L.[2] In our study the mean value of serum potassium was 3.64±0.67 mEq/L. Khandelwal found mean value of serum potassium 3.62 mEq/L.[10] Similarly Widodo et al, stated that prevalence of hypokalemia in 23% of the hospitalized patients with dengue fever.[19] Kalita et al observed hypokalemia in association with infectious diseases, particularly in dengue fever. [20] Rathod N et al cited that the incidence of abnormal electrolytes as 13% in dengue fever subjects. [21]

It was found that there exists significant correlation between difference in sodium and potassium levels with dengue spectrums (DF, DHF and DSS) which implies that as the difference between the levels increases, greater are chances of the Dengue spectrum towards DHF or DSS. Mild hyponatremia and hypokalemia were more common amongst patients of DF as compared to DHF and DSS. Arun Gogna et al quoted that the mean sodium levels were 135.5, and mean potassium levels were 4.1; The levels were significantly reduced among cases with severe dengue presented with warning signs.[22] Bandaru A et al stated that the prevalence of hyponatremia was 35.5% among DF cases and 53.5% among DHF cases and hypokalemia as 16.1%. They also observed that the prevalence of deranged serum electrolytes was more common among severe cases of Dengue hemorrhagic fever (DHF). [18]

Hence the present study proves the correlation between electrolyte levels and severity of Dengue viral infections.

CONCLUSION

The present study was conducted to assess the occurence of electrolyte disturbances in patients of Dengue viral infections with its association with severity of Dengue viral infections. Hyponatremia was the frequent electrolyte disturbance in patients of dengue fever and hyperkalemia was least common. Mild hyponatremia and mild hypokalemia were more common among patients of Dengue fever whereas moderate and severe hyponatremia and hypokalemia were more common among Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS).

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Orginal Article

Serum Electrolytes Levels in Irritable Bowel Syndrome

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ABSTRACT

BACKGROUND: *Irritable bowel syndrome (IBS) is one of the most gastrointestinal disorders that normally has an altered bowel habits in addition to abdominal discomfort. It significantly reduces patients' quality of life. Individuals diagnosed with IBS have "low-grade intestinal inflammation", and increased intestinal permeability. This can create an electrolyte imbalance.* ***OBJECTIVES:*** *The objectives of this study were to estimate serum electrolyte levels in patients with IBS.* ***MATERIALS AND METHODS:*** *This study was conducted in Prime Medical College, Rangpur from July 2019 to June 2020 on 108 individuals in the age group of 21-60 years of whom 54 were diagnosed IBS cases and 54 were normal controls. Estimation of serum electrolytes was done with the collected venous blood samples using the electrolyte analyzer. All the data thus obtained was arranged in tabulated from and analyzed using computer-based software SPSS 23.0 version for windows." Student t' test was used for statistical analysis and p value of less than 0.05 was considered as significant.* ***RESULTS:*** *Mean serum sodium and mean potassium levels slight decrease and with a statistically significant increase in the mean serum chloride and slight increase mean serum bicarbonate levels were the findings observed in our study group when compared with the controls.* ***CONCLUSION:*** *This study implies that serum electrolyte levels are not greatly altered in IBS cases probably due to the rapid transit in colon, mucoidal consistency and small volume of stools.*

Key word: Irritable bowel syndrome, Serum electrolytes

INTRODUCTION:

Irritable bowel syndrome is a gastrointestinal condition that normally has an altered bowel habits in addition to abdominal discomfort.[1] It is one of multifactorial, heterogeneous and complex gastrointestinal disorders. It has a significant medical and socioeconomic impact that reduces patients' quality of life and it also imposes a significant economic burden to the healthcare status of a country.[2]

The pathophysiology of IBS is still poorly understood. It is most likely mediated by a combination of mechanisms including inflammation, autonomic dysfunction, dietary and psychological factors. The diagnosis and management of this disorder can be challenging. Several pathogenic factors responsible for IBS have been suggested, such as genetic and environmental factors, alterations in digestive motility, visceral hypersensitivity, inflammatory and post-infection mechanisms, psychological morbidity, and bacterial overgrowth among others. However, none of them seem to clearly explain the real mechanisms that trigger the syndrome.[3] Individuals diagnosed with IBS have "low-grade intestinal inflammation", and increased intestinal permeability with changes in the intestinal microbiota. This can create an

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electrolyte imbalance. It is a well-known fact that maintaining normal serum electrolyte balance is essential for the efficient functioning of cells and organs in the body.[4]

Available studies regarding irritable bowel syndrome suggest controversial reports in the serum electrolyte levels. Some studies have shown that statistically significant improvement in abdominal discomfort or pain is observed when clinical trials with electrolyte supplementation were given.[5]

There is a paucity of literature directly linking the levels of the serum electrolytes and IBS, especially in south Indian studies. In addition, studies have suggested that the impact of IBS on health-related quality of life is equally as significant as in congestive heart failure and dialysis-dependent renal failure. Moreover, the association of the electrolyte levels with respect to the severity of the disease is not well established. Hence, the present study was taken up.

MATERIALS AND METHODS:

This cross-sectional analytical study was conducted in Prime Medical College & Hospital, Rangpur, Bangladesh on 108 individuals in the aged group of 21-60 years of whom 54 were diagnosed IBS patients and 54 were normal controls. All subjects were socio-economical condition matched. The objectives, nature, purpose and benefit of the study were explained to the subjects in details. Informed written consents were taken from all participants. Details were entered in a predesigned proforma that includes personal bio-data, presenting complaint, predominant symptoms, duration of illness and associated history relevant to exclusion criteria. After obtaining informed consent, under absolute aseptic precautions, 5 ml of venous blood samples were collected. Blood was allowed to clot and serum was separated by centrifugation of the sample at 5000 rpm for 10 minutes and this sample was estimated for serum electrolytes-sodium, potassium, chloride and bicarbonate ions using the direct electrolyte analyzer (Easylyte). Collected data were compiled and appropriate statistical analyzed by student "t" test were carried out using computer-based software, Statistical Package for Social Science (SPSS 23.0 version). and p value of less than 0.05 was considered as significant.

Inclusion Criteria:

Patients in the age group of 21-60 years diagnosed as IBS patients who fulfilled modified Rome III criteria for irritable bowel syndrome. i.e. recurrent abdominal pain or discomfort $\geq$ 3 days per month in the last 3 months associated with $\geq$ 2 of the following:

Pain or discomfort improved after defecation.

Change in the frequency of stool.

Change in form of stool, alternating between diarrhea and constipation.

No evidence of any inflammatory, anatomical, a metabolic or neoplastic process that could cause the symptoms.

Exclusion Criteria:

Patients with known and established causes of diarrhea.

Patients who had diabetes mellitus, hypertension, a salt-restricted diet, steroid therapy, bronchial asthma, previous GI disorders, other systemic disorders.

Patients on medications affecting serum sodium, potassium, chloride and bicarbonate levels.

RESULT:

The mean ±SD serum Na+and K+ levels were decreased and mean ±SD levels of serum Cl- and HCO3- is increased in IBS subjects than that of control subjects. **(Table-III)**

Table I: Age distribution among IBS patients & control

Age	Control	IBS patients
21- 30	27	25
31- 40	12	14
41- 50	7	6
51- 60	8	9

Table II: Gender distribution of the study population.

Gender	Control	IBS patients
Male	30	20
Female	24	34

Table III: Comparison of mean serum electrolyte levels between Control and IBS patients.

Mean SD of serum electrolytes in mEq/L	Number of subjects	Control	IBS subjects	P value
Na^+	54	140.28 ± 3.08	135.11± 4.09	0.14^{NS}
K^+	54	4.35 ± 0.51	4.17 ± 0.56	0.16^{NS}
Cl^-	54	101.11 ± 6.90	103.41± 5.23	0.01*
HCO_3^-	54	24.05 ± 0.93	28.05 ± 1.12	0.12^{NS}

Data were expressed as mean ± SD. Unpaired 't' test were done.
p value< 0.05 was taken as level of significance. NS= Non significant
Normal level of serum Na+: 135-145 mEq/L, K+:3.6 -5.2 mEq/L, Cl- :96-102 mEq/L
HCO3- : 22-28 mEq/L [6]

DISCUSSION :

This study aims to estimate the serum electrolyte values in IBS cases and the results suggested reduction in serum sodium and potassium levels in these cases when compared with normal controls. Though there were statistically significant increase in chloride and slight increase of bicarbonate levels in IBS cases. The possible explanation for this increase chloride could be due to defective chloride transporters on the intestinal mucosa[5]

Available studies regarding irritable bowel syndrome suggest controversial reports in the serum electrolyte levels. Individuals diagnosed with IBS have "low-grade intestinal inflammation", and increased intestinal permeability with changes in the intestinal microbiota. This can create an electrolyte imbalance. It is a well-known fact that maintaining normal serum electrolyte balance is essential for the efficient functioning of cells and organs in the body.[4]

Some studies have shown that statistically significant improvement in abdominal discomfort or pain is observed when clinical trials with electrolyte supplementation were given. One of the widely accepted views is that existing low-grade intestinal inflammation in IBS can cause increased intestinal permeability, which might possibly create an electrolyte imbalance.[5]

The values obtained are in accordance with the study done on IBS diarrhea patients by Vernia et al. which also opines, serum electrolytes and systemic acid-base balance were within the normal range. These data are in agreement with the lack of systemic changes observed in IBS patients even with profuse or longstanding diarrhea.[7] Aldosterone stimulates H+-ATPase dependent bicarbonate reabsorption in all collecting duct segments of type A intercalated cells in the connecting tubules.[8]

Although diarrhea is the predominant bowel dysfunction in as many as one-third of patients with IBS, it is unclear whether there is a specific disorder of intestinal fluid or electrolyte secretion in this syndrome, as there is no published evidence till date.[9]

Diarrhea in IBS is generally considered secondary to accelerated colonic transit and reduced volume of proximal colon. The mucoid consistency and the small volume of the stools do not significantly affect the levels of serum electrolytes.[10] This might be the probable reason for the lack of significant changes in the serum electrolyte levels in this study.

CONCLUSION:

The present study implies that serum electrolyte levels were not greatly altered in IBS patients probably due to the rapid transit in colon, mucoidal consistency and small volume of stools.

Further clinical studies are recommended withlarger sample sizes for correlation of dyselectrolytemia. Maintaining normal serum electrolyte balance is essential for the efficient functioning of living cells.

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ORIGINAL ARTICLE

Study on Use of Gabapentin to Prevent Succinylcholine Induced Myalgia.

