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EDITORIAL

Dietary Fibers and 'Health Wellbeing'

Anupam Sarker.

Dietary fiber or roughage is the portion of plant-derived food that cannot be completely broken down by human digestive enzymes[1] There are two components of dietary fibers. One is soluble fiber also called prebiotic fiber – which dissolves in water and generally fermented in the colon into gases and produce a physiologically active by-products, such as short chain fatty acid (SCFA) in the colon by the help of gut bacteria. Another is insoluble fiber which does not dissolve in water and inert to digestive enzymes in the upper gastrointestinal tract but triggers the secretion of mucus in the large intestine, providing bulking effects in colon[1, 2]. Dietary fibers are found in fruits, vegetables and whole grains when typically eaten whole, raw or cooked[3]. Some plants contain significant amounts of soluble and insoluble fiber such as : legumes (peas, soybeans, lupins and other beans), oats, rye, chia and barley; fruits including figs, avocados, plumes, berries, ripe banana and skin of apples, quinces and pears; vegetable such as broccoli, carrots, root vegetable sweet potatoes and onion; seed husks such as psyllium, flax seed nuts and almonds being the highest in dietary fiber[4]. Sources of insoluble fiber include whole grain foods wheat, corn, bran, legumes, nuts and vegetables such as green bean, cauliflowers, zucchini; some fruits including avocado unripe bananas the skins of some fruits, including kiwifruit, grapes and tomatoes[3,4].

Dietary fibers make three primary contributions in the gastrointestinal tract such as bulking, viscosity and fermentation[5]. Different fibers have different effects, suggesting that a variety of dietary fibers contribute to overall health. Some fibers contribute through one primary mechanism for instance, cellulose and wheat bran provide excellent bulking effects, but are minimally fermented. Alternatively, many dietary fibers can contribute to health through more than one of these mechanisms like psyllium provides bulking as well as viscosity[5]. Most bulking fibers are not fermented or are minimally fermented throughout the intestinal tract. Viscous fibers thicken the contents of the intestinal tract and may attenuate the absorption of sugar, reduce sugar response after eating, and reduce lipid absorption(notably shown with cholesterol absorption)[5,6]. Fermentable fibers are consumed by the microbiota within the large intestines, mildly increasing fecal bulk and producing short chain fatty acid (SCFA) as by products with wide-ranging physiological activities[7]. SCFAs are involved in numerous physiological processes promoting health, including: stabilize blood glucose levels by acting on pancreatic insulin release and liver control of glycogen breakdown stimulate gene expression of glucose tranporters in the intestinal mucosa regulating glucose absorption and provide nourishment of colonocytes[8]. The SCFA butyrate suppress cholesterol synthesis by the liver and reduce blood levels of LDL cholesterol and triglycerides responsible for developing atherosclerosis. SCFA also lower colonic pH (i.e., raises the acidity level in the colon) which protects the lining from formation of colonic polyps and increases absorption of dietary minerals as well as stimulate production of T helper cells, antibodies, cytokines and lymph mechanisms having crucial roles in immune protection improve barrier properties of the colonic mucosal layer, inhibiting inflammatory and adhesion irritants[9]. SCFAs affect major regulatory systems, such as blood glucose and lipid levels, the colonic environment, and intestinal immune functions[9,10].

The Academy of Nutrition and Dietetics (AND)

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recommends a minimum of 20–35 g/day for a healthy adult depending on calorie intake (e.g., a 2000 Cal/8400 kJ diet should include 25 g of fiber per day). The AND's recommendation for children is that intake should equal age in years plus 5 g/day (e.g., a 4-year-old should consume 9 g/day). No guidelines have yet been established for the elderly or very ill[11].

Persons who consume generous amounts of dietary fiber, compared to those who have minimal fiber intake, are at lower risk for developing CHD, stroke, hypertension, diabetes, obesity, and certain gastrointestinal diseases[12]. Increasing the intake of high-fiber foods or fiber supplements improves serum lipoprotein values, lowers blood pressure, improves blood glucose control for diabetic individuals, aids weight loss, and improves regularity. Emerging research indicates that intake of inulin and certain soluble fibers enhances immune function in humans. A high level of fiber intake has health-protective effects and disease-reversal benefits[13].

The food habits of the people have been changing over the years all over the world. The consumption of indigenous foods has decreased an everyday diet. Eating out has become less of a novelty and more of a necessity, and fast foods seem to have more appeal to the general consumer, especially in the urban regions. Improving dietary habits would be beneficial in preventing lifestyle-related diseases. This idea does not simply mean better nutrition; it includes a novel concept of consuming special health-promoting food substances or components in our daily lives. It can be easily maintained by the most widely consumed food in the country is collectively known as Dal–Bhat–Tarkari (rice–pulse–vegetable) with a pickle of seasonal vegetables or fruits, and fish or meat as a non-vegetarian option is commonly consumed twice a day for better health.

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ORIGINAL ARTICLE

Comparison of Angiotensin-Receptor-Neprilysin Inhibitor Versus Valsartan in Heart Failure Patients with Reduced Ejection Fraction.

Md. Abu Zahid[1], Shakil Ghafur[2], Haripada Sarkar[3], Rabindra Nath Barman[4], Hasanul Islam[5] Abdullah-Al-Mahmud[6], Mahbubur Rahman[7].

ABSTRACT

BACKGROUND: *Heart failure (HF) is a common clinical syndrome caused by a variety of cardiac disease. The prevalence of HF has risen steadily in recent years and this trend is expected to continue due to a growing aging population with more cardiovascular risk factors[1,2]. For patients with HF with reduced ejection fraction (HFrEF), no therapy has proven to be significantly effective in reducing morbidity and mortality[3]. Consequently, there was an urgent need for new therapies to prevent and treat HFrEF . To achieve the goal ARNi has been introduced in the last decade along with other few pharmacological agents. Here we have performed one prospective study on ARNi. We examined the effect and safe dose of angiotensin receptor neprilysin inhibitor (ARNi) in HFrEF.* ***RESULTS:*** *Occurrence of cardiovascular deaths occurred 4 (8%) in the ARNi treatment arm while 11(22%) in the Valsartan arm with significant hazard ratio in the ARNi group [Hazard Ratio=0.56; 95% CI: 0.34, 0.64; p<0.05] during a median of 88 days of follow up period and 2(4%) of the patients from theARNi treatment were hospitalized due to HF while in the Valsartan treatment arm 10 (20%) patients did so.Furthermore, a significant effect was found to have in LVEF , NT-proBNP, eGFR and Serum electrolytes at 95% level of significance (p<0.05). These effects resulted from somewhat increased in LVEF (30.44±6.71% to 38.78±8.17%) and intensely decreased in NT-proBNP (3066.5±1882.147 pg/ml to 808.20±592.50 pg/ml) in the ARNi group.*

Key words: Heart Failure, ARNi, NT-pro BNP

1. INTRODUCTION

Heart failure (HF) is generally observed as clinical observation caused by different kind of cardiac diseases[4]. Heart failure, a clinical syndrome resulting from structural or functional damage, has become a major global epidemic, with increasing prevalence, clinical impact and cost[5]. With the aging of the population and the therapeutic advancements, the survival of patients with HF improve significantly.

The prevalence of HF has steadily been increasing in recent years and this trend is expected to continue due to a growing aging population with more cardiovascular risk factors[5,6]. Heart failure with reduced ejection fraction responsible for 50% of the conditions[7], is complicated by means of considerable morbidity and mortality[8,9]. Previously, A lot of clinical trials were conducted with the pharmacological treatments including β blockers[10]calcium-channel blockers[11] angiotensin-converting enzyme inhibitors (ACEi)[12] and angiotensin receptor blockers (ARBs)[13]. But It did not able to demonstrate

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benefit as expected.

For patients with HF with reduced ejection fraction (HFrEF), no therapy has proven to be effective at reducing morbidity and mortality[14]. Consequently, there is an urgent need for new safe therapies to prevent and treat HFrEF. Angiotensin receptor neprilysin inhibitor (ARNi) is the new drug class and unprecedented scientifically which forms a one compound with molecular moieties of the neprilysin (neutral endopeptidase 24)[15] inhibitor prodrug AHU377 and the ARB valsartan[16]. Enzymatic cleavage absorbs AHU377 to sacubitril at (LBQ657), the active inhibitor of neprilysin. Sacubitril/valsartan is the first angiotensin receptor neprilysin inhibitor that are recommended to HFrEF patients[13,14]. Sacubitril/valsartan has been regarded as a more effective alternative to angiotensin-converting enzyme inhibitor to be used together with other evidence-based treatments for HFrEF[17].

2. METHODS

2.1. Study design and patients

We consecutively referred patients admitted to Rangpur Medical college hospital and diagnosed with heart failure from May10, 2018 and December 3, 2018. Figure1 was shown the flow chart for sampling methods.

A total 242 patients were screened between May10, 2018 and December 3, 2018. Out of which 142 patients were excluded due to not meeting inclusion and exclusion criteria, withdrawal of consent or adverse events [Figure 1]. In this single blind trial, the patients were enrolled with chronic HF aged on or above 40 years, considering based on NYHA class II –IV and LVEF 40% or less. Moreover, NT-proBNP were required to have 400 pg/ml or larger among the patients. In view of inclusion and exclusion criteria, 100 patients with heart failure were randomly assigned 1:1 to the treatment arms either angiotensin receptor neprilysin inhibitor (ARNi) or valsartan through purposive sampling technique and followed for a median of 88 days.

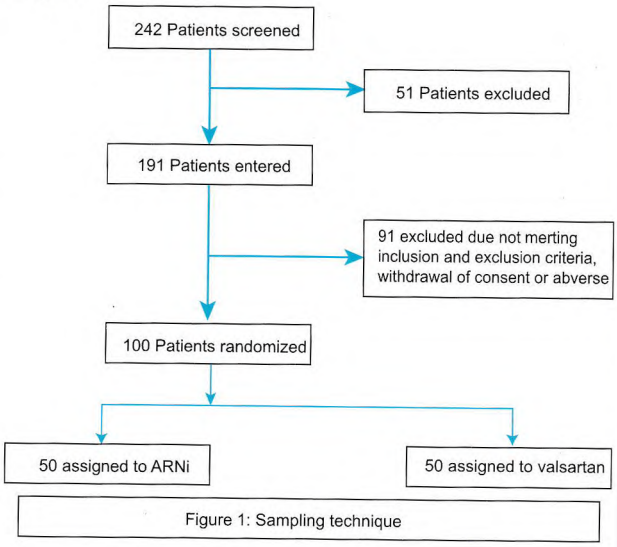


Figure 1: Sampling technique

any organic and/or psychiatric disorder that might hinder the content completion of health-related questionnaire.

2. 2 Procedures

Subsequent to randomization, the patients were underwent angiotensin receptor neprilysin inhibitor (ARNi) 50 mg and titrated to their final dose of 100 mg twice a day or valsartan 40 mg and titrated to the final dose of 80 mg twice a day to identify the effect of angiotensin receptor neprilysin inhibitor (ARNi) on cardiac status compared to valsartan in patients with chronic heart failure with reduced ejection fraction. Prior to be enrolled in the study, each of total 100 patients were discontinued on their background treatments (ACE-I or ARB) 24 hour earlier.

