ISSN 2518-3249

Vol. 2 No. 2
July 2016

Barind Medical College Journal

Functional dyspepsia (FD) is a clinical syndrome presented with persistent or recurrent pain or discomfort localized in the epigastric region without evidence of organic disease likely to explain the symptoms. For a very long time,

See Editorial Page 01

OFFICIAL JOURNAL OF
BARIND MEDICAL COLLEGE

BARIND MEDICAL COLLEGE JOURNAL (BMCJ)

Volume 2 Number 2 July 2016

Official Journal of Barind Medical College

Charaka was one of the principal contributors to the ancient art and science of Ayurveda a system of medicine and lifestyle developed in Ancient India in 2nd century BC. He is famous for authoring the medical treatise, the Charaka Samhita. Charaka has been identified as a native of Kashmir. He is well known as the "father of medicine".
He introduced tridosha theory in medicine. A body functions because it contains three dosha or principles, namely movement (vata), transformation (pitta) and lubrication and stability (kapha). These doshas are produced when dhatus (blood, flesh and marrow) act upon the food eaten. Health exists when there is a balance between three fundamental bodily bio-elements or doshas. Illness is caused when the balance among the three doshas in a human body are disturbed. To restore the balance he prescribed medicinal drugs.

Published By
Barind Medical College
Rajshahi, Bangladesh

Annual Subscription
Tk. 200/- for local subscribers
US$ 20 for overseas subscribers

BMCJ, a peer reviewed biannual medical journal, is the official journal of Barind Medical College, Rajshahi, Bangladesh.

BARIND MEDICAL COLLEGE JOURNAL (BMCJ)

Official Journal of Barind Medical College

Volume 2 Number 2 **July 2016**

Contents

■ **EDITORIAL**

Functional Dyspepsia: An unsolved dilemma 1-2
M. Manzurul Haque

■ **ORIGINAL ARTICLE**

Effect of vegetarian diet on Triglyceride (TG) level 3-6
Momena Khatun Munna, Md.Obaidullah Ibne Alib, Md.Mijanur Rahman Sardar, Farjana Yeasmin, Sohel Baksh, Gopal Chandra Sarker

Gender differences in anthropometric somatotype of adult santhals in north bengal, Bangladesh 7-10
Sumana Sutradhar, Shamim Ara, S.M. Akram Hosssain, Manjuara Khatun

Excessive vaginal discharge of reproductive age : common causative agents 11-14
Mst. Sultana Aktara, Md. Abdullah Siddiqueb, Md. Shah Alamc, Tapas Kumar Paula, Seema Sahaa, Md.Golam Maulad, Rezowana Sharmine

Chemotherapy in combination with Trastuzumab is better than chemotherapy alone in HER2 positive breast cancer patients 15-20
Md Dayem Uddin, Ipshita Zerin, Md Shafayat Habib, Arif Hosen, Julekha Khatun

Effect of Vitamin A on Lung Function Test in patient with Chronic Bronchial Asthma 21-24
M Obaidulla Ibne Ali, Nur-E-Atia, Tohorul Islam, Gopal chandra sarker

■ **REVIEW ARTICLE**

Alzhiemers Disease: An important cause of dementia 25-28
Md. Muazzem Hossain, Nasrin Jahan Shammi, Kazi Wali Ahmed , Rezowana Sharmin

■ **CASE REPORT**

Villous adenoma of the urinary bladder: A case report 29-32
Arefa Sultana, Shah Md Badruddoza

Information for Authors 33-36
Barind Medical College Journal (BMCJ)

Functional Dyspepsia: An unsolved dilemma.

M. Manzurul Haque

*Professor, Department of Surgery, Barind Medical College, Rajshahi, Bangladesh.