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ABSTRACT

CONTEXT: *Succinylcholine is the most commonly used depolarizing short acting muscle relaxant for endotracheal intubation. However it causes postoperative myalgia. Many agents are tried to reduce succinylcholine induced myalgia, but all have variable results and their own limitations. Gabapentin is commonly available drug which is being used in anesthesia for its many other useful effects.* ***OBJECTIVE:*** *To measure the effect of pretreatment with Gabapentin on succinylcholine-induced myalgia.* ***METHODS:*** *Total 30 patients of ASA Grade 1 and 2 of both sexes were randomly selected as- group G (Capsule Gabapentin). The patients of group-G were pretreated with capsule gabapentin 600 mg orally 2 hr before induction with a sip of water. All patients were given induction following same standard protocol. Standard monitoring is used and pulse, MAP, SpO2 is recorded intra operatively. Postoperative myalgia was assessed after 12 hrs, 24 hrs and 36 hrs of surgery and graded as grade 0, grade 1, grade 2 and grade 3 by another observer.* ***RESULTS:*** *Pulse, MAP was within physiological limit in group-G after 10 min and 15 min after induction. Myalgia was observed after 12, 24 and 36 hrs postoperatively. Myalgia was 40.0% in group-G. After 12 hours of post-operative time, 7(23.4%) patients of group-G had grade 1 and 5(16.7%) patients had grade 2 with mean score 0.56 in group G. After 24 hours, 6(20.0%) patients of group-G had grade 1 and 1(3.3%) patient detected grade 2 with mean score 0.26 in group G. After 36 hours, none of the case was detected myalgia. So precise control of myalgia was managed by drugs.* ***CONCLUSION:*** *Pre-treatment with gabapentin is effective to reduce succinylcholine-induced postoperative myalgia. Gabapentin decreases post-operative myalgia and rescue analgesics consumption without any significant complication.*

Key words: Gabapentin, Succinylcholine, Myalgia, muscle relaxant.

INTRODUCTION:

Succinylcholine is the most common depolarizing muscle relaxant agent used for endotracheal intubation. Its frequent side effect is postoperative myalgia.[1] It has the fastest onset of action (less than 1 min) and it is short-acting muscle relaxant.

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After administration of Succinylcholine fasciculations of the skeletal muscles are frequent, which may lead to muscle pain afterwards.[2]

Many agents are tried to reduce succinylcholine induced myalgia. Precurarization with NMDA, benzodiazepines, lidocaines, NSAID all are used with variable results. Atracurium is used to reduce succinylcholine induced myalgia.[3]

A meta-analysis that included data from 45 randomized and nonrandomized trials concluded that atracurium, d -tubocurarine, gallamine, pancuronium, diazepam, and lidocaine all significantly decreased the frequency of myalgia by approximately 30%.[4] Different pre-treatment modalities have been used in an attempt to reduce the incidence and severity of fasciculations and myalgia including non-depolarizing neuromuscular blockers, local anesthetics, chlorpromazine, benzodiazepines, phenytoin, ketorolac, vitamin E derivatives, pretreatment with rocuronium and ramifentanil.[5,6]

Gabapentin is being used in anesthesia for its useful effects in reducing postoperative pain, PONV. Study reported that prophylactic use of Gabapentin decreases the incidence and severity of myalgia and fentanyl consumption. Placebo controlled study by Pandey CK et al. suggests gabapentin as a possible preventative therapeutic option for postoperative succinylcholine adverse reactions. Gabapentin has an ideal safety profile and is very well tolerated-especially given a single dose of 600 mg used in the study.[7] The incidence of postoperative pain varies greatly depending on the nature of the procedure and patient-related factors. Postoperative pain is likely multi-factorial and separating myalgia ("muscle pain not related to surgical intervention") from surgical pain would seem a difficult distinction. More so, differentiating succiny lcholine-induced postoperative myalgia from multi-factorial postoperative myalgia (surgical positioning, stasis, baseline disease, etc.) would seem even more difficult to achieve. [8]

The proposed mechanisms to succinylcholine-induced myalgia are: increased myoplasmic calcium concentration, membrane phospholipid degradation, released free fatty acids and free radicals and damage to delicate muscle spindles. Investigators have shown that, in vitro, excessive repetitive contractile activity was associated with increased calcium uptake, activation of phospholipase A 2 , generation of arachidonic acid and synthesis of prostaglandins which may induce delayed onset of inflammation.[1] It is also postulated that influx of calcium into muscles caused an increase in muscle damage and pain.[9] Calcium influx enhances the speed and strength of the fasciculations and the contraction of the intrafusal muscle fibers, which increases the likelihood of spindle damage and subsequent muscle pain.[9]

Since intracellular calcium accumulation is important for enhancing the speed and strength of the fasciculations and the contraction of the intrafusal muscle fibers, an effect of gabapentin on voltage-gated calcium channels is possible. Gabapentin is known to bind to the $\alpha 2$ -δ-subunit of voltage-dependent calcium channels.[10] It reduces calcium influx into glutamatergic terminals, thus inhibiting the potassium-induced release of endogenous excitatory amino acids aspartate and glutamate. The inhibition of excitatory amino acid release conceivably leads to reduced postsynaptic excitability, providing one reasonable explanation for the antinociceptive efficacy of gabapentin in postoperative pain.[10,11] The above facts provide a plausible explanation for the antinociceptive efficacy of gabapentin in reducing the incidence of myalgia.[12]

The mechanism of postoperative myalgia is complex. It involves many steps. So different pretreatment agents can be used to target different steps of myalgia. The different pretreatment drugs represent different lines of actions on cellular mechanisms and thus a combination may be a sensible rationale for further decreasing postoperative myalgia. Therefore, in this randomized study, we observed the effect of prophylactic use of Gabapentin on Succinylcholine-induced myalgia in subjects undergoing upper abdominal surgery under GA.

MATERIALS AND METHODS

This Prospective Randomized Controlled Study was conducted in Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka from 8th June 2018 to 7th December 2018. Total 30(thirty) patients with ASA grade I, II undergone upper abdominal surgery under GA were included according to selection criteria & sample were selected by purposive sampling technique.

Patients undergoing elective upper abdominal surgery under GA with ASA physical status I, II, age between 20 to 50 years with informed consent were inclusion criteria in the study.

Hypersensitivity to drugs, patients with renal, liver or heart function disorders, morbidly obese, under anti-hypertensive medication, with anticipated

airway difficulties, taking analgesics prior to surgery, emergency surgeries were exclusion criteria.

The patients randomly assigned to receive Capsule Gabapentin (G group) for 600 mg of Gabapentin (two capsules of 300 mg each). After administration of Gabapentin, anesthesia was induced with fentanyl 1.5 mcg/kg and propofol 2 mg/kg body weight, followed by succinylcholine 2 mg/kg IV.

- Nil or grade 0: Absence of muscle pain
- Mild or grade 1: Stiffness limited to one area only or muscle stiffness or pain on specific questioning in nape of neck, shoulders and lower chest on deep breathing.
- Moderate or grade 2: Muscle pain or stiffness noticed spontaneously by patient, which may require analgesic therapy
- Severe or grade 3: Incapacitating generalized muscle stiffness or pain.

All information recorded in data collection sheet and statistical analysis of the continuous data analysed by Student's t-test while the categorical data by the chi-square test. Data processing work

Following administration of succinylcholine, oral endotracheal intubation was performed after one minute of succinylcholine injection and anesthesia was maintained with a mixture of Nitrous Oxide and Oxygen (2:1) and Halothane 0.5% using a Bain's coaxial circuit.

Controlled ventilation was facilitated, SBP, DBP, MAP, heart rate and SpO2 was recorded at regular intervals, i.e. Immediately after intubation, just after intubation and 3 minutes and 5 minutes after intubation and monitoring was continued at 15 minutes interval intraoperatively. At the end of surgery, neuromuscular blockade will be reversed by neostigmine and atropine.

All patients had same standard monitoring and analgesia postoperatively. Post-operative myalgia was recorded after 12 hrs, 24 hrs and 36 hrs of surgery. The grading of myalgia performed as follows:

consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data. The data were analyzed by using SPSS latest version. "P" value <0.05 was considered as significant.

RESULTS:

Table- I : Age distribution of the patients (N=30)

Age (years)	Number of patients
	Group G **(n=30)** *n(%)*
20-30	7(23.3%)
31-40	19(63.3%)
41-50	4(13.3%)
Mean ± SD	33.27±9.6

Total 30 patients were studied for myalgia.

Table- II: Sex distribution of the patients (N=30)

Sex of the respondents	Number of patients
	Group G (n=30) *n(%)*
Male	23(76.7%)
Female	7(23.3%)

Total of 30 patients were studied where 23 were male and 7 were female.

Table- III: Distribution of the study patients according to types of ASA status (n=30)

ASA status	Group G (n=30)	
	n	*%*
I	19	63.3
II	11	36.6

Table shows ASA status of the study patients, it was observed that 19 patients had ASA grade I & 11 patients had ASA grade II in group G.

Table- IV: Showing change of MAP of study patients in 1st hour (n=30)

Time point after general anaesthesia	Mean arterial pressure –MAP (mmHg)
	Group G (n=30)
Preanaesthesia	69.60±11.6
5 min after	83.45±8.2
10 min after	85.40±7.9
15 min after	76.92±8.1
20 min after	76.31±8.6
30 min after	75.57±10.2
45 min after	71.05±9.3
60 min after	59.55±6.8

After 15 minute and 20 minute of anesthesia MAP was decrease then it continued to decrease.

Table- V: Assessment of severity of myalgia at different follow-up time (n=30)

Myalgia	Group G (n=30)	
	N	*%*
After 12 hours		
Grade 0	18	60.0
Grade 1	7	23.4
Grade 2	5	16.7
Grade 3	0	0
Mean±SD	0.56	
After 24 hours		
Grade 0	23	76.7
Grade 1	6	20.0
Grade 2	1	3.3
Grade 3	0	0
Mean±SD	0.26	
After 36 hours		
Grade 0	30	0
Grade 1	0	0
Grade 2	0	0.0
Grade 3	0	0.0
Mean±SD	0	0

Table shows the grading of myalgia in group. After 12 hours, 7(23.4%) patients of group-G had grade 1 and 5(16.7%) patients of group-G had grade 2 with mean score 0.56. After 24 hours, 6(20.0%) patients of group-G had grade 1 and 1(3.3%) patient of group-G detected grade 2 with mean score 0.26. After 36 hours, none of the case was detected myalgia.

Table -VI: Showing averages of myalgia in patients (n=30)

Myalgia	Group G (n=30)
	Mean±SD
After 12 hours Mean±SD	0.56±0.01
After 24 hours Mean±SD	0.26±0.005
After 36 hours Mean±SD	0

Table shows theat after 12 hours, mean score 0.56 in group G. After 24 hours, mean score 0.26 and after 36 hours, none of the case was detected myalgia. So precise control of myalgia was managed by drugs.

DISCUSSION

Succinylcholine is the best drug for rapidly providing ideal intubating condition. Its use is associated with postoperative myalgia. Smith I et al described incidence of myalgia after using succinylcholine ranges from 41% to 92%. Total 30 patients were studied to determine the effectiveness of pretreatment with Gabapentin on succinylcholine-induced postoperative myalgia.[13]

In present study, majority of cases were between 31-40 years of age. Mean age of group G is 33.27. Heart rate and mean blood pressure were decreased in G group but all readings were within physiological limit.