Transthoracic echocardiography (LA diameter, LVIDD, LVIDS and left ventricular ejection

fraction) test was performed at baseline, 30 days and 90 days or end of the study. All the echocardiography were performed in the Department of Cardiology, Rangpur Medical College Hospital, Rangpur, Bangladesh. Measurent is made in accordance with the recommendation of the American society of Echocardiography. Echo was performed by using Philip iE-33 echo machine. NT-proBNP was measured at screening/baseline and 90 days or at early termination of visits by Getein 1100 immmunofluorescence Quantitative Analyzer. Level of blood sugar, serum creatinine, eGFR (estimated glomerular filtration rate) and level of serum electrolytes were also examined at baseline, 30 days and 90 days or at early termination of visit or end of the study. To define the functional capacity, the New York Heart Association (NYHA) functional classifcation (I, II, III, IV) was used.

2.3. Follow-up and end points

Patients were followed up by clinical visits, the median duration of follow-up was 88 days. The clinical composite assessment was done in accordance with the NYHA functional classifcation, patient-reported outcomes (PROs) or major adverse clinical events (or both)[18]. The patients were considered as improved based on improvement in NYHA functional classi?cation or patient-reported outcomes (PROs) and no major cardiovascular event was reported. In contrast, at the endpoint of follow up, the patients who did have major cardiovascular event or deteriorating of their NYHA class or patient-reported outcomes (PROs) during this single blind treatment were adjudicated to be inferior. The primary outcome were mode of cardiovascular death and rate of hospitalization for heart failure or overall mortality.

2. 4. Statistical analysis

All continuous variables are presented as the mean ± SD, and analysis of variance was used to compare means across multiple groups. Noncontinuous and categorical variables are presented as frequencies or percentages and were compared using the Chi-square test. The Chi-square test was used for the comparison of the endpoints. The absolute differences on endpoints between groups and the corresponding 95% confidence intervals were reported. The Kaplan-Meier curve method was used to calculate time to clinical endpoints, and the log-rank test was used to compare the survival curves.

A total 100 patients were randomly assigned through system generated block randomization into two comparison treatment arms, considering 80% power and at 5% level of significance, to perceive 25% in the ratio of the NT-proBNP at a median of 88 days over baseline between ARNi and valsartan group, we used a two-sided t-test on the logarithm of this ratio.

Table I: Demographic characteristics and clinical profile at baseline

Characteristics	ARNi (n=50)	Valsartan (n=50)
Age (years)	60.8±11.4	61.9±12.5
Age group (years)		
(40-50)	11 (22)	10 (20)
(51-60)	13 (26)	15 (30)
(61-70)	16 (32)	16 (32)
(71-80)	9 (18)	8 (16)
(81-90)	1 (2)	0 (0)
(90-100)	0 (0)	1 (2)
Female sex no. (%)	17 (34.0)	16 (32.0)
LA Diameter	43.3±3.7	43.4±7.6
LVIDD (mm)	63.7±7.2	61.9±6.8
LVIDS (mm)	53.00±8.95	51.1±7.4
LVEF (%)	30.44±6.707	30.57±6.047
Blood sugar (mmol/L)	8.14±3.039	8.97±7.826
Serum creatinine (mg/dl)	1.20±0.4	1.48±0.6
e GFR (ml/min/1.73m2)	53.42±18.15	46.62±18.85
NT_pro BNP (pg/ml)	3066.5±1882.15	3488.18±2912.219
Median NT_pro BNP (pg/ml)-IQR	2386	2041.5
NYHA functional class- no. (%)		
II	1 (2)	4 (8)
III	48 (96)	46 (92)
IV	1 (2)	0 (0)
Clinical symptoms		
Chest pain	28 (56)	33 (66)
Shortness of breath	38 (76)	45 (90)
Medical History		
Systolic blood pressure (mmHg)	119.78±19.8	124.4±29.6
BMI	22.9±3.2	23.5±2.8
Hypertension no. (%)	14 (28)	11 (22)
Diabetes no. (%)	14 (28)	11 (22)
Pretrial use of medication no. (%)		
ACE inhibitor	11 (22)	5 (10)
ARB	11 (22)	5 (10)
BB	44 (88)	41 (82)

Hypertension no. (%)	14 (28)	11 (22)
Diabetes no. (%)	14 (28)	11 (22)
Pretrial use of medication no. (%)		
ACE inhibitor	11 (22)	5 (10)
ARB	11 (22)	5 (10)
BB	44 (88)	41 (82)
Diuretics	38 (76)	41 (82)
MRA(Spironolactone)	37 (74)	38 (76)
Risk factors		
Tobacco smoking/chewing	14 (28)	16 (32)
Obesity	6 (12)	4 (8)
Family H/o CAD	4 (8)	5 (10)
Dyslipidemia	4 (8)	5 (10)
Sedentary lifestyle	4 (8)	5 (10)

No significant difference was found to have between two groups. Plus-minus values indicate mean±SD IQR denotes interquartile range. The body-mass index is the weight in kilograms divided by the square of the height in meters.

We used statistical software STATA (verson 13.0) for all of analysis according to inten-to-treat. For the primary endpoint of the single blind trial, we performed Cox-proportional hazards models and Kaplan-Meier estimates for comparing time-to-event cardiovascular deaths and rehospitalization due to heart failure between the treatment arms. We then adjusted the effect of all prespecified subgroups with dichotomas variables through Cox-proportional hazards models as well. To compare the occurrence of adverse event for undergoing both treatments, we perfomed Fisher's exact test.

3. RESULTS

Patient's demographic information and clinical Profiles:

Finally, a total of 100 patients with chronic heart failure were recruited to equally distributed between two groups. The patients were predominantly male (67%). The majority of patients reclined in the age group of (61-70) years (32%). The most collective symptom was found to have shortness of breath (83%) followed by chest pain (61%). The trial found tobacco smoking/chewing (30%) as the major risk factor followed by hypertension and diabetes (25% each). The both treatment arms were well-adjusted with reference to patient's baseline characteristics.

Clinical outcome

The primary endpoints, occurrence of cardiovascular deaths occurred 4 (8%) in the ARNi treatment arm, while 11(22%) in the valsartan treatment arm with significant hazard ratio in the ARNi group [Hazard Ratio=0.37; 95% CI: 0.34, 0.64; p=0.042] during a median of 88 days of follow up period [Table 2 (A) and figure 2]. 2 (4%) of the patients from the

ARNi treatment arm were hospitalized due to HF, while in the valsartan treatment arm, 10 (20%) patients were hospitalized due to HF followed by receiving treatment respectively with hazard ratio in the ARNi group [Hazard Ratio=0.80; 95% CI: 0.57, 0.92; p<0.037] [Table ii (A)]. The secondary outcomes of the trial were to examine the differences of ejection fraction, NT-proBNP and e-GFR between two groups

Primary and secondary outcomes

Table II (A):

Primary outcome no. (%)	ARNi	Valsartan	Hazard Ratio	p-value
Cardiovascular death	4 (8)	11 (22)	0.37 (0.34, 0.64)	0.042
Hospitalization followed by receiving treatment	2 (4)	10 (20)	0.80 (0.57, 0.92)	0.037

Table II (B)

Secondary outcome	ARNi			Valsartan			p-value
	n	Baseline	90 days	n	Baseline	90 days	
Elevated EF	50	30.4±6.7	38.8±8.1	50	30.6±6.0	35.0±7.9	0.017
Decreased NT-proBNP	50	3066.5±1882.1	808.2±592.5	50	3488.2±2912.2	1886.4±1017.8	0.000
Elevated e-GFR	50	53.4±18.1	56.2±16.6	48	46.6±18.8	48.9±22.3	0.045

EF denotes ejection fraction, e GFR denotes estimated glomerular filtration rate and NT-proBNP denotes N-terminal prohormone of B type natriuretic peptide

A significant effect was found to have in both ejection fraction and NT-proBNP at 95% confidence interval (p<0.05). These effects resulted from somewhat increased in ejection fraction (30.4±6.7% to 38.8±8.1%) and intensely decreased in NT-proBNP (3066.5±1882.1 pg/ml to 808.2±592.5 pg/ml) in the ARNi group, as compared to valsartan group in LVEF (30.6±6.0% to 35±7.9%) and in NT-proBNP (3488.2±2912.2 pg/ml to 1886.4±1017.8 pg/ml) respectively [Table ii (B)].

But no evidence of differences was found to have between the ARNi and valsartan groups with respect to the other echocardiography measurements (LA Diameter, p-value 0.53; LVIDD. p-value 0.78; LVIDS and p-value 0.50) except ejection fraction at a median of 88 days of follow up [Table III] . Similarly, the ARNi and valsartan groups did not differ with regard to the blood sugar (p-value= 0.38), potassium (K) (p-value=0.23) and chloride (Cl) (p-value=0.68) but sodium (Na) (p-value= 0.028) of serum electrolytes demonstrated the significance difference between ARNi and valsartan groups.

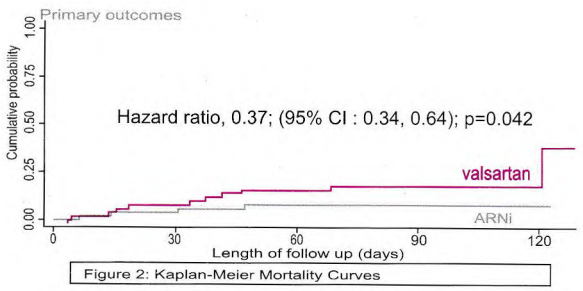


Figure 2: Kaplan-Meier Mortality Curves

Adverse event during treatment

In the ARNi group, 2 patients (4%) were re-hospitalized followed by receiving treatment while ratio of re-hospitalized increased to a greater extent in the valsartan group, 10 patients (20%) (p-value=0.014). No adverse effect was found in the ARNi.

Table III: Changes in echocardiographic measures and serum electrolytes at 90 days

Clinical parameters		ARNi		Valsartan			P value
	n	Baseline	90 days	n	Baseline	90 days	
LA Diameter	36	43.3±3.7	41.6± 7.6	38	43.4±7.6	41.8±7.3	0.53
LVIDD	50	63.7±7.2	59.7±5.8	50	61.9± 6.8	58.3± 8.8	0.78
LVIDS	50	53.0±8.9	49.8± 7.9	50	51.1±7.4	49.8±8.3	0.50
Blood sugar (mmol/L)	50	8.1±3.0	7.4±2.6	49	9.0±7.8	7.7±6.4	0.38
Sodium (Na)	48	139.1±5.6	138.0±6.0	48	137.0±6.9	135.0±8.5	0.028
Potassium (K)	48	4.1±0.6	4.9±6.7	48	4.0±0.5	4.1±0.6	0.23
Chloride (Cl)	48	99.7± 4.6	99.9±3.6	48	98.9±6.1	100.5±8.4	0.68
S. Creatinine	50	1.2±0.4	1.1±0.2	50	1.4±0.6	1.4±0.7	0.000

Subgroup analysis of endpoints

In the following analysis, we applied an interaction effect to figure out the relationship of different clinical factors to different anti-HF strategies. We first identified the potential clinical factors associated with CV death or HF hospitalization using a COX multivariate analysis, and the related factors are showed in Table IV Our study aimed to reveal the credible evidence in management of cardiovascular diseases with ARNi in adding with existing treatment. This study observed a benefit with regard to reduce cardiovascular mortality, was one of our primary endpoints which was met by the study.