Correspondence to : M M Haque drmanzur07@yahoo.com

Cite this as: BMCJ 2016; 2(2):

Functional dyspepsia (FD) is a clinical syndrome presented with persistent or recurrent pain or discomfort localized in the epigastric region without evidence of organic disease likely to explain the symptoms. For a very long time, dyspepsia has been defined in very different ways without any generally agreed consensus causing difficulties for both clinicians and researchers. Long back in 1865 Dr. Henry Browns MD defined dyspepsia to be an organic condition related to mouth, stomach and duodenum.[1] Only during late 1980s, an international working group, assembled in Chicago, suggested dyspepsia as epigastric or retrosternal symptom of gastrointestinal origin lasting for more than four weeks.[2] However concept of functional dyspepsia has been ventilated during the last 25 to 30 years and there has been a concerted effort to standardize the definitions. Functional dyspepsia has been defined more clearly by the Rome III criteria consisting of a sensation of pain or burning in the epigastrium, early satiety (inability to finish a normal-sized meal), fullness during or after a meal, or a combination of these symptoms which must be chronic, occurring at least weekly and over a period of at least 6 months and there is not an organic explanation.[3]

Functional dyspepsia has further been subdivided into two diagnostic categories of meal-induced Postprandial Distress Syndrome (PDS), characterized by postprandial fullness and early satiation and Epigastric Pain Syndrome (EPS) characterized by epigastric pain and burning.[4] However it is a great challenge for the physicians to differentiate between functional dyspepsia and organic conditions of the stomach or duodenum with similar symptoms.

A number of alarm symptoms have been identified to diagnose potentially hazardous serious underlying disease in dyspepsia, especially malignancy. These symptoms include new-onset dyspepsia in older age group, unexplained weight loss, anorexia, early satiety, vomiting, progressive dysphagia, odynophagia, bleeding, anemia, jaundice, an abdominal mass, lymphadenopathy, a family history of upper GIT cancer, or a history of peptic ulcer, previous gastric surgery or malignancy.

Patients without alarm symptoms are usually managed by testing for Helicobacter pylori, with subsequent treatment if positive (the "test and treat" approach), an empiric trial of acid suppression, or initial endoscopy.[5] In the first step patient reassurance and education, with use of H_2-blockers, or PPIs and a simple noninvasive H.pylori testing may be considered. Another strategy is prescription of empirical full-blown antisecretory therapy according to guideline proposed by the American College of Physicians. For either unresponsive patients or for those who will have an early symptomatic relapse further investigations are recommended . In another approach, the patients are initially subjected to comprehensive investigations including tests for H. Pylori and upper GIT endoscopy.

The potential adverse effects of long term PPI therapy has recently been brought into account in respect to the vast population receiving this medication over a prolonged period of time.[6] A recent report shows that Proton pump inhibitor use is associated with a higher risk of incident CKD.[7] Observational studies suggest a modest risk of osteoporosis and fracture, community acquired pneumonia, and *Clostridium difficile* infection in PPI users.[8] The PPIs are overprescribed in many patients and attempts should be justified to refrain from prescribing this medication where it is not needed.

In a placebo controlled trial of the tricyclic antidepressant amitriptyline or the selective serotonin reuptake inhibitor escitalopram, only amitriptyline showed a significant benefit over placebo in case of functional dyspepsia.[9]

Managing functional dyspepsia is challenging when both initial acid suppression therapy and *H pylori* eradication fail. Modification of eating habits, reducing stress, avoiding medications and foods that seem to exacerbate symptoms, and refraining from tobacco, caffeine, alcohol, and carbonated beverages have been advocated in different ways but of unproven value.[10]

We are trying to formulate a differential approach for the management of functional dyspepsia. We are suggesting full range of available investigations including upper GIT endoscopy, USG abdominal scanning, H. Pylori testing and others as and when necessary. Majority of our patients with functional dyspepsia appears to have psychosomatic components in predominance. However our suggestions must be validated by further studies. And definitely there are a lot of projections for studies in management of functional dyspepsia.