In this study 60% patient of group G did not experienced myalgia after 12 hrs. Wong SF in 2000 showed that the incidence of postoperative myalgia due to succinylcholine varies, being as high as 90% and generally thought to be approximately 50%1. The myalgia was described as similar to the pain or muscle soreness experienced after a significant physical activity8. The duration and intensity of this discomfort is highly variable. The different grades of muscle fasciculations observed are also shown in the same table. 26.7% patients developed mild and moderate fasciculations.[14-16]

The mechanism for the postoperative myalgia has not completely been elucidated. Postulated mechanisms include increased intracellular calcium concentrations, membrane phospholipid degradation, and release of free fatty acids and free radicals, which lead to increased membrane permeability.[17-19] It has been proposed that the pain occurs due to muscle damage produced by shearing forces associated with the fasciculations at the onset of phase one block.[20]

In our study, myalgia was experienced by 40% patients. In present study 12 out of 30 patients in gabapentin group experienced myalgia. Pandey CK

et al showed that in gabapentin group, 15 patients out of 35 had myalgia whereas 24 patients out of 35 had myalgia in the placebo group which was statistically significant. So, gabapentin could be used to prevent suxamethonium induced myalgia

CONCLUSIONS:

Pretreatment with magnesium sulphate had better result reducing incidence of myalgia than gabapentin. Magnesium sulphate significantly reduces the severity of myalgia in early postoperative period rescue drugs consumption. Therefore it can be used to prevent succinylcholine induced myalgia.

- Small sample size was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size.
- " We studied one dose; different doses can be studied.

Pretreatment with gabapentin can be used for prevention of suxamethonium induced myalgia if available.

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Original Article

Non-Alcoholic Fatty Liver Disease: "Ultrasographic diagnosis and Lipid Profile".

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ABSTRACT

BACKGROUND: *In Non-Alcoholic Fatty Liver Disease (NAFLD), there is excessive accumulation of triglyceride (IHTG) in liver. The prevalence of NAFLD is increasing globally. The growth of NAFLD as an epidemic is related to increasing prevalence of obesity and sedentary life-style. Risk factors for NAFLD include age, sex, central obesity leading to insulin resistance and development of metabolic syndrome.* ***OBJECTIVE:*** *The objective of this study was to evaluate NAFLD non-invasively by ultrasound and to compare ultrasonographically diagnosed various grades of fatty liver disease with serum lipid profile of the patient.* ***MATERIALS AND METHOD:*** *Patients (age more than 18 years) who presented to the Medicine and Gastroenterology (out-patient) departments of Enam Medical College between January 2018 and August 2018 with a ultrasonographic diagnosis of having fatty liver and who had no history of alcohol intake have been included in this study. Their fasting lipid profile were asked to do in the following morning. The results were recorded and analysis in SPSS 16. P value was calculated by using Analysis of variance test (ANOVA) and P value <0.05 was considered statistically significant.* ***RESULTS:*** *Total number of participants were 140; among them 83 were male (59.3%) and 57 were female (40.7%); the mean age of the participants were 40.79 + 13.21 years. Among the total 140 patients, 65.00% had grade-I fatty liver, 22.86% had grade-II and 12.14% had grade-III disease. Serum total cholesterol, LDL and triglycerides, levels were above normal in 20.71%, 15.71% and 67.14% patients respectively. Serum HDL levels were below normal in 70.17% of patients. It was observed that increasing grades of NAFLD (Grade-I, Grade-II, and Grade-III) were significantly associated with increasing levels of serum total triglycerides (P value-0.0009), and decreasing levels of serum HDL (P value-0.0053). It was also observed that, triglyceride levels have significantly increased as age increased, (P value-0.0016).* ***CONCUSSION:*** *Non-invasive technics like ultrasonography and simple blood test like lipid profile may help us to screen more cases of NAFLDs. This may help us to proceed further to confirm and treat them with life-style modification and with other early interventions.*

Key words: Non-Alcoholic Fatty Liver Disease, lipid profile, hyperechogenicity,

INTRODUCTION:

The hallmark feature of Non-Alcoholic Fatty Liver Disease (NAFLD) is steatosis, means excessive accumulation of intrahepatic triglyceride (IHTG). Steatosis, has been chemically defined as IHTG content >5% of liver volume or liver weight,[1] or histologically defined when 5% or more of the hepatocytes contain visible intracellular triglycerides (TG).[2]

NAFLD covers a wide histopathological range of disease and subtypes varies from simple steatosis with very mild inflammation to more aggressive necro-inflammation to fibrosis and ultimately liver cirrhosis and finally hepatocellular carcinoma (HCC). Non-alcoholic steatohepatitis (NASH) is presumed to progress into cirrhosis in quarter of the affected person[3].

The growth of NAFLD as an epidemic is related to increasing prevalence of obesity and sedentary life-style. Risk factors for NAFLD include age, sex, central obesity, leading to insulin resistance and

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development of metabolic syndrome. The genetic predisposition is also presumed to have a role as the prevalence varies amongst different ethnic groups[4,5].

NAFLD was believed to be a disease of the developed world, but various studies now have been highlighted NAFLD as a global epidemic. Studies have suggested a wide amount of diversity in prevalence based on the country of interest. The average prevalence in Europe is 20-30%, in China 5-24% and in India between 16-32%. This is believed to be due to the increasing industrialization, along with changes in lifestyle and diet. Although, NAFLD is associated with high body mass index (BMI) in western world; it can also affect seemingly nonobese Asians. This has revealed a new concept of lean NAFLD[6-9].

In the context of Bangladesh, about one-third of the population of Bangladesh is affected by NAFLD. Individuals with higher body mass index (overweight and obese), diabetics, midlife adults, married individuals, and rural women are more at risk of having NAFLD than others.[10] Bangladesh is experiencing an increasing trend of NAFLD due to changing dietary patterns and sedentary lifestyles.[11-13]

The World Health Organization (WHO) has been documented in May 2014, stating that 2.82% of total deaths in Bangladesh are due to liver diseases. It is the eighth most common cause of death in Bangladesh; the age adjusted death rate is 19.26 per 1,00,000 populations.[11-14] Chronic liver diseases (CLDs) are responsible for 37-69% of liver diseases in Bangladesh, and NAFLD is a significant contributor to the burden of chronic liver diseases.[13]

Most patients with NAFLD have no symptoms or signs of liver disease at the time of diagnosis, although many patients report fatigue or malaise and a sensation of fullness or discomfort on the right side of the upper abdomen. Hepatomegaly is the only physical finding in most patients.[15]

A NAFLD classification system (grade-I to grade-III) has been proposed, that correlates certain histologic features and with the long-term prognosis [16,17]. In this classification system: Grade-I constitute simple steatosis, Grade-II is steatosis with lobular inflammation and ballooned hepatocytes and Grade-III is steatosis, lobular inflammation, ballooned hepatocytes and mallory hyaline or fibrosis.

The objective of this study was to evaluate NAFLD non-invasively by ultrasound and to compare ultrasonographically diagnosed various grades of fatty liver disease with serum lipid profile of the patient.

Grading of non-alcoholic fatty liver on ultrasonography

The grade of fatty liver was recorded, mild (grade-1), moderate (grade-II), or severe (grade-III) according to the findings of liver brightness, hepatorenal echo contrast, deep attenuation of the ultrasound signal, and the blurring of vessels.

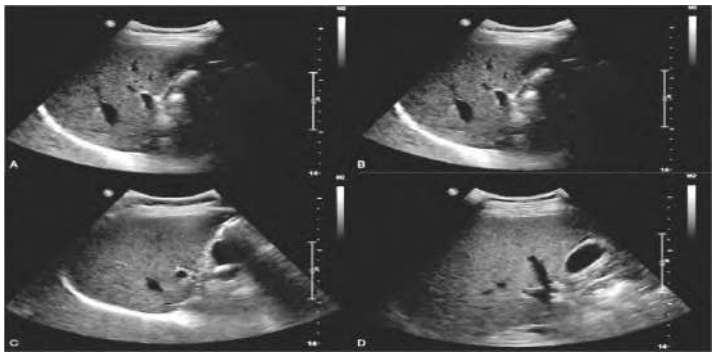

Figure 1 shows: Normal liver echogenicity (A); Mildly fatty liver or Grade-I: diffusely increased hepatic echogenicity with appreciable periportal and diaphragmatic echogenicity (B). Moderately fatty liver or Grade-II: diffusely increased hepatic echogenicity obscuring periportal echogenicity, but diaphragmatic echogenicity is still appreciable (C). Severely fatty liver or Grade III: diffusely increased hepatic echogenicity obscuring periportal, as well as diaphragmatic echogenicity (D).

MATERIALS AND METHOD

Patients (age more than 18 years) who presented to the Medicine and Gastroenterology out-patient department of Enam Medical college in between January 2018 and August 2018 with a ultrasonographic diagnosis of having fatty liver are requested to participate in this study.

Subjects were considered as a case if they have fatty liver according to the standard criteria accepted by the American Gastroenterology Association i.e., an increase in hepatic echogenicity as a reference, the presence of enhancement and lack of differentiation in the periportal intensity and the vascular wall due to great hyperechogenicity in the parenchyma. The degree of involvement was standardized with a semi quantitative scale of the degree of hepatic involvement. The diagnosis of hepatic steatosis was made on the basis of characteristic sonographic features: increased echogenecity of liver; increased liver contrast compared to kidney; vascular blurring, mainly of portal veins; attenuation of echogenic level in deep seated area.

The patients who had negative history of alcohol intake and gave consents to participate in the study are included in this study. Total participants in this study were 140 and they were considered as having ultrasonographically proven NAFLD.

Participants were asked about their symptoms if they had any and were investigated for fasting serum lipid profile; total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglyceride. Serum lipids were considered normal when, total cholesterol was <200 mg/dL, HDL was >40 mg/dl in female & >50 mg/dL in male, LDL was <130 mg/dL and Triglyceride was <150 mg/dL.

The actual levels of various lipid were recorded with few additional information like age, sex and their alcohol intake history; a structured questionnaire was used in this purpose. The results were recorded and analysis in SPSS 16. P value was calculated by using Analysis of variance test (ANOVA) and P value <0.05 was considered statistically significant.

RESULTS:

Prevalence: Among 140 ultrasonographically diagnosed NAFLD cases included in the study, 65.00% had grade-I, 22.86% had grade-II and 12.14% had grade-III disease.

Age & Sex and Prevalence: Among them, 83 (59.3%) were male and 57 (40.7%) were female. The mean age of the participants were 40.79 years with a standard deviation of 13.21 years.
Table I shows the distribution of patients according to their sex and grades of NAFLD.

Table I: Distribution of patients according to the sex and NAFLD grade

	Male	Female	Total	Percentage
Grade-I	51	40	91	65.00
Grade-II	22	10	32	22.86
Grade-III	10	7	17	12.14
Total	83	57	140	

The majority of patients, 40.00% were in 31 to 45 years' age group, followed by 27.9% in the age group of 30 years and below, 22.10% in the age group between 46 to 60 years and 10% belongs to the age group 65 years and above.

Table II shows patients having different grades of NAFLD according to their age group.