Table IV: Sub group analysis with multiple adjustments for all variables shown in Cox proportional Hazards Models with time dependent coverable

Sub group	ARNi n (%)	Valsartan n (%)	Hazard Ratio	p-value
Age				
< 65 years	31 (62)	25 (50)		
≥ 65 years	19 (38)	25 (50)	1.00 (0.79 1.86)	0.997
Age				
< 75 years	41 (82)	41 (82)		
≥75 years	9 (18)	9 (18)	0.48 (0.42 2.62)	0.326
Sex				
Male	33 (66)	16 (32)		
Female	17 (34)	34 (68)	0.60 (0.15 2.41)	0.475
NYHA class				

II	1 (2)	4 (8)		
III or IV	49 (98)	46 (92)	0.51 (0.57 0.82)	0.047
Estimated e GFR				
< 60 ml/min/1.73 m^2	34 (68)	37 (74)		
≥ 60 ml/min/1.73 m^2	16 (32)	13 (26)	0.17 (.26 1.14)	0.076
LA Diameter				
≤ Median	9 (25)	12 (31.6)		
> Median	27 (75)	26 (68.4)	1.77 (0.23 3.19)	0.579
LVIDD				
≤ Median	25 (50)	27 (54)		
> Median	25 (50)	23 (46)	1.47 (0.22 9.78)	0.688
LVIDS				
≤ Median	24 (48)	33 (66)		
> Median	26 (52)	17 (34)	0.30 (.04 2.07)	0.222
Ejection fraction (%)				
≤ Median	28 (56)	26 (52)		
> Median	22 (44)	24 (48)	0.14 (0.03 0.79)	0.034
NT_pro BNP (pg/ml)				
≤ Median	22 (44)	28 (56)		
> Median	28 (56)	22 (44)	9.01 (1.10 3.56)	0.040

The patients who received ARNi did have consistently much lower levels of NT-proBNP (reflecting reduced cardiac wall stress) all over the trial in comparison with valsartan which is consistent with the evidence previously reported[27]. NT-proBNP is an indicator of left ventricular tension and decreases in NT-proBNP was associated with better-quality outcomes in patients with heart failure, which was our secondary outcome and achieved expectedly.

4. DISCUSSION

Approximately half of hospitalizations for the syndrome of heart failure occurred in patients with reduced ejection fraction. The angiotensin receptor neprilysin inhibitor

sacubitril/valsartan shown to be superior to enalapril in patients with heart failure with reduced ejection fraction and reduced both death and heart failure hospitalization[19].

The study revealed that participated patients with chronic heart failure by means of reduced ejection fraction, the angiotensin receptor neprilysin inhibitor (ARNi) was to a greater extent effective in dropping the risk of cardiovascular deaths and re-hospitalization resulting from heart failure than did valsartan followed by a median of 88 days. ARNi was also found as superior in powerfully reducing NT-proBNP and increasing ejection fraction compared to valsartan which was consistent with a few study previously conducted[20,21]. The results of these extensive benefits of angiotensin receptor neprilysin inhibitor compared to valsartan was found to have strong significant effect. In the ARNi group, improvement of NYHA class was significant compared to valsartan.To inhibit deteriorating of clinical condition in patients with heart failure, previously conducted few trials have reported advances in exercise tolerance or functional class or reductions in the risk of hospitalization for heart failure[22,23]. In accordance with these generated findings, this trial recommends that the patients of heart failure with reduced ejection fraction have a greater chance of having a beneficial effect who receive ARNi. In patients with this disorder,further testing of this composite could be justified. Current treatment of heart failure with reduced ejection fraction is continued through both symptom-based and empiric without acceptance of specific treatment for this indication[24]. Even though ACE inhibitors and ARBs have the evidence improving the symptoms, increasing the functional capacity and reduction of hospitalization in patients with this conditions[12,13]. Existing guidelines announced that to decrease morbidity or mortality, current treatment could not show the credibility[25].

Our study demonstrated that ARNI can reduce the outcome incidence in HF patients coexisted with atrial fibrillation, it has been reported that atrial fibrillation could increase the serum brain natriuretic peptide[26] indicating the severity of heart function. The increasing vasoactive peptides strengthen the effect of neprilysin inhibitor.

ARNi was found sound endurable as a whole and its adverse-eftect proftle was less frequent in comparison with valsartan in this study. Fewer patients of the study participants underwent the adverse events in the ARNi with respect to re-hospitalization and no adverse event was found in regard to renal impairment while in the valsartan group, significant increase in the level of serum creatinine and re-hospitalization were more frequent Table V.

Table V: Adverse events during treatment

Events	ARNi	Valsartan	p-value
Re-hospitalization	2 (4)	10 (20)	0.014
Elevateds. creatinine			
	0 (0)	4 (10.26)	0.026
Elevated Potassium			
mEq/L)	1 (2.22)	1 (2.56)	0.918
Elevated Blood sugar			
	7 (15.22)	3 (7.69)	0.283

This outcome of ARNi on renal impairment is found consistent in the experimental studies[27,28]. Biomarkers and substitute endpoints were the major determinants for this result of the study, whether the experimental outcomes will interpret into better clinical consequences need to conduct further prospective testing in an appropriately sampled outcomes study.

LIMITATION OF THE STUDY:

Several potential limitations apply to our results. First, the features, triggers, prognosis, and response to therapy of patients with reduced EF are different from those with preserved EF. Due to the relatively small sample, we did not separate patients diagnosed with HFmrEF and HFpEF. Second, there was a limited sample size.

5. CONCLUSIONS

Chronic treatment with the angiotensin receptor neprilysin inhibitor (ARNi) significantly decreases the progressive NT-proBNP, slightly changes sodium (Na) and e-GFR levels[29]. ARNi also increases ejection fraction including decreasing the risks and rates of a number of indicators of clinical worsening of enduring patients with heart failure compared to valsartan. As a result, ARNi has a greater impact on reducing morbidity and mortality in patients with chronic heart failure than valsartan. Beside the treatment effect of ARNi, it steady the progression of heart failure is likely to have significant effect for quality of life in this disorder.

Many of the results of our analysis show ARNI is an efficacy treatment strategy to improve the outcome , while further studies are needed to replicate and extend our findings including the measurement of the structure and diastolic function during the follow-up period.

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ORIGINAL ARTICLE

Effects of Tobacco Chewing on Serum Glucose Level.

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ABSTRUCT:

BACKGROUND: *In recent decades there have been a massive global increase in tobacco consumption. In Bangladesh tobacco is used in both smoke and or smokeless form. Immediate availability and the low price leads to high consumption of chewing tobacco, which may cause alteration in serum glucose level. Use of tobacco therefore may be a modifiable risk factor for causing type 2 diabetes mellitus.* ***OBJECTTIVES:*** *To assess the effects of tobacco chewing on fasting serum glucose level and serum glucose level 2 hours after ingestion of 75gm glucose.* ***METHODS:*** *This cross sectional study was conducted from July 2015 to June 2016 in the Department of Physiology, Rangpur Medical College, Rangpur. For this a total number of 100 age & socioeconomic condition matched male subjects were selected, among them 50 were apparently healthy non-tobacco chewer non-smoker subjects (group A), 50 were apparently healthy tobacco chewer nonsmoker subjects (group B). The subjects were selected from Rangpur district. The study parameters were fasting serum glucose level and serum glucose level 2 hours after ingestion of 75 gram glucose. For statistical analysis Unpaired student's 't' test was performed by computer based software SPSS- 17.0 version for windows.* ***RESULTS:*** *Fasting serum glucose level and serum glucose level 2 hours after ingestion of 75 gm glucose were significantly ($p<0.001$) higher in tobacco chewer nonsmoker subjects as compared with the healthy control subjects.* ***CONCLUSIONS:*** *The increased level of fasting serum glucose and serum glucose level 2 hours after ingestion of 75 gram glucose occurs due to tobacco consumption, which is the evidence of development of type 2 diabetes mellitus in tobacco chewers nonsmokers .*

Key wards: Serum glucose, tobacco chewer, nicotine.

INTRODUCTION

"Tobacco" is an English word originates from the Spanish and Portuguese word "tabaco"[1]. In the developing world tobacco use is increasing rapidly. One of the biggest threats to current and future health is the use of tobacco. It is one of the leading cause of diseases, disability and important avoidable cause of death in the world[2]. From tobacco related illness nearly about 5 million people die annually and this number will be more than double by the recent years globally. In Bangladesh, more than 57000 people die each year from tobacco related diseases[2,3].

It has been observed that in Bangladesh 43.3% of adults (41.3 million) currently use tobacco in smoking and/or smokeless form. 44.7% men, 1.5% women, and 23.0% overall (21.9 million adults) currently use tobacco in smoke form, whereas, 26.4% men, 27.9% women, and

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27.2% overall (25.9 million adults) currently use smokeless tobacco[4]. Snus that is smokeless form of tobacco delivers the same amount of nicotine as cigarettes[5].

Characteristics of diabetes mellitus is uncontrolled hyperglycemia, which may lead to life threatening complication and acute metabolic aberrations[6]. In a study the researchers have observed that the prevalence of type 2 diabetes mellitus was equally increased in both smoker & nonsmoker tobacco users diagnosed by OGTT[7]. A good number of primary studies have assessed the association between smoking and incidence of serum glucose abnormalities. They suggested that use of any form of tobacco could be independently associated with glucose intolerance, impaired fasting glucose, and type 2 diabetes. Therefore, tobacco consumption may be a modifiable risk factor for causing type 2 diabetes mellitus[8].

To the best of our knowledge few researches have been done on the tobacco chewer nonsmoker to observe the effects of tobacco use on glycemic control in our country. As many people in our country are tobacco chewer, so we have selected this group of people to assess the effects of tobacco consumption on fasting serum glucose level and serum glucose level 2 hours after ingestion of 75 gm glucose.

MATERIALS & METHODS

This cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur from July 2015 to June 2016. A total number of 100 male subjects, aged 35-45 years were included in this study from different community of Rangpur district. Among them 50 non-tobacco chewer non-smoker subjects were included in control group and was denoted as group A & 50 tobacco chewer and non smoker subjects were included in experimental group and denoted as group B. They were age and socio-economic condition matched. History of chewing tobacco regularly minimum 5 times in a day for five years was taken as inclusion criteria. Study was carried out with prior protocol approved by the thesis protocol review committee and ethical committee of Rangpur Medical College. Before collection of sample all the subjects were informed about the objectives of the study and then informed written consent was taken from each of the study subjects. A standard questionnaire was filled up after taking history and thorough clinical examinations. Obese & known diabetic subjects and subjects with liver, kidney, heart, lungs and other diseases were taken as exclusion criteria. None had donated or received blood in last 3 months. Serum creatinine & ALT level were estimated to exclude kidney and liver diseases respectively. For calculation of BMI weight in kg & height in m2 of each subject was taken by measuring tape and medical weighing machine.

All the subjects were advised to be in overnight (8-10 hrs) fasting state then to attend next day at 8.00 A.M. in the Department of Physiology of Rangpur Medical College. Three (3) ml of blood was collected from ante-cubital vein from each subject under all aseptic precaution by a disposable syringe. The needle was detached from the nozzle and then the blood was immediately transferred into a de-ionized test tube with a gentle push to avoid hemolysis & blood was kept in standing position till formation of clot. Serum was separated by centrifuging the blood at 3000rmp for 5 minutes. The clear supernatant was taken and kept in ependorffs. All tests were carried out as early as possible.