Table II: Distribution of patients according to the age and NAFLD grade

	Grade I	Grade II	Grade III	
30 years and below	**27**	**7**	**5**	39
31 to 45 years	**35**	**17**	**4**	56
46 to 60 years	**18**	**6**	**7**	31
61 years and above	**11**	**2**	**1**	14
Total	**91**	**32**	**17**	140

Age & Sex and Lipid profile: Serum total cholesterol, LDL and triglycerides, levels were above normal in 20.71%, 15.71% and 67.14% patients respectively. Serum HDL levels were below normal in 70.17% of patients.

Table III shows distribution of patients as per their lipid profile in various sex and age groups.

Table III: Distribution of patients, showing abnormal serum lipid profile in various age group

	Total Cholesterol		HDL		LDL		Triglyceride	
	Normal	High	Normal	Low	Normal	High	Normal	High
Age of the patients in groups								
30 years and below	32	7	12	27	34	5	15	24
31 to 45 years	47	9	20	36	50	6	23	33
46 to 60 years	20	11	3	28	22	9	5	26
61 years and above	12	2	6	8	12	2	3	11
Sex of the patients								
Male	67	16	21	62	73	10	29	54
Female	44	13	20	37	45	12	17	40

Signs and symptoms: More than 50% (76 out of 140) patients were asymptomatic, remaining 64 patients have symptoms like upper abdominal pain, discomfort & feeling of heaviness in the abdomen, malaise & fatigue and a few presented with mild hepatomegaly (Table IV shows).

Table IV: Showing signs and symptoms in NAFLD patients.

Symptoms	Grade I	Grade II	Grade III	
Asymptomatic	54	17	5	76
Abdominal pain, discomfort & heaviness	35	12	9	56
Malaise	18	6	7	31
Fatigue	13	10	6	29
Hepatomegally	7	7	3	17

Lipid values in different age group: Table V shows comparison of changes of lipid values in different age groups of patients. It was observed that there was no significant relationship exist between changing in lipid values with increasing age except triglycerides, the level of which has significantly increased as age increased, (P value-0.0016).

Table V: comparison mean lipid values and SD within various age group

	30 years and below		31 to 45 years		46 to 60 years		61 years and above			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F-Stat	P-Value
Total Cholesterol	191.90	91.02	173.88	38.05	187.81	45.05	166.50	49.52	1.1022	0.3506
HDL	41.21	8.52	41.23	10.73	36.25	7.63	40.79	13.12	2.0859	0.1049
LDL	114.90	14.70	110.47	17.04	118.46	23.62	107.43	27.62	1.6796	0.1742
Triglycerides	174.97	43.23	202.13	79.38	240.26	78.89	225.93	74.40	5.3811	0.0016

Lipid values in different grades of NAFLD: Table VI shows comparison of changes of lipid values in different grades of NAFLD. It was observed that increasing grades of NAFLD had statistically significant association with increasing levels of serum total triglycerides (P value-0.0009), and statistically significant association with decreasing levels of serum HDL (P value-0.0053). But association between increasing grades of NAFLD with increasing levels of total cholesterol and LDL was not statistically significant.

DISCUSSION

In our study, we found two-third of our patients (65.00%) had grade-I fatty liver disease. This defers from a study done by Dhumal Uttareshvar Mahaling et al; they found little less than half (47.15%) of their patients had grade-I and 42.85% had grade-II disease. they also found serum triglycerides, total cholesterol, LDL and VLDL levels were raised in 67.14%, 45.71% 34.28%, 25.71% of participants respectively; low serum HDL levels were seen in 62.85% of patients.[18] But in our study, we found serum total cholesterol, LDL and triglycerides, levels were above normal in 20.71%, 15.71% and 67.14% patients respectively; serum HDL levels were below normal in 70.17% of patients. In another study, Roli Agrawal et al reported hypertriglyceridemia in 63.7%, hypercholesterolemia in 50%-80% patients, elevated LDL in 25% patients and elevated VLDL in 56.5% patients. They also reported low HDL in 45.16% of patients.[19]

Most of the patients with NAFLD are asymptomatic. The disease is discovered either incidentally during routine laboratory examination or when the patient is investigated for conditions like hypertension, diabetes or obesity. In our study, 76 (> 50%) patients were asymptomatic. Different studies done in India, have reported 30.8 to 38% patients to be asymptomatic which is much lower than our finding. But we found similarity with few other studies done in developed countries, reported 47.7 to 64% patients to be asymptomatic.

We found that increasing grades of NAFLD has statistically significant association with increasing levels of serum total triglycerides (P value-0.0009), and with decreasing levels of serum HDL (P value-0.0053).

Other plasma lipid values have also increased with increasing grades of NAFLD, but association did not show statistical significance at 95% confidence interval level (P-values are 0.8268 and 0.1038 for total cholesterol and LDL-cholesterol). But another study done in India, they found increasing grades of NAFLD had statistically

significant association with increasing values of total cholesterol (P value-0.001), LDL (P value-0.000) and VLDL (P value-0.003) and decreasing values of HDL (P value-0.000).[20] Increasing serum triglyceride values also shown significant association with increasing age of the participants.

Our aim was to evaluate NAFLD with ultrasonography and to compare the ultrasonographic gradings of NAFLD with serum lipid profile to find out association between these two investigations. Liver biopsy is a sensitive method for diagnosis of NAFLD. However, liver biopsy is a painful and invasive procedure[21] with rare, but potentially life-threatening complications like bleeding [22,23] and is prone to sampling errors [24,25]. In addition, given the numbers of patients with NAFLD, the use of liver biopsy is clinically and financially impractical.

Ultrasonography can be used for the early detection of NAFLD. Sonographically diagnosed NAFLD patients showed statistically significant association with serum HDL and serum triglyceride. Ultrasound is the least expensive modality for detecting changes associated with NAFLD and Lipid profile may add up more information towards confirming NAFLDs.

CONCLUSION

This is an observational study only; just to find out association between NAFLD and serum lipid profile. As the current trend of NAFLD is increasing in developed countries as well as in different Asian countries including Bangladesh, non-invasive technics like ultrasonography and simple blood test like lipid profile may help us to diagnose more cases of NAFLDs. This may help us to proceed further to confirm and treat them with life-style modification and with other early interventions.

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Orginal Article

Evaluation of Vitamin D Level Among Type 2 Diabetic Chronic Kidney Disease Stages-3 to 5 Pre-dialysis Patients

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ABSTRACT

BACKGROUND: *Diabetes mellitus is a group of metabolic disorders with various etiologies that are characterized by hyperglycemia due to a lack of insulin secretion, insulin action, or both. The most common cause of chronic kidney disease (CKD) is diabetic nephropathy. CKD is frequently misdiagnosed and undertreated due to its slow onset, unpredictable course, and long time to overt renal failure. In people with CKD, vitamin D deficiency is more common, and it worsens as the disease progresses.* ***OBJECTIVE:*** *To evaluate vitamin D level among type 2 diabetic chronic kidney disease stages 3 to 5 pre-dialysis patient.* ***METHODS:*** *This cross-sectional study was conducted in the Department of Biochemistry, molecular biology, and nephrology, BIRDEM, Dhaka, from July 2016 to June 2017. In this study, 138 subjects were enrolled (21-stage 3, 43-stage 4 and 74-stage 5 CKD patients). Stages of CKD were assessed by calculating eGFR. The ANOVA test and Pearson's correlation coefficient test were done to determine the association between vitamin D status and the stages of CKD. Vitamin D was measured by HPLC. SPSS (12) was used for data analysis.* ***RESULTS:*** *The Mean of serum vitamin D concentration of type 2 diabetic CKD was 9.81±8.48 in stages 3, 8.56±6.62 in stage-4 and 4.84±3.53 in stage 5 pre-dialysis patients ($p<0.001$). Vitamin D deficiency was observed in CKD patients in a decreasing trend from stage 3 to stage 5 pre-dialysis patients. Vitamin D concentrations differed significantly across CKD stages ($p=0.001$). Vitamin D was found to have a significant positive correlation with eGFR in type 2 diabetic CKD patients ($r=0.426$; $p=0.001$).* ***CONCLUSIONS:*** *This study found that low vitamin D levels decreased as CKD progressed from stage 3 to stage 5. The vitamin D level positively correlated to eGFR.*

Key Words: Type 2 Diabetes, CKD, eGFR, Vitamin D.

INTRODUCTION:

Diabetes mellitus is a group of etiologically distinct metabolic disorders characterized by hyperglycemia caused by a defect in insulin secretion, insulin action, or both.[1] It affects nearly 6.28 percent of the world's population.[2] According to the International Diabetic Federation (ADA), 381.8 million people worldwide had diabetes in 2013, and this figure is expected to more than double by 2035.[3]

According to a recent meta-analysis, the prevalence of diabetes in Bangladesh increased significantly from 4% in 1995 to 2000, 5% from 2001 to 2005, and 9% from 2006 to 2010. The International Diabetic Federation predicts that by 2035, the prevalence will be 10.1 percent.[3]

Diabetes' chronic hyperglycemia is linked to long-term damage, dysfunction, and failure of various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels.[4] In the developed world, diabetes is the leading cause of chronic kidney disease. Approximately 40.0% of diabetics developed CKD.[5] The global prevalence of CKD is estimated to be 8-10%.[6]

Vitamin D plays wide range of functions in our body such as regulation of mineral homeostasis, bone remodeling and in immune system, also plays important role in β-cell functions, insulin sensitivity and secretion by both direct and indirect actions. Vitamin D directly acts on Vitamin D receptor, enhances the transcriptional activation of insulin gene, and thus increases insulin secretion. Vitamin D stimulates expression of insulin receptor and thus

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improves insulin sensitivity. Indirectly vitamin D can affect insulin resistance by regulating Renin Angiotensin Aldosteron System. In the tissue of vascular and skeletal muscle, action of insulin is inhibited by Angiotensin II thus causes impaired glucose uptake.[7]

Recent studies in the general population have revealed a high prevalence of vitamin D deficiency, which is even more prevalent in patients with chronic kidney disease (CKD).[8] Vitamin D deficiency has also been linked to a decrease in renal 1α-hydroxylase activity, diabetes, and proteinuria in CKD patients.[9] It is estimated that one billion people around the world suffer from vitamin D deficiency or insufficiency.[10] Vitamin D deficiency is a common condition that affects between 30 to 50 percent of the general population.[11] This is higher in patients with chronic kidney disease (CKD) and increases as the disease progresses.[12]

There are several machanisms involved in the decreased levels of vitamin D that occur in the different stages of CKD. As a result, a decrease in renal mass will obviously limit the amount of 1α-hydroxylase available for the production of the active vitamin D metabolite. A decrease in GFR may limit substrate delivery to the 1α-hydroxylase, limiting the kidney's ability to produce vitamin D.[13] The aim of the study is to evaluate the vitamin D level of diabetic patients with different stages of CKD 3 to 5 in BIRDEM General Hospital.

METHODS:

This Cross sectional study was conducted in the Department of Biochemistry and Molecular Biology and Nephrology, BIRDEM, Dhaka from July 2016-June 2017 over a period of one year. According to the selection criteria, 138 Type 2 diabetes mellitus patients of both sexes aged 40 to 70 years with chronic kidney disease stage 3 to 5 who had not undergone dialysis were enrolled in this study from the Inpatient Department of Nephrology, BIRDEM, General Hospital. Patients with Acute kidney disease, chronic liver disease, disorder of parathyroid gland and malabsorption syndrome were excluded from this study.

A structured questionnaire was filled up for each patient after taking informed written consent. Type 2 diabetes mellitus was diagnosed according to the World Health Organization criteria and chronic kidney disease was diagnosed according to the National Kidney Foundation. Blood sample was collected from study subjects after an overnight fasting of 10-12 hours. 8 ml venous blood was drawn from the anterior cubital vein in a disposal syringe with an aseptic precaution.

The ANOVA test was used to compare different parameters between CKD stages. All statistical tests were considered significant at the 5% level ($p<0.05$ was used as the test of significance). Pearson's correlation coefficient test was used to determine the statistical significance, direction, and strength of linear correlation between two quantitative variables. All statistical analyses were carried out using the SPSS for Windows (Statistical Package for Social Science) 12 versions software.

RESULTS:

Table I: Distribution of study participants according to stages of CKD (N=138)

CKD stages	Frequency (n)	Percentage (%)
Stage 3 (eGFR: 30-59)	21	15.2
Stage 4 (eGFR: 15-29)	43	31.2
Stage 5 (eGFR: <15)	74	53.6

In this study 15.2% were stage 3 CKD, 31.2% were stage 4 CKD and 53.6% were stage 5 CKD patients.

Table II: Statistical analysis of vitamin D level (mean ± SD) of the study participants (n=138)

CKD stages	Mean ± SD (ng/dl)	P value
Stage 3/ Stage 4	9.81±8.48 / 8.56±6.62	<0.05*
Stage 3/ Stage 5	9.81±8.48 / 4.84±3. 53	<0.001***
Stage 4/ Stage 5	8.56±6.62 / 4.84±3. 53	<0.001***

Stasistical analysis was done by anova test to compare among groups.
*= Significant
*** = Highly significant

The mean ± SD vitamin D levels were 9.81±8.48 ng/dl in stage 3, 8.56±6.62 ng/dl in stage 4 and 4.84±3.53 ng/dl in Stage 5.

In this Study differences of mean Vitamin D level were compared between stage 3 and stage 4, stage 3 and stage 5, stage 4 and stage 5. The mean vitamin D levels were significantly ($p < 0.001$) lower in stage 4 than stage 3, stage 5 than stage 3 and stage 5 than stage 4 (Table II). The serum vitamin D was significantly decreased according to the progression of CKD ($p<0.001$).

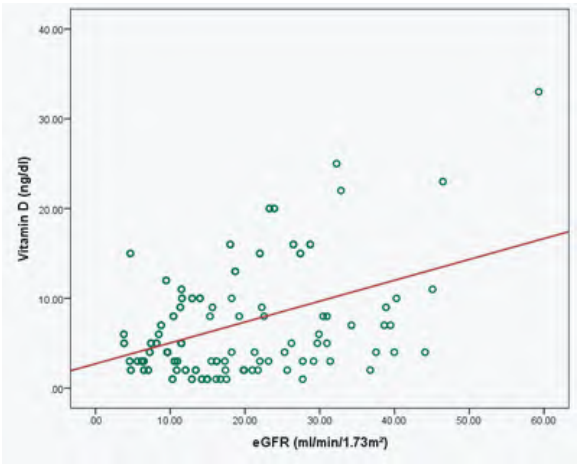

Figure 6: Correlation of Vit D with eGFR

DISCUSSION

A total of 138 subjects were enrolled in the study, with 21 being stage 3, 43 being stage 4, and 74 being stage 5 CKD patients based on eGFR. In this study, vitamin D levels were found to be significantly lower as CKD progressed ($p<0.001$). This finding is consistent with the findings of numerous other studies.[12,14]

The Pearson correlation coefficient test was used to assess the relationship between renal function loss as measured by eGFR and vitamin D levels. There was a statistically significant ($p<0.001$) positive correlation. The findings were consistent with the findings of Aggarwal et al.[14]

This study is supported by Lu et al.[15], who found no significant difference in BMI in advanced stages of CKD. Hossain et al.[16] and Inassi and Vijayalakshmy[17] found an association between long duration of diabetes and the development of diabetic nephropathy, but this study did not.

Low vitamin D levels in type 2 diabetic CKD stage 3,4 & 5 patients could be due to proteinuria, low physical activity, diabetes mellitus, impaired tubular reabsorption, reduced skin synthesis, calcineurin inhibitor prescription, reduction of liver CYP 450 isoform in SGPT and reduced VDR(vitamin D receptor). Because vitamin D level was measured in a single laboratory, the comparison of vitamin D levels across stages was deemed valid. This study suggests that a longitudinal study among type 2 diabetics with CKD stages 3, 4, and 5 pre-dialysis patients, can provide purposeful awareness about vitamin D level screening in type 2 diabetic CKD patients.

CONCLUSIONS:

According to the findings of this study, vitamin D level is decreasing in the course of CKD from stage 3 to stage 5, as measured by levels of 25 hydroxy vitamin D. Vitamin D level was found to be positively related to eGFR. This research can help clinicians manage advanced stages of CKD more effectively. This will allow for the initiation of early treatment as well as the avoidance of complications.

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ORIGINAL ARTICLE

Comparative Study between Caudal Block and Penile Block for Postoperative Analgesia Following Circumcision

Mohammad Abu Taher[1], Md Mushfiqur Rahman[2].

ABSTRACT

BACKGROUND: *Circumcision is a frequently performed surgery in children worldwide. For circumcision, penile and caudal epidural blocks are commonly used. Nerve blocks not only decrease the systemic analgesia requirement intraoperatively but also increase the length of pain relief postoperatively.* ***OBJECTIVES:*** *The aim of the study was to compare the postoperative analgesia efficacy following circumcision between caudal block and penile block.* ***MATERIALS AND METHODS:*** *This study was conducted in pediatric patient scheduled for circumcision. Total 60 samples (n=60) were taken and divided into two groups of 30 each. The group C received caudal block and group P received penile block. The blocks were performed after general anaesthesia. The patients were keenly observed for change in heart rate and all other vital parameters in both groups. The postoperative consumption of pain killers were also noted in both the groups.* ***RESULTS:*** *In group C patients with caudal block did not show any significant surgical response, whereas group P patients with penile block showed increased heart rate during surgery. There was no complain of pain in group C in the recovery period, whereas complains of pain were recorded in most of the children in Group P, hence pain killers were given to the patients in this group.* ***CONCLUSION:*** *It can be concluded from this study that caudal block was better than penile block for pain relief following circumcision.*

Key words: : Caudal block, Penile block, Analgesia, Circumcision.

INTRODUCTION:

Circumcision is a painful intervention that is frequently performed in pediatric surgery.[1] To eliminate fear and anxiety, it is generally performed under general anaesthesia.[2] Postoperative pain relief is an important aspect of surgery. It decreases morbidity, helps in early rehabilitation of the patient and decrease the need for narcotic analgesics.[3] There is evidence that inadequate postoperative pain relief may have deleterious effects on the patient's recovery and return to daily life activities.[4] Children are more prone to behavioral problem due to fear of pain.[5] Regional techniques are more effective than systemic opioids, non-steroid anti-inflammatory drugs and acetaminophene for postoperative analgesia in circumcision.[6] The most preferred techniques are caudal epidural block and penile block.[7]

Penile block has been commonly used for postoperative analgesia. The efficacy of penile block is well established. Penile block can either be based as anatomical landmarks or ultrasound guided.[8] The penile block is safe and effective method as well.[8] The penile block as compared to the caudal block does not cause sensory or motor block to the lower limbs and the patient can ambulate early.[9]

Caudal block is a cheap, easy and effective method used in pediatric surgery as a postoperative analgesia and as sole anaesthetic technique.[10] Caudal block is used as an adjunct to general anaesthesia in many procedures below the level of umbilicus. Caudal anaesthesia provides

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good postoperative analgesia. As compared to penile block, caudal anaestheia is technically demanding. The duration of postoperative analgesia depends on the anaesthetic used, concentration and dose of the drug. Urinary retention, systemic toxicity because of needle displacement into vessels and intrathecal displacement causing total spinal anaesthesia are some of the drawbacks of the caudal block.[11] It also adds to the duration of patient's time in operating room.

Pain is one of the most complicated, under-diagnosed and untreated medical problems, particularly in children. Postoperative pain may result in non-cooperative and restless child. Postoperative pain is a subjective feeling and accurate measurement is difficult in children. Several methods are used to determine the intensity of pain. Most of these methods rely on the facial expression and behavior of the pediatric patient.[12]

In this study, we aim to find out the comparison of postoperative analgesia efficacy of caudal block versus penile block for elective circumcision cases.

MATERIALS AND METHODS:

This comparative study was carried out at Prime Medical College Hospital, Rangpur from January 2019 to June 2019. After obtaining institutional approval and parents written consent, 60 patients (each group 30) of ASA grade I, aged 3-10 years were scheduled for elective circumcision surgery. They were randomized into two groups, group C (n = 30) patients were given caudal block and group P (n=30) patients were given penile block. Patients were excluded if they had any systemic disease, seizure disorder or any neurological or spinal cord disorder or any coagulopathy or any infection of skin or any subcutaneous tissue at the site of injection. All children were fasted before operation and were taken to the operating room in the morning. Peripheral IV access with 24 G IV cannula was secured. Anaesthesia was delivered with intravenous bolus of propofol (2 mg/kg) until loss of eyelash reflex with oxygen inhalation via facemask.Group (C) Caudal block (n = 30): After the patient is positioned in the left side, the sacrococcygeal area is sterilized with viodine solution and sterile wraps were applied. The sacral hiatus is localized and punctured with a needle before the ventral wall of sacrum is reached, inclined before the lack of resistance due to the dural puncture occurs, placing it horizontally and then advanced to the cephalad when sucking. Confirmation of correct placement of the normal hypodermic needle is done by injection of 1 to 2 ml of air while a stethoscope is fixed over the lumbar vertebrae. If there is no formation of weal in the subcutaneous tissue, the anaesthetic is injected bupivacaine 0.25% (1mg/kg) slowly with frequent aspiration during the injection.

Group (P) Penile block (n=30): After the patient has been put in a supine position with exposed genitalia, the area is sterilized with viodine solution and sterile wraps were applied. Using 27G needle to lift the skin wheals at 2 and 10 o'clock levels and then gradually introduce the needle within the middle of each skin wheal. The needle is guided to the middle of the shaft deeply for about 0.5 cm or to the point where the lack of resistance is felt to indicate that the tip is within the Buck fascia. Aspirate to make sure that the needle is not in the blood vessel and gently inject about 2 ml of bupivacaine 0.25% on each side.

Intraoperatively, Patients were monitored for heart rate, blood pressure and SpO2. After the completion of Surgery, patients were transferred to recovery room. All children were observed and recorded for pain, sedation and side effects (nausea, vomiting, penile haematoma, bleeding, motor block and urinary retention). Postoperative pain and sedation scores were assessed on the 10th, 30th minutes and 1-6 hours by nurses and parents. For follow-up of postoperative pain, the FLACC pain scale (Table I) was used and for the sedation follow- up, the Ramsey sedation scale (Table II) was used.