For collection of next sample 75gm glucose dissolved in 250 ml of distilled water was ingested to each subject and directed to come after 2 hours. Just after 2 hours 3 ml blood was collected and prepared for centrifuge for estimation of serum glucose as early as possible.

All data were recorded systematically in a preformed history sheet and all statistical analysis was done by computer using the software SPSS 17.0 version for windows. Fasting serum glucose, serum glucose level 2 hours after ingestion of 75 gm glucose levels were compared between the groups by unpaired student's 't' test. In the interpretation of results, < 0.05 level of probability (p) was accepted as significant.

RESULTS

The mean age of control subjects (group A) was 36.60±2.14761 years and the tobacco chewer subject (group B) was 42.74±3.13512 years. The mean height was 1.68 meter in group A & 1.67 meter in group B and mean weight was 61.6 kg in group A & 65.8 kg in group B. The mean BMI were 21.82 Kg/m^2 & 22.99 Kg/m^2 in group A & group B respectively (Table I)

Table I: Distribution of subjects according to mean age height, weight and BMI.

Groups	Age (years)	Height (m)	Weight (Kg)	BMI (Kg/m^2)
Group A (n=50)	36.60±2.14761 (35-45)	1.68	61.6	21.82
Group B (n=50)	42.74±3.13512 (35-45)	1.67	65.8	22.99

Group A: control (non tobacco chewer & nonsmoker)
Group B: experimental (tobacco chewer & nonsmoker)
n= number of subjects.
Figures in parenthesis indicate ranges

The mean ± SD fasting serum glucose level was 4.9020 ± 0.55420 mmol/L in group A(control) & 7.4520 ± 0.78409 mmol/L in group B(tobacco chewer &nonsmoker). The mean fasting serum glucose level was significantly ($p<0.001$) higher in tobacco chewer &nonsmoker subjects (group B) than control subjects (group A).The mean ±SD serum glucose level 2 hours after ingestion of 75 gm glucose was 6.0220 ± 0.65971 mmol/L in group A(control), 10.6740 ± 1.56033 mmol/L in group B (tobacco chewer & nonsmoker subjects).Again, the mean serum glucose level 2 hours after ingestion of 75 gm glucose was significantly ($p < 0.001$) higher in group B (tobacco chewer & nonsmoker) subjects than group A(control) (Table II).

Table II: Mean ± SD serum fasting glucose & serum glucose level 2 hours after ingestion of 75gm glucose in group A & group B subjects

Variables	Group A (n=50)	Group B (n=50)
Fasting serum glucose (mmol/L)	4.9020 ± 0.55420 (3.60 – 5.80)	7.3680 ± 0.80621*** (6.00 – 10.30)
Serum glucose level 2 hours after ingestion of 75gm glucose (mmol/L)	6.0220 ± 0.65971 (4.80 – 9.50)	9.6400 ± 1.04491*** (7.30 – 12.00)

Data were expressed as mean± SD. Unpaired student's 't' test was done.
Group A : control (non tobacco chewer & nonsmoker)
Group B : experimental (tobacco chewer & nonsmoker)
n= number of subjects.
*** = P<0.001
Figures in parenthesis indicate ranges.

DISCUSSION

The present study was carried out to compare the fasting serum glucose and serum glucose level 2 hours after ingestion of 75 gm glucose in between tobacco chewer non smoker and non tobacco chewer non smoker control subjects.

In this study, the mean fasting serum glucose level and serum glucose level 2 hours after ingestion of 75 gm glucose were significantly higher in tobacco chewer non smoker subjects than those of control subjects. Similar observations were made by some other investigators[2,3,9,10]. It cannot be elucidated from this study the exact mechanism of high glucose level due to tobacco chewing but researchers have observed that the use of nicotine like products caused adverse effects like hyperglycemia[11,12]. The nicotine present in tobacco might hamper the maintenance of blood glucose level of insulinpossibly by lowering insulin sensitivity. Moreover, adiponectin, hormone secreted by adipocytes,level decreases in smokers due to nicotine component of tobacco. Adiponectin is also involved in the maintenance of serum glucose levels. So, decrease level of adiponectin had been linked to the possibility of developing type 2 diabetes mellitus[13].
Moreover, some authors found for the first timean association between heavy use of oral moist snuff and type 2 diabetes as they got same plasma insulin level during smoking and snuffing[8].

Again, increased smokeless tobacco consumption increases the lipid metabolism and accumulation of fat content in the blood stream, which leads to development of greater intra-abdominal fat mass that is larger upper body fat distribution, as a results there is accumulation of fat specially abdominal or visceral fat. Central (intra-abdominal) adiposity is more strongly linked to insulin resistance. Visceral fat is metabolically more active than non visceral fat. It is more lipolyticaly active than subcutaneous fat because of its greater complement of adrenergic receptors. In addition to these, abdominal adipose tissue store is resistant to the antilypolitic effect of insulin. So, there is increase lypolysis in adipocytes and alteration

in the production of adipokines such as tumor necrosis factor alpha (TNF-α), adeponectin and resistine, resulting in insulin resistance and promotes to develop type 2 diabetes mellitus.

CONCLUSION

From this study it may be concluded that tobacco chewing may increase fasting serum glucose and serum glucose level 2 hours after ingestion of 75 gram glucose in tobacco chewers non- smokers, which is the evidence of development of type 2 diabetes mellitus due to tobacco consumption. In this respect we recommend to build awareness among the tobacco chewer, so that they may refrain from tobacco consumption in order to reduce mortality and morbidity caused by type 2 diabetes mellitus.

LIMITATIONS AND RECOMMENDATIONS

The limitations of this study were that it was conducted in a selected area,the sample was taken purposively and serum nicotine level could not be measured. To overcome the limitations we recommend this type of study with large sample size along with estimation of serum nicotine level,plasma free fatty acid level, fasting serum insulin level, insulin sensitivity and insulin resistance, TNF-α, adiponectin level in tobacco chewer non-smoker subjects.

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in the production of adipokines such as tumor necrosis factor alpha (TNF-α), adeponectin and resistine, resulting in insulin resistance and promotes to develop type 2 diabetes mellitus.

CONCLUSION

From this study it may be concluded that tobacco chewing may increase fasting serum glucose and serum glucose level 2 hours after ingestion of 75 gram glucose in tobacco chewers non- smokers, which is the evidence of development of type 2 diabetes mellitus due to tobacco consumption. In this respect we recommend to build awareness among the tobacco chewer, so that they may refrain from tobacco consumption in order to reduce mortality and morbidity caused by type 2 diabetes mellitus.

LIMITATIONS AND RECOMMENDATIONS

The limitations of this study were that it was conducted in a selected area,the sample was taken purposively and serum nicotine level could not be measured. To overcome the limitations we recommend this type of study with large sample size along with estimation of serum nicotine level,plasma free fatty acid level, fasting serum insulin level, insulin sensitivity and insulin resistance, TNF-α, adiponectin level in tobacco chewer non-smoker subjects.

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ORIGINAL ARTICLE

Comparative Study Between General and Spinal Anaesthesia in Laparoscopic Appendicectomy

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ABSTRACT

BACKGROUND: *The introduction of laparoscopy has revolutionized the surgical field with its advantages of reducing morbidity with early recovery. Laparoscopic appendicectomy is rapidly increasing in the treatment of acute appendicitis. Spinal anaesthesia has some advantages over general anaesthesia in providing analgesia while avoiding some of the complications of general anaesthesia.* ***OBJECTIVES:*** *To study the overall outcome, safety and side effects of Spinal anaesthesia in laparoscopic appendicectomy and its comparison with general anaesthesia.* ***METHODS:*** *This comparative study was conducted on 60 patients undergoing laparoscopic appendicectomy. Total patients were divided into two groups of 30 patients each. Group (G) was done under general anaesthesia (30 patients) and group (S) was done under spinal anaesthesia (30 patients).* ***RESULTS:*** *Anaesthetic procedures and surgeries for all patients were successfully completed. From 1 min to 12 hours post-operative, there was significant increase in mean heart rate and mean arterial blood pressure in group G than group S. In group S, 2% was converted to open due to shoulder pain and inappropriate level of anaesthesia. The operative time between both groups was insignificant. Shoulder pain was found in 4% of group (S). Mean Visual analogue scale (VAS) score was significantly lower at 1,2,4 and 12 h with significantly less analgesic requirements in group (S). Nausea and vomiting was found in 4% patient of group (G). 6% in group S had retention of urine and needed urinary catheterization.* ***CONCLUSION:*** *Spinal anaesthesia can be used safely using a combination of 0.5% hyperbaric bupivacaine mixed with fentanyl provided effective anaesthesia for laparoscopic appendectomy compared to general anaesthesia .*

KEY-WORDS: General anaesthesia (GA), Spinal anaesthesia (SA), Pneumoperitoneum, Laparoscopic appendicectomy, Heart rate (HR), Arterial blood pressure (ABP)

INTRODUCTION

The introduction of laparoscopy in the field of surgery in the mid 1950s revolutionized surgical techniques due to reduced bleeding, less complications and early recovery. The gradual shift of laparoscopy to include more complicated surgical procedures resulted in modification of existing anaesthetic techniques. The various effects of induction of pneumoperitoneum can result in respiratory embarrassment and cardiovascular changes best manged by use of general anaesthesia (GA)[1]. The evolution of anaesthetic medicine on scientifically and clinically relevant scales has propelled innovations and initiatives for newer safer techniques[2]. Advancement

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in anaesthesiology have been made as many fronts besides clinically relevant scales[3,4,5].

Acute appendicitis is one of the most common surgical causes of acute abdominal pain throughout the world[6]. The cumulative incidence of acute appendicitis in western countries approximately 9% and the incidence of acute appendicitis have been increasing both in developed and developing countries[7]. Open appendicectomy was the choice of surgery earlier and now it is gradually replaced by laparoscopic appendicectomy (LA)[8]. The laparoscopic approach has rapidly increased in popularity due to early recovery, shortened hospital stay and decrease chance of infectious complications[9].

It is evident that spinal anaesthesia has a significant and excellent outcome in the care of patients undergoing laparoscopic surgery[10]. Spinal anaesthesia is a less invasive anesthetic technique that has lower morbidity and mortality compared with general anaesthesia[11]. Spinal anaesthesia has the advantage of providing analgesia and muscle relaxation in a conscious patient. Spinal anaesthesia is still preferred for patients who are high risk for general anaesthesia and basing on this, laparoscopic surgeries being performed under spinal anaesthesia in selected patients have started coming in[12].

Spinal anaesthesia has got many advantages over general anaesthesia is that the patient is awake and oriented during the procedure, tend to ambulate earlier and complications related to intubation or extubation is avoided in spinal anaesthesia for patients undergoing laparoscopic interventions[13]. Some complications as pressor response to endotracheal intubation, increased release of stress hormones, sore throat, post-operative pain, post-operative nausea and vomiting (PONV) are associated disadvantages of GA[14,15].