Table I: FLACC pain evaluation scale[13]

Categories	0	1	2
Face expression	No special expression	Slight frowning grimace	Mop, teeth clenching
Feet	Normal position	Tight, stressful	Kick at anybody
Activity (movements)	Calm	Tum around	Hop off, jerk
Crying	No cry	Groan, moaning	Shouting, cry
Condolence	Relaxed	Consoled with hug or touch	Never consoled

Table II: Ramsey sedation scale[14]

1. Fully awake and oriented
2. Awake, sleepy
3 Asleep but easily awaken by verbal command
4. Asleep but easily awaken by motor stimulation
5. Asleep and cannot be awaken by verbal or motor stimulation

Table III: Demographic data (mean value± SD), anaesthesia and operation time.

	Group C (n=30)	Group P (n=30)	P
Age (years)	6±3	7±2	0.297
Weight (kg)	23±9	26±6	0.225
Duration of surgery (min)	26±9	33±2	0.078
Duration of anaesthesia (min)	52±10	58±13	0.073

The FLACC pain scale is a behavioral scale for scoring postoperative pain in young children. If the FLACC pain score was 5 or over, 2 mg/kg of diclofenac sodium suppository as a supplemental analgesia was administered. Probable local or systemic complications were recorded.

Table IV: Postoperative follow-up parameters

Follow up	Group C (n=30)	Group P (n=30)	P
The number of patients who were pain free for the first 6 hours	28 (93.3%	13 (43.3%)	0.0001
The number of analgesic administration (min)	458±73	376±68	0.000033
The number of paracetamol demand (in 24 hours)	(median=451) 2.1±0.6	(median=382) 2.4±0.7	0.102
The time to first walking (min)	(median=2) 163±32	(median=2) 134±27	0.004
The time to first micturition (min)	(median=158) 205±54	(median=130) 184±46	0.110
Motor block (0/1/2)	(median=190) 16/10/4	(median=172) 30/0/0	0.00007

Statistical analyses were performed using SPSS for windows 11.5. Continuous variables were presented as mean ± SD and median categorical variables were presented as frequencies and percentage. Significance level was stated at 0.05.

RESULTS

The total number of 60 patients was included in the study. These patients were divided into two groups, Group C (n=30) underwent caudal block and group P (n=30) underwent penile block. None of the patients were withdrawn from the study as neither group C nor group P had failed block. There was no difference in respect to demographic data (Age, weight, duration of surgery and duration of anaesthesia). None of the patients were reported due to bleeding and required rescue analgesics in operation theatre or post anaesthesia care unit.

Patients were allocated to each group by closed envelop method. There were no serious complications after caudal or penile block. A significant decrease in pain scores was found. The number of patients, who were pain free for the first 6 hours, was significantly higher in group P (28/30 [93.3%]) than group P (13/30 [43.3%]) (P=0.0001). The time to first analgesic administration were longer in group C (group C median = 451) and group P (group P median = 382) [P= 0.000033]. The rescue analgesic demand in 24 hours were similar between two groups (P=0.102). As might be expected, motor block occurred in 14 of 30 patients in group C (P = 0.00007). There was a delay in time to first walking in group C (C median = 158) and group P (P median = 130) [P = 0.004]. There was a delay in time to first micturition in group C (C median = 190 min) and group P (P median = 172 min). It was not statistically significant (P = 0.110).

The vitals of patients in both groups remain stable during operation and the incidences of emergence agitation were much less in both groups rather than the patients undergoing surgery under general anaesthesia without caudal block.

There was no major difference in sedation score between the two groups after recovery. Sedation scores (time to waking) were similar in both groups according to the Modified Aldrete kroulik Recovery scores at all times (p > 0.05).

All of the patients were discharged on the same day after being comfortable, mobile, tolerating oral fluids and passing urine (before 6 hours).

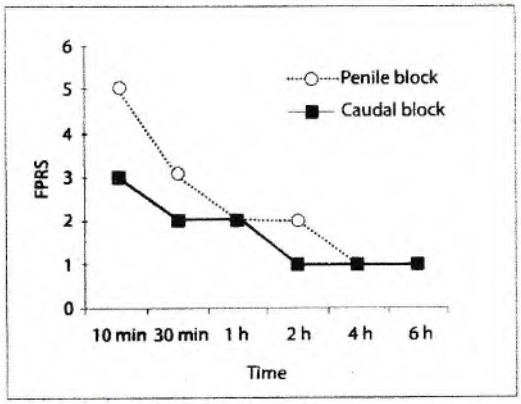

Figure 1. FPRS (Faces Pain Rating Scale) was lower in Group C on the 10th, 30 th minutes and 2nd hour ($p<0.05$).

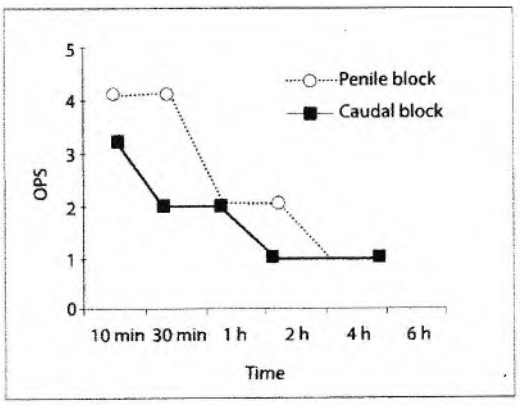

Figure 2. OPS (Observer Pain Score) was lower in Group C on the 10th, 30 th minutes and 2nd hour ($p<0.05$)

DISCUSSION

Mode of anaesthesia is very important regarding postoperative pain following circumcision surgery. Pain relief after surgery continues to be a major medical challenge despite improvement in understanding mechanism of acute pain. A randomized controlled trial of caudal block (group C) versus penile block (group P) in patients undergoing circumcision surgery was conducted to determine postoperative active pain. The study revealed that postoperative pain was significantly less with caudal block than penile block. For the measurement of pain, FLACC pain score based on five categories; face, leg, activity, cry, consol ability was used.[15]

Ease of performance and reliability makes caudal block the most commonly performed block in children. Caudal administration of bupivacaine is a widespread regional anaesthetic technique for effective postoperative analgesia and pain control following circumcision. Although, local anaesthetics are generally quite safe and effective, but they may affect heart and brain in case of inadvertent use. Therefore excessive doses of drugs, intravascular absorption and inadvertent intravascular or intraosseous application became more important.[16]

In connection with this study, a distinction was made between caudal and penile block with respect to postoperative pain score, rescue analgesia time and total analgesia dose. The current study discovered postoperative pain scores were significantly lower in caudal group than penile group. The duration of rescue analgesia was significantly longer in the caudal group compared to the penile group and the average dose of rescue analgesia was much higher in the penile group compared to caudal group.

Vater et al.[17] and Demiratan et al.[18] is have found that caudal block and penile block are generally effective and safe when applied for circumcision. Although Gauntlett[19] used lower dose of bupivacaine in caudal analgesia than in penile block. He reported statistically significant motor blocks and delayed micturition with no difference in the incidence of nausea and vomiting. They preferred penile technique to caudal block due to incidence of complication. But penile block provides analgesia just on the ¾ dorsal side of the penis, so caudal block should be superior in circumcision surgery.[20] Margetts et al.[21] used higher dose of caudal bupivacaine and compared with penile block. Bupivacaine provided better analgesia and did not affect the time to micturition or increase the incidence of adverse effects; but they reported delayed walking. Therefore they concluded that both techniques provided effective postoperative analgesia; but caudal block had a longer postoperative analgesia period. In a Cochrane review published in 2003, it is reported

that in children old enough to walk, penile block may be preferred over caudal block due to temporary leg weakness which is parallel to our study[22].

In this study, the time to first analgesic requirement and walking were longer in patients with caudal block Delayed time to first walking and better analgesia in the caudal block are also supported findings.

CONCLUSION

The use of either caudal or penile block in children undergoing circumcision is effective in postoperative analgesia. Caudal block using 0.25% bupivacaine is a better alternative for postoperative analgesia than penile block in circumcision23. The caudal block appeared to be more efficient than the penile block in lowering postoperative pain scores and decreasing the need for rescue analgesia by prolonging the length of the block.

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ORIGINAL ARTICLE

Evaluation of Parasympathetic Nerve Function by Heart Rate Response to Standing in Obese Adolescents

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ABSTRACT

BACKGROUND: *Increasing trend of obesity among adolescents is a worldwide phenomenon and considered as one of the major public health challenge of the 21st century. Obesity is an important and independent risk factor for non-communicable diseases and associated with parasympathetic nervous system dysfunction.* ***OBJECTIVES:*** *To assess parasympathetic nerve function by heart rate response to standing in obese adolescents.* ***METHODS:*** *This cross-sectional analytical study was conducted from July 2018 to June 2019 in the Department of Physiology, Rangpur Medical College, Rangpur. After obtaining permission, subjects who would meet the inclusion and exclusion criteria were enrolled in the study after briefing them objectives of the study. A total number of 60 adolescents were selected, among them 30 were healthy adolescents with normal weight (Group-A) and 30 were healthy obese adolescents (Group-B). The evaluation of parasympathetic nerve function in obese adolescents were done by heart rate in response to standing. The individuals were selected from different areas of Rangpur district. For statistical analysis unpaired t test was performed by computer based software SPSS-23.0 version for windows.* ***RESULTS:*** *Heart rate response to standing was significantly ($p<0.01$) lower in obese adolescents than those of normal weight adolescents.* ***CONCLUSION:*** *The study concluded that decrease heart rate response to standing in obese adolescents indicate in the parasympathetic nerve dysfunction.*

Key words: Obese, Adolescents, Parasympathetic nerve function, 30th : 15th ratio.

INTRODUCTION:

Overweight and obesity are recognized as an "escalating epidemic" affecting both developed and developing countries. Among adolescents, obesity has been observed as one of the serious public health challenges of the 21st century by World Health Organization (WHO).[1] Overweight and obesity are nutritional disorders emanating from calorie imbalances. These disorders develop when calorie consumption surpasses calorie expenditure and the excess calorie gradually accumulates which later results into abnormal weight gain.[2] Obesity is a condition of excess fat deposition in the body. Body mass index (BMI) is most widely used to categorize normal weight, overweight and obese populations.[3] The World Health Organization (WHO) recommends the cut off values of BMI for the definitions of overweight and obesity for Asian populations which are as normal weight: BMI 18.5 to 22.9 kg/m^2, overweight: BMI 23 to 24.9 kg/m^2 and obese: BMI $\geq$25 kg/m.[4]

Adolescence is the period of transition between childhood and adulthood. There are physical, intellectual, social and emotional changes occur during these period.[5] According to World Health Organization (WHO), adolescence as the period of life between the age of 10 and 19 years.[6] Adolescence is a crucial part of their life and is considered to be one of the critical periods for the

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development of obesity.[7,8] According to UNFPA and WHO, adolescents currently comprise one-sixth of the world's population and over 90% of adolescents live in sub-Saharan Africa and in South and South-east Asia in 2017.[9] There were about 36 million adolescents in Bangladesh, who make up about more than one-fifth of total population (BBS, 2015) and the obesity among boys was found 3% and 2.3% among girls in 2016.[10] According to World Health Organization (WHO), there were about more than 700 million obese aged 15 and above in 2015.[8] The prevalence of overweight and obesity among adolescents has risen dramatically from just 4% in 1975 to just over 18% in 2016 and has increased over the last three decades particularly in Asia.[2,11] Over the past 30 years, the prevalence of obesity has quadrupled among adolescents in the United States.[12]

All obese individuals are overweight but all overweight individuals are not necessarily obese.[4] Overweight and obesity negatively affects body strength, lower body mobility and daily activities.[13] Overweight and obesity are the fifth leading preventable causes of death worldwide1. Adolescents who are obese often experience significant social pressure, stress and difficulties accomplishing developmental tasks.[14] Obesity in adolescence is a significant risk factor for developing non-communicable diseases in adulthood such as cardiovascular diseases, diabetes mellitus, stroke, psychological problem and increased risk of mortality[1]. But in addition to increased future risks, obese children experience breathing difficulties and sleep apnea, increased risks of fractures, hypertension, early markers of cardiovascular diseases, insulin resistance and psychological effects.[11] Autonomic nerve dysfunction also co-exist in addition to recognized complication caused by obesity.[3] The autonomic nervous system (ANS) is responsible for regulation and integration of internal organs functions.[15] Excess weight induces ANS dysfunction, which may be involved in the hemodynamic and metabolic alterations that increase the cardiovascular risks of obese individuals, i.e: hypertension, insulin resistance and dyslipidemia.[16] The assessment of ANS requires recording the response of an end organ to physiological maneuvers. Changes in heart rate by a stimulus which reflects parasympathetic modulation.[17] The simple, reliable and non-invasive cardiovascular reflex test that is heart rate response to standing is useful tool for evaluation of parasympathetic modulation of the heart. Normally heart rate varies continually but this depends on an intact parasympathetic nerve supply. During the change from lying to standing a characteristics immediate rapid increase in heart rate occurs but the result is lower in obese.[18,19] The change of posture from lying to standing puts hydrostatic stress on the venous return which causes decrease in venous return due to pooling of blood in the lower limbs results in decrease in the blood pressure. The decrease in blood pressure activates the baroreflex resulting in rise of the heart rate which raises the blood pressure towards the resting values. The recovery of blood pressure results in the decrease in the heart rate later.[20]

Overweight and obesity related health problems are becoming quite common in our community.[21] Its health consequences ranges from increased risk of serious chronic conditions that reduce the overall quality of life to premature death.[22] Therefore, emphasis should be laid on early detection of the autonomic dysfunction in obese adolescent population.[8] So, the present study has been designed to assess the changes of cardiac parasympathetic nerve function status in obese adolescents.

METHODS

The cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur from July 2018 to June 2019. A total number of 60 healthy adolescents, aged 17-19 years were included in this study from different areas of Rangpur districts. Before perform the parasympathetic nerve function tests and collection of sample all the subjects were explained clearly about the objectives and the procedure of the study. Informed written consent of the study subjects were taken in easily understandable Bengali phrases. A standard questionnaire was filled up after taking history and thorough clinical examinations.

All the study subjects were divided into two groups on the basis of their body mass index, among them 30 normal weight adolescents were denoted as group A and 30 obese adolescents were denoted as group B. They were matched with age, sex and socioeconomic condition. Study was carried out with prior protocol approved by the thesis protocol review committee and ethical committee of Rangpur Medical College, Rangpur. Obese and history of diabetes mellitus, hypertension, chronic renal failure, cardiac complication, obstructive lung diseases and liver diseases, tobacco users and alcoholics, any neurological disorders, psychiatric disorders (depression), endocrine disorders (thyroid, adrenal etc), previous history of head injury and trained athletes were taken as exclusion criteria.

For calculation of BMI weight in Kg and height in m^2 of each subjects was taken by medical weighing machine and measuring tape respectively.

From the previous night up to the examination, they should not undergo any physical or mental stress and not to take any sedatives or any drugs affecting

RESTING PULSE RATE[23]

The subjects were asked to take rest for 10 minutes in supine position and radial pulse rate was recorded in supine position and expressed as beats/min. Three reading were taken and the average of the three was taken as the resting pulse rate.

central nervous system. Then the autonomic nerve function parameters were assessed by cardiovascular autonomic reflex tests using sphygmomanometer (mercury manometer) and ECG machine. Blood glucose, serum creatinine and serum alanine amino transferase level were measured to exclude diabetes mellitus, chronic renal failure and liver diseases respectively. FEV1 was also measured to exclude obstructive lung disease. Heart rate response to standing was conducted in a comfortable environment in the departmental physiology laboratory from 9.00am - 2.30 pm.

HEART RATE RESPONSE TO STANDING:[18, 19]

The test was performed with the subject lying on a bed quietly and heart rate was recorded continuously on an electrocardiograph. Then subjects was asked to stand from lying as quickly as possible without any support and the point of starting to stand was marked on the electrocardiogram. The characteristics heart rate response expressed by 30^{th}:15^{th} ratio.

30^{th}:15^{th} ratio: Ratio of longest R-R interval around 30th beat after standing to shortest R-R interval about 15 beats after standing.

30th:15th ratio - Normal: $\geq$ 1.04, Borderline: 1.01-1.03, Abnormal: $\leq$ 1.00

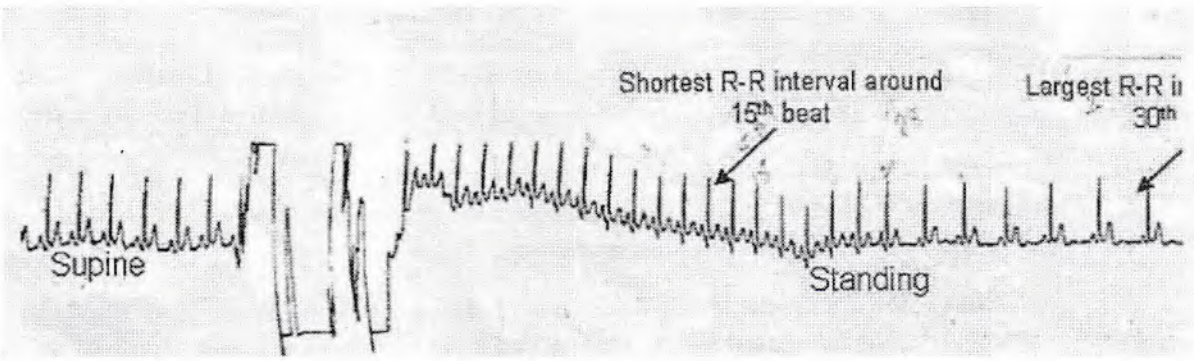

Figure 1. Representative tracing of lying to standing test 20

All data were recorded systematically in a preformed history sheet and all statistical analysis was done by computer using the software SPSS-23.0 version for windows. Comparison between obese with normal weight adolescents were done by unpaired t tests. In the interpretation of results, < 0.05 level of probability (p) was accepted as significance.

RESULT

The mean ± SD of age were 18.000 ± 0.871 years in group A and 18.233 ± 0.728 years in group B. The mean ± SD of height were 1.548 ± 0.045 m in group A and 1.540 ± 0.047 m in group B. The mean ± SD of weight were 49.300 ± 3.779 kg in group A and 65.267 ± 7.492 kg in group B. The mean ± SD of body mass index were 20.516 ± 1.302 kg/m2 in group A and 27.559 ± 2.277 kg/m2 in group B.The age and height were statistically non-significant between the groups but weight and BMI were statistically highly significant in group B than group A (Table - I).

Table I: Showing mean ± SD of age, height, weight and body mass index of the study subjects in group A and group B

Variable	Group A (n=30)	Group B (n=30)	P value
Age-years	18.00 ± 0.87	18.00 ± 0.87	0.869 NS
Height-m	1.54 ± 0.04	1.54 ± 0.04	0.987 NS
Weight-kg	49.30 ± 3.77	65.26 ± 7.49	0.000***
BMI (kg/m^2)	20.51 ± 1.30	27.55 ± 2.27	0.000***
BMI range (kg/m^2)	18.5 - 22.9	23 - 24.9	

Data were expressed as mean ± SD. Unpaired t test was done.
Group A are healthy adolescents of normal weight.
Group B are healthy adolescents of obese.
n = Number of subjects. SD = Standard Deviation.
p value < 0.05 level taken as level of significance.
NS = P > 0.05 *** = p < 0.001

The mean ± SD of resting heart rate were 73.9333 ± 6.69500 beats/min in group A and 84.1333 ± 10.76627 beats/min in group B. The mean resting heart rate were significantly (p<0.01) higher in group B than A (Table - II).

Table II: Showing mean ± SD of resting heart rate of study subjects in Group A and Group B

Variables	Group A (n=30)	Group B (n=30)	P value
Resting heart rate (beats/min)	73.93 ± 6.69	84.13 ± 10.76	0.001**

Data were expressed as mean ± SD. Unpaired t test was done.
Group A are healthy adolescents of normal weight.
Group B are healthy adolescents of obese.
n = Number of subjects. SD = Standard Deviation.
p value < 0.05 level taken as level of significance.
** = p < 0.01
Normal Heart rate = 60 - 90 beats / min.[24]

The mean ± SD of 30th : 15th heart rate ratios were 1.1313 ± 0.07482 and 1.0444 ± 0.03658 in group A and group B respectively.

Table III: Showing mean ± SD of heart rate response to standing (30th : 15th ratio) of study subjects in Group A and Group B

Variables	Group A (n=30)	Group B (n=30)	P value
Standing (30^{th} : 15^{th} ratio)	1.13 ± 0.07	1.04 ± 0.03	0.000***

Data were expressed as mean ± SD. Unpaired t test was done.
Group A are healthy adolescents of normal weight.
Group B are healthy adolescents of obese.
n = Number of subjects. SD = Standard Deviation.
p value < 0.05 level taken as level of significance.
*** = p < 0.001
Normal value:
Heart rate response to standing: ≥1.04.[18,19]

DISCUSSION

The present study was carried out to observe the changes in heart rate response to standing in between healthy normal weight and obese adolescents. BMI was calculated to differentiate normal weight and obese individuals. Our result showed significantly lower values of 30th : 15th ratio in obese adolescents when compared to normal weight adolescents indicating reduced vagal or parasympathetic activity. The finding is in consistent with that of some other investigators.3,19 In contrast some other researchers did not find any significant difference in obese and normal weight adolescents.[8,25]

The exact mechanisms involved for the impairment of cardiac autonomic nerve functions in obese adolescents cannot be established clearly. Changes in the autonomic nervous system activity begin in the overweight and may become more prominent in the obese thus indicating increased cardiovascular risk.[26] The result of our study suggested that with increased body mass index, modification in the autonomic nervous system and the frequency of involvement of cardiovascular autonomic function impairment also increased in obese adolescents.