MATERIALS AND METHODS

This comparative study was carried out at Prime Medical College Hospital, Rangpur from October 2018 to December 2019. Total 60 Patients in age group ranging from 20-35 years, body mass index 28 kg/m^2 and ASA grade I were included in this study after a written informed consent was obtained. Both anaesthetic techniques either general or spinal anaesthesia were considered for each patient and the patients were randomized either general anaesthesia (Group G) 30 patients or spinal anaesthesia (Group S) 30 patients. Patients preoperative evaluation and preparation were completed and all patients with acute appendicitis undergoing laparoscopic appendicectomy were included in this study. Patients with contraindication to laparoscopic appendicectomy were excluded from this study. After obtaining base line vital signs, both groups were preloaded with 8 ml/kg of Ringers lactate solution via peripheral vein. The patients of both groups were pre-medicated with 5 mg diazepam and 8 mg ondansetron before induction of anaesthesia.

GA PATIENTS (Group G)

Patients of group G were induced with intravenous propofol 2mg/kg, fentanyl 0.75µgm/kg and succinyl chlorine 1.5 mg/kg and then intubated with suitable size endotracheal cuffed tube. Anaesthesia was maintained using combination of halothane and nitrous oxide in oxygen and vecuronium as neuromuscular blocking agent. Ventilation was maintained with tidal volume of 7-8 ml/kg and ventilatory rate was adjusted to maintain $PaCO_2$ of 35-40 mm Hg. Non invasive arterial

blood pressure, electrocardiography, pulse oximetry and end tidal carbon dioxide ($ETCO_2$) were monitored continuously. At the end of surgery, residual neuromuscular block was reversed by neostigmine 0.04 mg/kg and atropine 0.02 mg/kg and patient was extubated and transferred to post anaesthesia care unit.

SA PATIENTS (Group S)

Under all aseptic technique, patients in sitting position at the level of $L_{3,4}$ or $L_{4,5}$ in midline approach, lumbar puncture was performed using 27 gauge pencil point spinal needle. Once flow of clear CSF is seen, 15 mg bupivacaine (hyperbaric) with 25 microgram fentanyl injected intra-thecally and patient asked to lie in supine position. The sensory block level was assessed by pin prick and motor block level was assessed by modified Bromage scale. Ringers lactate solution (4-6 ml/kg) was infused during the surgery. Non-invasive arterial blood pressure, electrocardiography, pulse oximetry were monitored continuously. Intraoperative hypotension was managed by intravenous ephedrine sulphate. At the end of surgery, patients were transferred to PACU. In both the groups, mean ABP, heart rate and SPO_2 were recorded prior to induction, following induction, immediately after pneumoperitoneum, every 15 min thereafter and 1,2,4,8 and 12 h post-operatively. Post-operative pain was analyzed by using visual analogue scale (VAS) and assessed at 1,2,4 and 12 hrs following operation.

RESULTS

In this study, total 60 patients in the age group ranging from 20-35 years were included. Fifty five patients were male and five patients were female. There was no statistically significant difference between both studied groups regarding age, sex distribution, mean body mass index (BMI) and other co-morbidities.

Table I : Comparison between group G and group S regarding mean heart rate at different times.

Mean HR	Group (G)	Group (S)	Independent t-test	
	Mean ± SD	Mean ± SD	t	p-value
Basal	88± 1.78	87± 2.67	1.982	0.160
After induction	92± 1.5	76± 1.65	33.870	<0.001
Pneumoperitoneum	102± 1.20	79± 2.08	41.839	<0.001
Intra op 15	100 ± 2.48	86± 3.10	24.14	<0.001
Intra op 30	96± 2.80	85± 1.10	16.567	<0.001
Intra op 45	92± 2.65	84 ± 2.50	1.935	<0.001
Intra op 60	90 ± 1.27	79 ± 2.07	20.256	<0.001
Post op 1 h	94± 3.70	85± 1.50	9.880	<0.001
Post op 2 h	95± 3.08	86± 3.60	8.580	<0.001
Post op 4 h	97±2.30	81± 2.83	20.540	<0.001
Post op 8 h	93± 1.25	82± 2.67	17.690	<0.001
Post op 12 h	90±2.82	85± 3.62	6.907	<0.001

The table shows that, at basal time there was no statistically significant difference found between group G and group S. But since induction to 12 h post-operative the table shows that there was highly statistically significant increase in mean heart rate in group G than group S with p-value <0.001.

Table II : Comparison between group G and group S regarding mean arterial blood pressure at different times.

Mean HR	Group (G)	Group (S)	Independent t-test	
	Mean ± SD	Mean ± SD	t	p-value
Basal	109.20 ± 1.80	109.10 ± 2.06	0.224	0.829
Pneumoperitoneum	96.90 ± 3.16	86.36 ± 3.98	9.376	<0.001
Intra op 15	95.42 ± 2.87	84.7 ± 3.61	8.456	<0.001
Intra op 30	93.22 ± 2.95	88.9 ± 3.64	6.038	<0.001
Intra op 45	92.04 ± 3.45	86.52 ±4.24	5.580	<0.001
Intra op 60	91.86 ± 4.17	88.21 ±6.86	4.512	0.002
Post op 1 h	108.76 ± 2.37	94.3 ± 2.82	19.847	<0.001
Post op 2 h	109.65 ± 2.88	95.01±3.34	16.942	<0.001
Post op 4 h	106.22 ± 2.29	96.35±2.74	12.152	<0.001
Post op 8 h	104 ± 2.78	98 ± 2.66	7.983	<0.001
Post op 12 h	102.38 ± 3.38	99.05 ± 3.81	3.920	0.006

The table shows that at basal time there was no statistically significant difference found between group G and group S, but since induction to 12 hours post-operative the table shows that there was highly statistically significant increase in mean arterial blood pressure in group G than group S with p-value <0.01.

As for post-operative pain, VAS score was recorded for both groups with mean score 3.2 ± 0.8 in group (G) and 1.7 ± 0.4 in group (S) at 1 hour Post-operative with p-value <0.001. At 12 hours Post-operative the mean score was 2.9 ± 0.80 in group (G) and 2.2 ± 0.37 in group (S) with p-value <0.001. Group (G) needed analgesics more than group (S).

Three patients of group (S) had nausea and one patient had vomiting. Two patients in group (S) had retention and needed catheterization to evacuate the bladder but none needed further catheterization. Early post-operative mobilization was noticed in group (S) 12.0 ± 1.4 h as compared to 17.0 ± 2.7 h for group (G) with p-value <0.001. Group (G) had a higher mean cost of the operation and hospital stay.

DISCUSSION

With the advancement of medical science, the popularity of laparoscopic surgery for abdominal cases are rapidly increasing. Though general anaesthesia is the most acceptable form of anaesthesia for laparoscopic procedures but some patients having co-morbidities like COPD, Bronchial asthma are more prone to develop risk and complications under GA. Rise in the airway

pressure, atelectasis, hypercapnoea and PONV are common risk associated with GA. In this context, spinal anaesthesia offers a safer alternative to general anaesthesia with some additional advantages in pain management and that enhances the speedy recovery of the patient and reduces hospital stay time markedly.

Now-a-days, laparoscopic appendicectomy is one of the common surgical procedure worldwide. In this study,7.8% of the spinal anaesthesia group (S) of patients showed bradycardia, which was almost similar to Gurudatta and Arif's study of spinal anaesthesia in lower abdominal surgeries found 12% of the patients had bradycardia[15], while Mehta et al compared general and spinal anaesthesia in laparoscopic cholecystectomy and found no evidence of bradycardia[16]. 6% of group (S) patients had hypotension in our study while it was 24% in Gurudatta and Arif's paper15, 30% in Mehta et al, 18.21% in Sinha et al. study discussing laparoscopic surgeries under spinal anaesthesia[17].

The measurement and assessment of post-operative pain was carried out by VAS score that was in favor of group (S) throughout the post-operative period (1,2,4,12 h) with p-value <0.001, while Gurudatta and Arif,s study and Bessa et al. study found that the difference was non-significant after 6,8 h but Imbelloi et al. showed significant difference found at 2,4 h but non-significant difference at 12 hours in his study[18].

The requirement of analgesic ampoule at mean number in spinal anaesthesia group 0.7 ± 0.30 ampoule/patient as compared to 1.8 ± 0.7 ampoule/patient in general anaesthesia group. Bessa et al, did a study and compared general and spinal anaesthesia group and found significantly lower values being 0.5 to 1.113. Shoulder pain was recorded in 2 patients (5%) of group (S) which was less than reported by Gurudatta and Arif 24%15, Van Zandart et al. 25% in a study of laparoscopic cholecystectomy under spinal anaesthesia[19].

Some other complications like post-operative nausea and vomiting were 3 cases (7.5%) of group (G) and none of group (S) compared to 32% and 8% respectively in Gurudatta and Arif's study15. As for urinary retention, 2 patients (5%) of group (S) suffered from urinary retention and needed catheterization although Imbelloni et al. showed no cases of retention in their study[18].

Post-operative mobilization and return of bowel sounds were early in spinal anaesthesia group over general anaesthesia group due to better pain control outcome. The mean h for post-operative mobilization was 17.0 ± 2.6 h for group (G) and was 12.0±1.5 h for group (S) which was significant on p-value <0.001. Bowel sounds were heard earlier in group (S) after meantime of 6.2 ± 1.4 h as compared to 7.1 ± 2.3 h in group (G).

CONCLUSION

Laparoscopic appendicectomy performed under SA using a combination of 0.5% hyperbaric bupivacaine and fentanyl provided effective anaesthesia. The evidence suggests the safety of the use of spinal anaesthesia with minimal side effects which can easily be managed with the available drugs. SA can provide certain advantages over GA, such as lack of airway manipulation, maintenance of spontaneous respiration, effective post-operative analgesia, minimal nausea and vomiting, less operating room costs and early recovery and ambulation. So, the use of spinal anaesthesia for laparoscopic appendicectomy in a patient with risks for general anaesthesia may

bring far better outcome in upcoming days of advancement of medical science.

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ORIGINAL ARTICLE

Effects of Tobacco Consumption on Serum Creatinine & eGFR Levels in Tobacco Chewers.

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BACKGROUND: *The recent decades have been a massive global increase in tobacco use. Tobacco use is a major preventable cause of premature death and diseases. Immediate availability and the low price gives rise to high consumption of tobacco chewing and causes alteration of renal functions.* ***OBJECTIVES:*** *To observe the effects of tobacco consumption on renal functions in tobacco chewers.* ***METHODS:*** *This cross sectional analytical study was conducted from July 2016 to June 2017 in the Department of Physiology, Rangpur Medical College, Rangpur. A total number of 60 subjects were selected, among them 30 were apparently healthy non-tobacco chewer non-smoker subjects as control group (group A) and 30 were apparently healthy tobacco chewer non-smoker subjects (group B)). The subjects were selected from different area of Rangpur city. The effects of tobacco chewing on renal functions were studied by measuring the levels of serum creatinine and eGFR. For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows.* ***RESULTS:*** *Serum creatinine levels were significantly higher ($p<0.001$) & eGFR levels were significantly lower ($p<0.001$) in tobacco chewer subjects as compared with the healthy control subjects.* ***CONCLUSION:*** *The increased serum creatinine & decreased eGFR levels in tobacco chewer subjects were evidence of development of renal function impaired due to tobacco consumption.*

KEYWORDS: Smokeless tobacco, Nicotine, Creatinine, eGFR.