Cardiac parasympathetic dysfunction present in obese subjects could be associated with higher carbohydrate intake and lower fat and protein intake which results in parasympathetic abnormality.[27]

Gradual development of insulin resistance in target tissues with the beginning of excess weight gain in obesity is responsible for subsequent development of hyperinsulinemia. This hyperinsulinemia has got a role in low cardiac vagal activity. But several researchers made various suggestions such as high insulin level or insulin resistance might cause damage to autonomic nerves at any level of their reflex arc, insulin resistance might cause deterioration of microcirculation in many tissues including nerves which might lead to neural ischemia and thereby damage of cardiac parasympathetic nerve terminals occur at the level of cardiac muscle or vascular wall.[3]

From this above discussion, it has been shown that significantly lower values of heart rate response to standing indicates parasympathetic impairment or decreased vagal tone may occur due to decrease baroreflex activity in obese adolescents.

CONCLUSION

After analyzing the results of the study, it can be concluded that decreased parasympathetic nerve activity in obese adolescents, as evaluated by heart rate response to standing strongly indicates the need for the early diagnosis and care of these adolescents to avoid the onset of future complications. However further studies with large size samples of different age groups and comparison between sexes are

recommended for more precise evaluation to aid in identification of those prone to weight gain and are at higher risk of cardiovascular complications.

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ORIGINAL ARTICLE

Association of Anemia with CKD: A Tertiary Care Hospital Based Cross Sectional Study

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ABSTRACT

BACKGROUND: *Chronic kidney disease (CKD) is a worldwide public health problem. It is usually associated with anemia and prevalence of anemia increases with progression of CKD. OBJECTIVE: To find out the association of anemia with different stages of CKD.* ***MATERIALS & METHODS:*** *This cross-sectional study was conducted in the Department of physiology in Mymensingh Medical College, Bangladesh over a period of one year from January to December 2016. A total number of 174 subjects were enrolled in this study among which 87 were CKD patients and 87 were healthy participants. On the basis of inclusion and exclusion criteria study subjects were divided into case and control group. Hemoglobin concentrations in the blood were measured in all study subjects by using auto-analyzer.* ***RESULT:*** *Hemoglobin concentration in the blood was decreased in both male and female CKD patients, which were 9.55±1.13 gm/dl and 9.11±0.95 gm/dl respectively and result was statistically significant (p<0.01).) 55% were anemic in stage 1, 61% in stage 2, 70% in stage 3, 75% in stage 4 and 86% in stage 5 of CKD.* ***CONCLUSION:*** *This study revealed that prevalence of anemia is common in all stages of CKD patients in Mymensingh, Bangladesh. It emphasizes the need for regular checking of anemia in CKD patients and early referral to the nephrologists.*

Key words: Chronic kidney disease (CKD), anemia, hemoglobin concentration.

INTRODUCTION:

With an increasing incidence, prevalence and poor outcomes chronic kidney disease (CKD) has become a major public health burden. Consequences of kidney disease includes kidney failure, decreased kidney function and cardiovascular diseases.[1]

Again, anemia is a common manifestation in CKD. The concentrations of hemoglobin begin to decrease in early renal impairment. It also leads to fatal outcomes, such as mortality and cardiovascular complications.[2,3]

Anemia is defined as the Hb level <13 g/dl in men and <12.0 g/dl in women (According to WHO). Normal hemoglobin distribution differs also with physiological status and ethnicity.[4] The cause of anemia in chronic kidney disease is relative deficiency of erythroprotien, declined erythropoiesis due to toxic effects of uremia on marrow precursor cell, reduced red cell survival, blood loss due to increased capillary fragility and low platelet function, decreased dietary consumption and absorption of iron and other hematinics.[5]

The objective of this study was to find out the association of anemia with different stages of CKD. To the best of our knowledge this type of study was not done in Mymensingh region of Bangladesh. So, it necessitates finding out the actual pattern of association between anemia and CKD in this region of Bangladesh.

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MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Physiology in Mymensingh medical college from January to December, 2016. A total number of 174 subjects participated in this study. Among them 87 were CKD patients and 87 healthy individuals. Persons below 20 years and above 70 years, pregnant woman, persons having arthritis, chronic liver disease, endocrine disease, malignancy and history of regular alcohol consumption were excluded from our study. During visit the available age matched CKD patients and healthy persons were interviewed, examined and sample of blood were collected with informed written consent. The patients were selected on the basis of history, clinical examination and relevant investigations. Hemoglobin concentration in blood was determined by using auto analyzer. Anemia was defined as hemoglobin concentration <13 g/dl in case of male and <12 g/dl in case of female. Stages of CKD were determined by calculating estimated GFR. Statistical analysis was done by using SPSS , version 20 and level of significance was determined by unpaired student's `t' test.

RESULT

Out of 174 study subjects, 87(48 male and 39 female) were CKD patients and 87(44 male and 43 female) were healthy individuals. The hemoglobin concentration of control group male & case group male were 13.76±0.12 g/dl & 9.55±0.17 g/dl respectively. Hemoglobin concentration was decreased in case group male, and the result was statistically significant ($p<0.01$) than that of control group.The hemoglobin concentration of control group female & study group female were 12.35±0.12 g/dl & 9.11±0.14 g/dl respectively. Again, In study group female, hemoglobin concentration was decreased & result was significant ($p<0.01$) than that of control group (Figure:1)

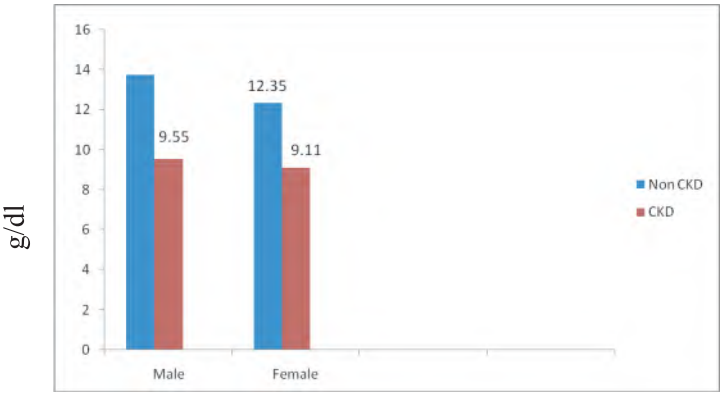

Figure 1: Mean hemoglobin concentration of study population

In our study we found increased serum creatinine and decreased eGFR in CKD patients which is shown in the Table I below.

Table I: mean± SD Level of serum creatinine and estimated GFR of study subjects.

Variable	S. Creatinine (mg/dl)		eGFR(ml/min)		P –value
	Control	Case	Control	Case	
Male	1.03±0.18	3.08±1.38	85.89±2.02	28.65±1.11	0.001***
Female	0.98±0.16	2.98±1.92	70.58±1.92	30.14±0.92	0.001***

*** = highly significant

There was various number of CKD patients in different ages. Table II is showing number of CKD patients in different ages with percentage.

Table II: Age distribution of CKD patients

Age range (years)	**Number of patient (%)**	**Percentage (%)**
20-30	08	09
31-40	13	15
41-50	18	21
51-60	27	31
61-70	21	24
Total	**87**	**100**

Table III: Distribution of CKD patients by stage

CKD stage	**Number of patients**	**Percentage**
Stage 1	18	21%
Stage 2	23	26%
Stage 3	27	31%
Stage 4	12	14%
Stage 5	07	08%
Total	87	100%

Anemia was found to be increased gradually with declining GFR and advancement of CKD. The frequency and percentage of anemia in CKD is

Table IV: Distribution of anemia in chronic kidney disease patient by stage.

CKD stage	Non anemic	Anemic	Percentage of anemia
Stage 1	8	10	55%
Stage 2	9	14	61%
Stage 3	8	19	70%
Stage 4	3	9	75%
Stage 5	1	6	86%
Total (87)	**30**	**57**	**65% (Avg)**

The hemoglobin concentration is gradually decreased with the advancement of CKD (Table V).

Table V: Mean hemoglobin concentration for stages of CKD

CKD stage	Hb Concentration (g/dl) (Mean±SD)
Stage 1	11.18±2.13
Stage 2	10.76±2.08
Stage 3	8.89±1.73
Stage 4	8.24±1.94
Stage 5	7.58±2.24

DISCUSSION

This study has demonstrated high prevalence (65%) of anemia in CKD patients in Mymensingh district, Bangladesh. This prevalence is almost similar with other studies.[6-8]

It is shown in our study that, there is a gradual increase in the prevalence of anemia according to stage, which is 55% anemia in stage 1, 61% in stage 2, 70% in stage 3, 75% in stage 4, 86% in stage 5 of CKD. Similar result was found in another study where they found 21% anemic in stage 1 with gradual increasing in anemia reaching 98% anemic in stage 5.[9]

Another study, which was done on 345 patients, showed that, 26.4% (n = 91) had anemia and 29.6% had moderate to severe renal failure (GFR < 60 ml/min). The association between anemia and a higher prevalence of renal failure was statistically significant (p = 0.005).[10] therefore, anemia is a risk factor for renal disease progression.[11]

We have found in our study, hemoglobin concentration in male is greater than female, because of male sex hormone testosterone, which stimulates erythropoietin and ultimately causes more red blood cell production and greater hemoglobin concentration.[12]

Reduced erythropoietin, declined red cell survival, increased loss of blood due to capillary fragility and poor platelet function as well as less dietary intake and absorption of iron and other hematinics are responsible for anemia in CKD.[5]

Anemia in patients with CKD is a multifactorial process, in which chronic inflammation, erythropoietin deficiency, iron metabolism disorders, blood loss on hemodialysis sessions, uncontrolled hyperparathyroidism, deficiency of essential nutrients like iron, folic acid, and vitamin B12, the use of some drugs, including ACE inhibitors and uremic toxins play the most

important role. The understanding of underlying mechanisms of anemia in CKD is important due to the fact that in some patient's erythropoietin stimulating agents (ESA) treatment might be least ineffective or even deleterious.[13-15]

Again, in CKD there is increased level of inflammatory cytokines such as interleukin-6 which enhance production and secretion of hepcidin, a hepatic protein that inhibits intestinal iron absorption and impairs iron transport from the reticulo-endothelial system to bone marrow. Erythroprotien which normally enhances iron transport from macrophages to the blood stream is impaired thereby exacerbating relative iron deficiency. [16]

Some studies showed anemia may worsen renal medullary hypoxia leading to renal interstitial injury and fibrosis which progress kidney disease.[17,18]

CONCLUSION

This study has documented a relatively high prevalence of anemia in all stages of CKD. The prevalence of anemia has increased from CKD stage one to stage five. A strong association has found between anemia and CKD. As we know that anemia with CKD has a lot of adverse consequences, so, immediate measure should be taken for the management of anemia and early referral to nephrologists should be confirmed.

This study was a single centered study and sample size was small. Only hemoglobin concentrations were tested for anemia determination. But CBC, red cell indices, iron profile, PBF, Vitamin B12 and folic acid concentration was not done. Though anemia can be identified by simply investigating hemoglobin concentration but the etiology and pattern of anemia couldn't be evaluated without doing those investigations.

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