INTRODUCTION

The English word "tobacco" originates from the Spanish and Portuguese word "tabacco". Tobacco is a product prepared from the plant by curing them[1]. Tobacco contains the alkaloid nicotine, which is an extremely addictive drug[1,2]. In addition to nicotine, tobacco contains thousands of other chemicals such as cresol, pyrene, DDT, carbon monoxide, ammonia, hydrogen cyanide, acetone, methanol, formaldehyde, arsenic, cadmium etc[3,4]. There are two kinds of commonly used tobacco products in Bangladesh i.e. smoking and smokeless tobacco products[4]. Smokeless tobacco products used include a wide range: betel quid with zarda, zarda only or zarda with supari; betel quid with sada pata; pan masala with tobacco; sada pata chewing; gul, khoinee[4,5].

Tobacco consumption is one of the leading causes of premature death, disease and disability in the world. In Bangladesh 43.3% of adults (41.3 million) use tobacco in smoking and or smokeless form. More than five million

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people die globally each year due to tobacco related illness, the figure expected to increase to 8.3 million by 2030[5,6].

Tobacco consumption in any form has negative consequences on health and it has become a significant public health concern around the globe[5]. The short term effects of chewing tobacco are addiction to nicotine, receding gums, permanent gum loss, sensitive teeth, tooth decay, sores, patches and lumps in mouth, bad breath, bad taste in mouth, stained teeth etc. Long term effects of tobacco chewing has many adverse effects on the heart, several types of cancers eg. lung, pancreas, breast, liver, kidney and different organ[2].

Now a days the adverse effects of tobacco chewing on renal function have gained more attention, because it is associated with excessive morbidity and mortality. In addition to its known cardiovascular consequences of tobacco chewing are also considered to be the common particular risk factor for the renal function disorders[7]. Some researchers observed tobacco chewing identified as an important risk factor cause renal dysfunction, not only in subjects with pre-existent primary renal disease, hypertension and diabetes mellitus but also in healthy subjects[8].

Smokeless tobacco has been associated with periodental disease, precancerous oral lesions, oral cancer and cancer of the kidney. In addition the involvement of its highly reactive radicals in carcinogenesis, DNA damage, alteration of cellular antioxidant defense system. And reduction in kidney glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as the induction of lipid peroxidation in kidney, raises a lot of public health concern[9].

Consumption of tobacco is now increasing rapidly throughout the developing world and is one of the biggest threats to current and future world health. Because of vigorous efforts toward increase awareness of adverse effects of tobacco, smoking has declined consistently over the last few years, paradoxically the use of smokeless tobacco and snuff has greatly increased[10].

The purpose of this study was to asses the effect of tobacco on some renal parameters of tobacco chewer subjects of northern region because the rate of tobacco use is more among the people of this region. As far as our knowledge, this kind of study is not previously done in our country. This study would increase awareness about the adverse effects of unjudicial tobacco use on renal system.

METHODS

The Cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur from July 2016 to June 2017. The Rangpur Medical college ethical committee and thesis protocol review committee approved the study protocol. Total number of 60 apparently healthy subjects of both sexes with age 30-45 years were divided into following groups: Group A - 30 apparently healthy non-tobacco chewers non smokers and Group B - 30 apparently healthy tobacco chewers non-smokers. The subjects included in each group matched in their age and socio-economic condition. The duration of chewing is more than three years. All the subjects were free from history of liver, heart, lung and other chronic systemic diseases, obesity & diabetes mellitus, hypertension, pregnancy and lactating mother.

After selection of subjects, the objectives and the procedure of the study were explained in detail to them and their informed written

consent were taken. A standard questionnaire was filled after taking history and through clinical examinations. At the first day all study procedures were maintained and advised the subjects to be in overnight (8-10 hrs) fasting state. Then attended next day at 8.00 A.M. at the Department of Physiology, Rangpur Medical College, Rangpur. Fasting venous blood sample was collected from the subjects. 5 ml of blood was collected from antecubital vein from each subject under all aseptic precaution by a disposable syringe. The test tube containing blood was kept in standing position till formation of clot. Serum was separated by centrifuging the blood at 3000 rpm for 5 minutes. The clear supernatant was taken and kept in ependorffs. All biochemical tests were carried out as early as possible and done by enzymatic colorimetric method at the Department of Biochemistry, Rangpur Medical College, Rangpur.

eGFR (estimated glomerular filtration rate) is calculated by Cockcroft-Gault formula by using serum creatinine level, age, sex and body weight of the patients[11].

For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows.

RESULTS

The data depicted in Table –I. In this cross sectional study, the mean serum creatinine levels are significantly higher ($p<0.01$) and eGFR levels are significantly lower ($p<0.01$) in tobacco chewer non-smoker subjects than those of healthy control subjects.

Table-I: Mean ± SD serum Creatinine and eGFR levels in two groups (n=60)

Variables	Group A (non - tobacco chewers non smok ers) Mean ± SD Range (L - H)	Group B (Tobacco chewers non -smokers) Mean ± SD Range (L - H)	p value
Serum Creatinine mg/dl	0.8967 ± 0.13515 (0.70 – 1.10)	1.3200 ± 0.15403 (1.00 – 1.60)	0.000***
GFR ml/min/1.73m ^{2} of body surface ar ea	96.4440 ± 19.40323 (66.30 – 139.68)	67.0617 ± 8.81058 (56.31 – 88.64)	0.000***

A= Apparently healthy subjects of non-tobacco chewers non-smokers (Control).
B= Apparently healthy subjects of tobacco chewers non-smokers (Experimental).
n= Number of subjects. ***= $p<0.001$.
# Normal range of serum creatinine level is 0.6 – 1.3 mg/dl[12].
# Normal range of eGFR level is ≥ 90 ml/min per m^2 body surface area[13].

DISCUSSION

In this cross sectional study, serum creatinine levels were significantly higher ($p<0.01$) and eGFR levels were significantly lower ($p<0.01$) in tobacco chewer non-smoker subjects than those of healthy control subjects which is comparable to others[7,14].

Literature review suggested several mechanisms for these changes of serum creatinine and eGFR levels in tobacco chewer non-smoker subjects. Higher levels of serum creatinine and lower levels of eGFR in tobacco chewer non-smoker subjects might be due to tobacco contains nicotine and also some toxic components which are nephrotoxic cause alteration of the kidney functions. The effects of heavy metals in tobacco like Cadmium (Cd) and Lead (Pb) cause glomerular dysfunction lead to renal damage. Tobacco chewing induces renal damage through enhancing the synthesis of free radicals lead to alter the glomerular functions and increase the serum creatinine and decrease eGFR levels. For this causes impairment of renal functions. Nicotine increases mesangial cell proliferation through activation of nicotinic receptors. Tobacco chewing responsible for impairment of renal function which indicate increase serum creatinine and decrease eGFR levels[7].

The tobacco and its constituents undergo metabolic activation and nitrosation, which together produce the ultimate carcinogenic derivatives. Then, these derivatives cause DNA mutations and strand breaks, as well as biochemical and structural changes that increase cell proliferation, pre-neoplastic changes and carcinogenesis. The expression patterns of tumor suppressor genes, such as P53, BRCA1 and BRCA2, are strongly altered in people who overuse tobacco; these alterations are likely to diminish their tumor suppressor properties and favor carcinogenesis. These might be due to impairment of renal functions which indicate increase serum creatinine and decrease eGFR levels[14].

From the results of the present study, higher serum creatinine and lower eGFR levels in tobacco chewer non-smoker subjects might be due to tobacco chewing for a prolong period of time which induced sustained rise of blood nicotine, carboxyhemoglobin levels and also free radicals cause impaired renal functions in tobacco chewers.

CONCLUSION

In this present study, it has been concluded that higher serum creatinine and lower eGFR levels in tobacco chewer non-smoker subjects might be due to renal functions impairment in tobacco chewing for a prolong period of time which induced sustained rise of blood nicotine level. But exact mechanism of high levels of serum creatinine and lower levels of eGFR in this group of people could not be demonstrated from this type of study. So, estimation of serum nicotine level, in same study population with large sample size which may help us to avoid bias. Reduction in tobacco consumption improves renal functions impairment & reduce mortality and morbidity in tobacco chewers non-smokers.

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ORIGINAL ARTICLE

A Dermatoglyphics Study of Total Finger Ridge Count of β Thalassemia Major Patients in Bangladesh.

Afroj Zahan[1], Maskura Benzir[2], AHM Mazharul Islam[3], Sharna Moin[4], Tahmina Akter[5], Tamanna Mahmud Urmi[6].

ABSTRACT

CONTEXT: *Palmer dermatoglyphics of an individual can dictate the types of genetic diseases to which that person is susceptible. Total finger ridge count (TFRC) is a special feature of palmer dermatoglyphics. Many studies were carried out in various populations to determine TFRC of β-thalassemia major patients. However, there is no published article on this topic in Bangladesh. So, this study was aimed to establish the standard data of TFRC of β-thalassemia major patients and to make comparison with healthy individuals, previous studies on other populations.* ***MATERIALS AND METHODS:*** *This cross sectional analytical type of study was carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka, Bangladesh from January 2016 to December 2016. This study recruited 55 β thalassemia major patients aged between (5-35) years were considered as case group and 55 healthy individuals of the same age & sex were considered as control group were enrolled in this study. Dermatoglyphic prints of the study subjects were taken by ink & paper method . Total Finger Ridge count (TFRC) on the distal phalanges of the β thalassemia major patients were studied with 6X magnifying glass and compared with healthy individuals.* ***RESULTS:*** *The mean ± SD of Total Finger Ridge count (TFRC) were higher in β thalassemia major patients in comparison to the healthy individuals.* ***CONCLUSION:*** *This study concludes that, TFRC can be useful in the management of β thalassemia major specifically in early prediction & at the level of prevention.*

Key words: Dermatoglyphics, β thalassemia major, Total Finger Ridge count, Bangladeshi populations.

INTRODUCTION

The study of epidermal ridge of palms & soles running parallel in small fields known as dermatoglyphics[1,2,3]. All the physical traits or features of the human body including dermatoglyphics are controlled genetically and passed from generation to generations governed by the law of inheritance propounded by Mendel. Dermatoglyphics has long been recognized as a valuable research tool in the field of human genetics, forensic science, medico-legal & anthropological. Dermatoglyphics has a great importance in personal identification (e.g.- passport, legal issue, assurance of attendance in offices) as the various dermatoglyphic features differ from person to person and remains unchanged

Authors afiliations

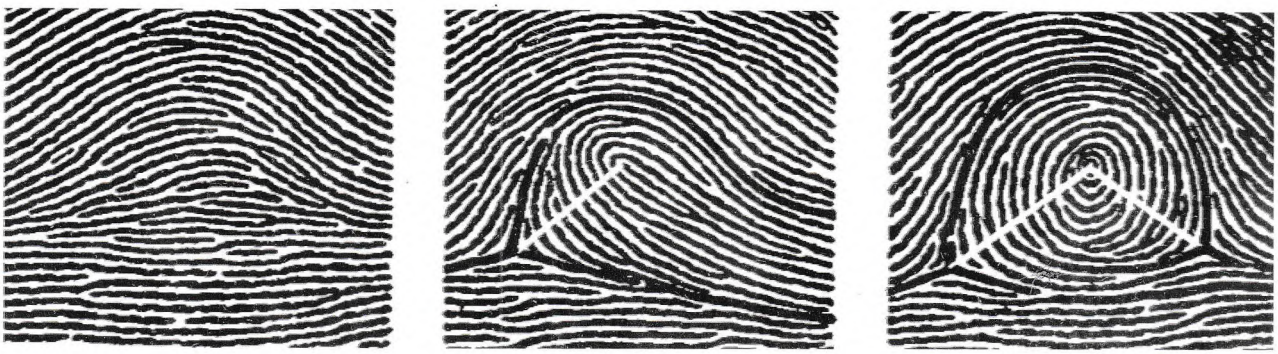
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throughout life[4]. Thalassaemia and the haemoglobin disorder are the most common clinically serious single gene disorder in the world. About 60,000-70,000 children are born each year with severe form of thalassaemia[5]. In Bangladesh, more than 7000 children are born with thalassemia each year[6]. β thalassemia is most common among all types of thalassemia with sever adverse consequences[7]. Abnormal chromosomes affect the development of various dermatoglyphic features, like–β thalassemia major, Down´s syndrome child have distinctive dermatoglyphic features on their hands and feet which have diagnostic value[8]. Substantial differences in selected dermatoglyphic feature of β thalassemia major patients have been noted in studies from different parts of the world. These differences appear to be racial/ethnic in origin. Distinctive dermatoglyphic features can be used to reinforce clinical judgment in the diagnosis of beta-thalassemia patients. TFRC is one of the most important feature of dermatoglyphics. In β thalassemia major patients TFRC can be used as risk indicator. This may be used as a preliminary screening to determine those at risk of developing β thalassemia major and proper monitoring can be instituted to prevent morbidity and mortality associated with this condition[9]. This paper provides the TFRC research methods, application and the relationship between β thalassemia major patients with healthy individuals.

MATERIALS AND METHODS

This analytical type of cross sectional study was carried out in the department of anatomy, Sir Sallimullah Medical College, Dhaka, Bangladesh between the periods of January, 2016 to December, 2016. Fifty five β thalassemia major patients aged between (5-35) years were considered as study group and fifty five healthy individuals of the same age & sex were considered as control group were enrolled in this study. All the subjects were free from other congenital or acquired deformities of finger and palm of hand. Study group were selected from the day care unit of transfusion medicine department (where patients receive transfusion of blood and blood component service which is an alternative to hospital admission) of Bangabandhu Sheikh Mujib Medical University, Dhaka, on the basis of Hb electrophoresis. The healthy individuals of the same age & sex were considered as control group. After selection of the subjects, dermatoglyphic print was taken by the ink & paper method[10]. Two white papers were fixed on clip board to take the print of both hands. Both hands were painted with ink and both hand prints were taken on white paper. Then dermatoglyphics of each hand were studied with 6X magnifying glass to identify the finger ridges for determination of TFRC. Total finger ridge count (TFRC) represents the sum of ridge counts of all ten digits[11]. Total finger ridges were counted by taking the number of ridges from the tri-radius to the core pattern connected by a straight line of all the digit of both hands (Fig :1 .a,b,c). The core forms the center of the pattern area (Fig : 2). Delta or tri-radius is located at the meeting point of three opposing ridge systems (Fig : 3). A triangle is formed at the center[12]. Ethical permission was taken from the Institutional Review Committee of Sir Salimullah Medical College, Dhaka. Data were expressed as mean ± SD and statistical significance of difference among the group was calculated by unpaired student's t test. Statistical analysis was done by using Statistical package of social service (SPSS) for windows version- 21. P value <0.05 was considered as significant.



(a) No tri-radius in arch (b) tri-radius in loop (c) Two tri-radius in whorl

Fig 1: Diagrammatic representation of (a) arch (b) loop (c) whorl pattern.

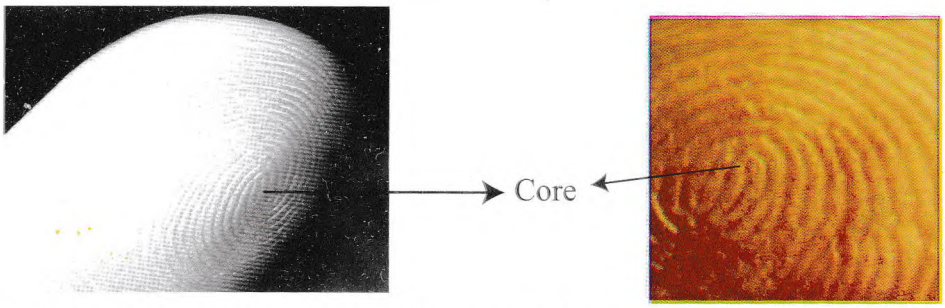


Fig 2: Diagrammatic representation of core or center of a pattern area.

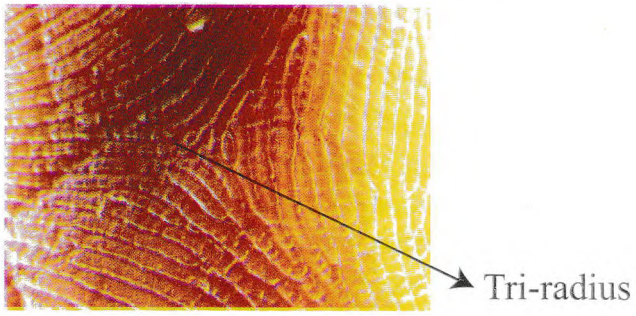


Fig 3: Diagrammatic representation of delta or Tri- radius of a pattern area.

RESULTS

In the present study TFRC in the distal phalanges of hands were studied. It was noticed that mean total finger ridge count was higher in both male ($P<0.000$) and female case ($P<0.05$) groups than in male and female control groups.

As shown in Table I, the mean ± SD of total finger ridge counts were 105.70 ± 30.18 and 68.04 ± 28.27 for the male case and control groups respectively. Highly significant difference of total finger ridge counts were found when compared between two groups ($P<0.00$). The mean ± SD of total finger ridge count in female case group was 94.04±24.78 and in female control group was 80.03±32.72. Significant difference of total finger ridge count was found when compared between two groups ($P<0.05$).

Table I: Comparison between total finger ridge count between two groups.

Sex	Group	Total finger ridge count (Mean ± SD)	P value
Male	Ca se (n=30)	105.70±30.18 (28.0 -165.0)	0.000**
	Control (n=24)	68.04±28.27 (16.0 -128.0)	
Female	Case (n=25)	94.04±24.78 (36.0 -141.0)	0.047*
	Control (n=31)	80.03±32.72 (34.0 -145.0)	

Figure in parentheses indicate range. Comparison between study group done by unpaired students "t" test, **= significant at P value < 0.01,
*= significant at P value < 0.05.
Case: β Thalassemia major patients.
Control: Healthy individuals.

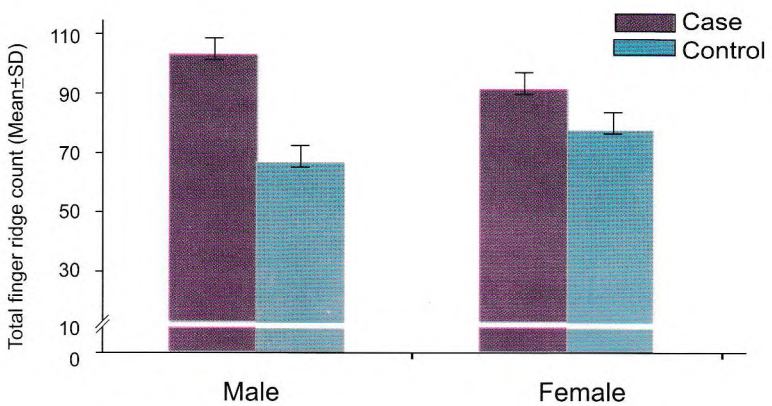


Fig 4: Distribution of total finger ridge count of hands in case and control group.

Case: β Thalassemia major patients.
Control: Healthy individuals.

DISCUSSION

This study attempts to analyse whether any specific dermatoglyphics feature like TFRC is exist for β thalassemia major and whether that serve as an early diagnostic tool. Our study shows that there is significant increase in TFRC in both male & female β thalassemia major patients. This observation coincides with the study of Ganorkar YS[13] and Dogramaci AC[14], they observed that total finger ridge count was significantly more in both male and

female case than control group. This finding was similar with the present study. Saha KC, Chatterjea JB and Mukherjee DP[15] reported that TFRC were higher in female β thalassemia major patients than male patients. This finding was dissimilar with the present study. Stomeo C and Tannonia N[16] reported that TFRC was lower in both male and female study group. This result was dissimilar with the present study. Observed results of different variables showed some similarities as well as dissimilarities with the available information present on different publications. The similarities might be due to the fact that palmar dematoglyphics and β thalassemia major both are genetically determined and once established, dermatoglyphic patterns remain unchanged throughout life. Substantial dissimilarities have been noted in studies from different parts of the world. These differences appear to be racial/ethnic in origin.

CONCLUSION

This study was aimed to establish a standard baseline data of TFRC of β thalassemia major patients in Bangladesh and to make comparison with healthy individuals. In the present study we observed that, significant increase in number of total finger ridge count is found in both sex of β thalassemia major patients. Our findings can be useful in the management of β thalassemia major specifically at the level of prevention.

ACKNOWLEDGEMENT

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ORIGINAL ARTICLE

Susceptibility Pattern of Antibiotics in Urinary Tract Infection: a Study in a Teaching Hospital.

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ABSTRACT

OBJECTIVES: *Urinary tract infections (UTI) remain the common infection in outpatients as well as hospitalized patients. In high percentage of cases urinary tract infection may be recurrent and progresses from urinary bladder to other parts of urinary trac leading to renal parenchymal damage. Likewise it is responsible for high morbidity and mortality. Complete cure especially in male sex and with organic lesion of urinary tract and also in patients with co-morbidity like diabetic mellitus, cancer, immunosupression and with instrumentation is very difficult and have high failure rate. So it needs to be meticulous in treating patients of UTI. Updated knowledge on antimicrobial sensitivity pattern is essential for appropriate therapy targated to complete cure and eradication. The aim of the study is to determine the changing pattern of antibiotic susceptibility among uropathogen causing urinary tract infection.* ***METHODS:*** *Midstream urine samples were collected from patients of different age-groups in both sex and subjected to microscopical and appropriate biochemical tests followed by culture for proper identification of causative agent. Antimicrobial susceptibility testing was performed by Kirby Bauer's disc diffusion method. Results: In our study, 50 samples of clinically suspected, routine examination confirmed urine showed growth of pathogens among which the most prevalent were E.Coli (64%), followed by Enterococci (12%). The majority (76%) of the isolates were from female. 56% of the isolates are susceptible to Amikacin, while 50% are susceptible to nitrofurantoin and 38% to imepenem. Very high rate of resistance observed against cefixime (88%). The sensitivity pattern to other antibiotics are ceftriaxon 26%, ciprofloxacin 24%, gentamicin 22%, cefuroxime 20%, azithromycin 16%, doxycycline & cotrimoxazole 14%,. E.Coli showed high susceptibility to amikacin 71.87% followed by nitrofurantoin 59.37%.* ***CONCLUSION:*** *The study revealed E.Coli as the most common etiological microb and remains sensitive susceptible to amikacin. Imipenem and nitrofurantoin are good alternatives. The high incidences of multiple antibiotics resistance was identified. So urine culture and sensitivity must be performed prior to antibiotic therapy.*

KEYWORDS: Urinary tract infection, Causative organism, Antibiotic response.

INTRODUCTION

Urinary tract infection

(UTI) is one of the most common clinical condition encountered in general and gynecological practice[1]. It is the second most common type of infection accounting for about 8.1 million visit to health care providers each year[2]. Because of its anatomy and favorable chemical composition human urine can support growth of several different strains of bacteria [3,4]. E. Coli is the cause of 80-85% of UTI, with staphylococcus being the causes in 5-10%[5]. Other bacterial species that causes the UTI include klebsiella, proteus, enterobacter and strep. agalactae. UTI may also be less commonly due to fungal or viral infections[6], and usually related to abnormalities of the urinary system or urinary catheterization[7].

Microbial infections of urinary tracts are generally classified as uncomplicated or complicated[8]. Uncomplicated UTIs occur in sexually active healthy female patients with

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structurally and functionally normal urinary tracts. UTI in male patients are considered as associated with co-morbid conditions and other pathologies.Those prolong treatment period and there is increased chance of therapeutic failure.

These conditions include abnormalities of urinary tract that slows down urine flow, (outflow obstruction) the presence of foreign body (e.g., indwelling catheter, stone) or infection with resistant pathogens [9,10] .

The inappropriate and non judicious use of antimicrobial agents invariably results in the development of antibiotic resistance. In recent years it has become a major problem worldwide[11]. Four large scale studies reporting in vitro susceptibility of E.Coli causing uncomplicated UTI in North America and Europe were conducted [12,13,14].

To ensure appropriate treatment, informations about the organism that causes UTI and their antibiotic susceptibility response is mandatory[15]. The aim of study was to assess the changing behavior of urinary pathogens to antimicrobial agents in UTIs.

METHODS

This study was conducted on 50 culture positive UTI patients in Prime Medical College Hospital, Rangpur between January 2018 to January 2019. Only patients who have clinical symptoms of UTI and positive urine culture (>105organisms/ml) were studied. The midstream urine specimens were obtained by clean catch method. The sample were collected in sterile universal containers and cultured within 30 minutes of collection. The samples were placed out on macconkey and blood agar media and incubated., aerobically overnight at 37^0C. Samples that showed pure growth of isolate in a count of > 105 colony-forming unit (CFU) per ml of urine after overnight of incubation were considered to indicate significant bacteriuria. Antibiotic sensitivity testing was performed using Kirby Bauer disc diffusion method as described by the National committee for Clinical laboratory Standard (presently called Clinical Laboratory Standard Institute)[16].

Interpretation as sensitive or resistant was done on the basis of inhibition of bacterial growth as recommended by disc manufacturer. The antibiotic used for susceptibility testing were Ciprofloxacin, Cotrimoxazole, Cefuroxime, Doxycycline, Imepenem, Amikacin, Gentamicin Nitrofurantoin, Cefixime, Cefuroxime, Azithromycine and Ceftriaxione.

RESULTS

Table –I outlines the demographic profile of UTI. The patients were between 18 and elderly age group (18-70).Usually reproductive age counted from 12 years in case of female and 13 years in case of male Due to unavailability of patient we enrolled the age group from 18 years. The prevalence of UTI is high among females (76%) than males (24%). Females of the reproductive age group (18-49 years) constitute 68 % of total patients with UTI. However, elderly (more than 50 years) males had higher incidence of UTI (16%) compared to the elderly females (8%)

Table-I: Age and sex distribution of patients with urinary tract infections

Age group (in years)	Females No (%)	Males No (%)
18-29	10 (20%)	1(2%)
30-49	24 (48%)	3(6%)
50-70	4 (8%)	8 (16%)

The commonest isolates were E.Coli, Enterococci, Pseudomonas, Klebsiella, Micrococcus, Stap.Aureus, Strep.Agalactae. (These represented 64%, 12%, 6%, 4%, 4%, 2% and 2% of isolate respectively), Pie chart showed the distribution of organism.

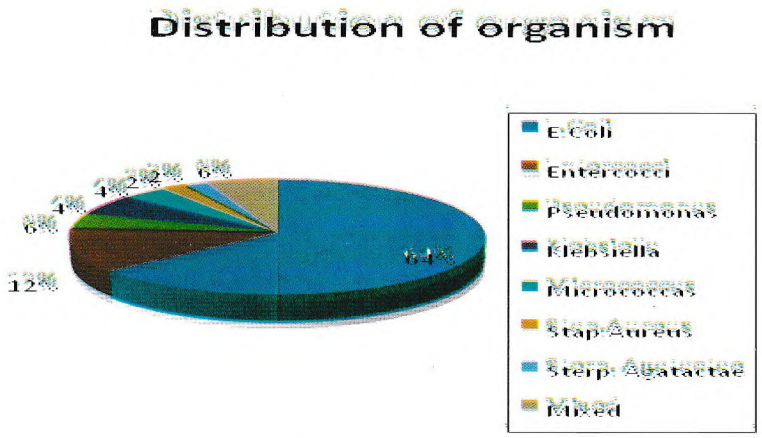


Figure1: The pie chart showing organism isolated

The antimicrobial potency and spectrum for 11 selected antimicrobial agents of different classes against the seven most frequent UTI pathogens is summarized in table-II.

Table-II: Antibiotic susceptibility and resistance pattern of isolated organisms in UTI

	E Coil (n-32)		Enterococcas (n=6)		Pseudomonas (n=3)		Klebsiella (n=2)		Staph Aureus (n=2)		Micrococcas (n=1)		Strep Agalactae (n=1)	
S	R	S	R	S	R	S	R	S	R	S	R	S	R	S
Amikacin	24.13%	71.87%	50%	50%	33.34%	66.66%	0%	100%	50%	50%	100%	0%	0%	100%
Nitrofurantoin	40.63%	59.37%	50%	50%	33.34%	66.66%	100%	0%	50%	50%	100%	0%	100%	0%
Imcepenem	62.5%	37.5%	75%	25%	0%	100%	0%	100%	50%	50%	100%	0%	100%	0%
Ceftriaxon	65.63%	34.37%	50%	50%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%
Ciprofloxacin	38.75%	31.25%	75%	25%	66.67%	33.33%	0%	100%	100%	0%	100%	0%	100%	0%
Lomifloxacin	75%	25%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%
Gentamicin	74.13%	21.87%	50%	50%	66.67%	33.33%	100%	0%	100%	0%	0%	100%	100%	0%
Azithromycin	81.25%	18.75%	75%	25%	66.67%	33.33%	100%	0%	100%	0%	100%	0%	100%	0%
Cotrimoxazole	84.38%	15.62%	100%	0%	66.67%	33.33%	100%	0%	100%	0%	0%	100%	100%	0%
Doxycycline	84.38%	15.62%	100%	0%	33.34%	66.66%	100%	0%	100%	0%	100%	0%	100%	0%
Cefixime	84.38%	15.62%	75%	25%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%

S=Susceptible, R=Resistant

E. Coli showed high susceptibility to Amikacin(71.87%), Nitrofurantoin (59.39%), Imepenem (37.5%) followed by Ceftrinxone (34.37%), Ciprofloxacin (31.25%),Cefuroxime (25%),Gentamicin (21.87%), Azithromycin (18.75%), Cotrimoxazole, Doxycycline, Cefixime (15.62%). Enterococci is highly sensitive to Amikacin, Nitrofurantoin, Ceftriaxone (50%) followed by Imepenem, Ciprofloxacin, Azithromycin, and Cefixim (25%). Pseudomonas is highly sensitive to Amikacin,Nitrofurantoin,Doxycycline (66%) followed by Ciprofloxacin, Gentamycin, Azithromycin, Cotrimoxazole (33%). Klebsiella is very highly susceptible to Amikacin, Nitrofurantoin and Cefuroxime (100%). Amikacin, Nitrofurantoin and Imepenem (50%) sensitive against Staph.Aureus. Micrococci is very highly susceptible to Gentamicin and Cotrimoxazole (100%). Strep. Agalactae is also very highly susceptible to Nitrofurantoin (100%).

Table III depicts the overall percentage of uropathogens sensitivity to antibiotics. More than 56% of the isolates are sensitive to Amikacin, while 50% are sensitive to Nitrofurantoin. 38% to Imipenem and 26% to Ceftriaxone.

Table III: Overall percentage of uropathogens susceptibility to antibiotics

Antibiotic	Susceptibility (%)	Resistance (%)
Amikacin	56%	44%
Nitrofurantoin	50%	50%
Imepenem	38%	62%
Ceftriaxon	26%	74%
Ciprofloxacin	24%	76%
Gentamycin	22%	78%
Cefuroxime	20%	80%
Azithromycin	16%	84%
Cotrimoxazole	14%	86%
Doxycyeline	14%	86%
Cefixime	12%	88%

DISCUSSION

The study observed that the prevalence of UTI is higher among females (76%) than males (24%) sex. Females of reproductive age group (18-49 years) constituted (68%) of the total patients of UTI. This study was supported by Akram et al[17]. In another study, UTI was observed more in middle age groups and accounted for 54.3% of total cases[18].

It has been reported that adult women have a higher prevalence of UTI than men principally due to anatomical and physiological factors[17]. Among males an increased prevalence of UTI was recorded in age group of more than 50 years (16%) than younger male (8%). This is probably because with advancement of age of male patients. The incidence of UTI increases in men due to enlarged prostate and also neurogenic bladder[19].

The study demonstrated that E.Coli remains as the leading pathogens being responsible for 64% of UTI. This is in consistant with findings of other studies in which E.Coli was the most frequently reported isolate from patients[20]. In another study, it was reported that predominant uropathogens are E. Coli which also supports our study results[21]. Following E. Coli, our study shows enterococci species (12%), Proteus(6%), Klebsiella (4%) as the other common uropathogens. Our findings are in accordance with study by Dias Neto et al[22]. Enterobacteriaceae have several factors favouralbe for their attachment to the urothelium. These gram negative aerobic bacteria colonize the urogenital mucosa with adhesion, pilli, fimbrae[19].

In this study it is revealed that Cefixime, Doxycyclin, Cotrimoxazole and Cefuroxime are virtually useless against uropthogens and

were sensitive in 12%, 14%, 14%, 16% and 20% of all isolated organism respectively. Amikacin shown strong activity against 56% of all isolated organism very active in E.Coli, Klebsiella and Pseudomonas particularly. Our result was almost similar to another study where the susceptibility rate of E. Coli to amikacin in remained 93-100%[23]. Nitrofurantoin also showed strong activity against 50% of all isolated organism and very active against E. Coli and Pseudomonas sp. particularly. A recent study conducted in India showed that Nitrofurantoin had the best in vitro susceptibility profile against E. Coli[24] Imipenem and Amikacin showed strong activity against Klebsiella 100%. Klebsiella isolate higher suscepssibility against Imepenem(88%) and Amikacin(59%) in the study by Akram et al[17]. The isolate shows low degree of susceptibility (24%) to fluoroqunolone which indicates that they can no more be opted for treating UTI.

CONCLUSION

In our study, culture positive uropathogens was studied for sensitivity to drugs. Majority are adult female patients. E. Coli was the most common etiological agent and remained sensitive to Amikacin. Imipenem and Nitrofurantoin are also good choice along with Amikacin.

We like to emphasize that empirical antibiotic selection should be based on the finding of prevalence of microbial organisms and their antibiotic sensitivities rather than on universal guidelines and also clinical experience Although our study was very small one for opinion with greater confidence, but it highlighted the overall situation in our community.

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