References:

1. Browns H. On Oral, Gastric, and Duodenal Dyspepsia. BMJ 1865;2:679.
2. Colin-Jones D, Bloom B, Bodemar G, et al. Management of dyspepsia: report of a working party. Lancet 1988;1:576–9.
2. Talley NJ, Ford AC. Functional Dyspepsia. N Engl J Med 2015;373: 1853-63.
4. Tack J, Talley NJ, Camilleri M, et al. Functional gastroduodenal disorders. Gastroenterology 2006; 130:1466–79.
5. Shaukat A, Wang A, Acosta RD, et al. The role of endoscopy in dyspepsia. Gastrointestinal Endoscopy 2015; 82: 2:227-32.
6. Johnson DA; Edward C. Oldfield IV. Reported Side Effects and Complications of Long-term Proton Pump Inhibitor Use. Clin Gastroenterol Hepatol. 2013;11(5):458-64.
7. Lazarus B, Chen Y, Wilson FP et al. Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease. *JAMA Intern Med.* 2016;176(2):238-46.
8. Moayyedi P, Leontiadis GI. The risks of PPI therapy. Nat Rev Gastroenterol Hepatol 2012;9:132-9.
9. Locke GR, Bouras EP, Howden CW, et al. The functional dyspepsia treatment trial (FDTT) key results. Gastroenterology 2013;144:140.
10. Malone M, Managing Dyspepsia. *Clinician Reviews*. 2015;25(6):350-7.

Effect of vegetarian diet on Triglyceride (TG) level.

Momena Khatun Munna[a], Md.Obaidullah Ibne Ali[b], Md.Mijanur Rahman Sardar[c], Farjana Yeasmin[d], Sohel Baksh[e], Gopal Chandra Sarker[f]

Abstract

Background: Vegetarians consume higher amount of dietary fiber, polyunsaturated fatty acid and anti-oxidant in comparison to non-vegetarians. Vegetarians have lower incidence of heart disease, hypertension, diabetes mellitus and malignancy. Although, the relationship between vegetarian and triglyceride have been investigated extensively, but the studies have showed conflicting results. **Objective:** To observe the effect of vegetarian diet on Triglyceride level. **Methods:** This cross sectional comparative study was carried out in the department of Physiology in collaboration with the department of Biochemistry of Rajshahi Medical College, Rajshahi between July 2014 to June 2015. Fifty healthy adults male and female aged 18 to 45 years were studied. Twenty five healthy adult, vegetarians (lacto vegetarians) enrolled in study group and twenty five healthy adult non-vegetarians were in control group. Serum Triglycerides were measured by colorometric method. Data were analyzed by unpaired student's t-test. **Results:** Serum Triglyceride level did not show any significant difference between vegetarians and non-vegetarians. **Conclusion:** This study suggested that lactovegetarian diets have no effect on Triglyceride level.

Key words: vegetarians, non-vegetarians, triglyceride.

[a] Lecturer, Department of Physiology, Rajshahi Medical College, Rajshahi, Bangladesh.

[b] Associate professor & Head, Department of Physiology, Rajshahi Medical College, Rajshahi, Bangladesh.

[c] Assistant Professor, Department of Physiology, Khulna Medical College, Rajshahi, Bangladesh.

[d] Assistant Professor, Department of Physiology, Diabetic Association Medical College, Faridpur, Bangladesh.

[e] Lecturer, Department of Physiology, Cox's Bazar Medical College, Cox's Bazar, Bangladesh.

[f] Professor, Department of Physiology, Barind Medical College, Rajshahi, Bangladesh.

Correspondence to :
M K Munna
Munna37rmc@gmail.com

Cite this as:
BMCJ 2016; 2(2):

Introduction

The lipids are a heterogeneous group of compounds, including fats, oils, steroids, waxes and related compounds, that are related more by their physical than by their chemical properties. They have the common property of being relatively insoluble in water and soluble in non-polar solvents such as ether and chloroform. They are important dietary constituents not only because of their high energy value, but also because of the-fat-soluble vitamins and the essential fatty acids contained in the fat of natural foods. Fat is stored in adipose tissue, where it also serves as a thermal insulator in the subcutaneous tissue and around certain organs.[1]

Triacylglycerols (formerly triglycerides) are the most abundant group of lipids that primarily function as fuel reserves of animals. The fat reserve of normal humans (men 20%, women 25% by weight) is sufficient to meet the body's calorie requirements for 2 – 3 months.[2]

Adipocytes of adipose tissue predominantly found in the subcutaneous layer and in the abdominal cavity are specialized for storage of triacyglycerols. The fat is stored in the form of globules dispersed in the entire cytoplasm. And surprisingly, triacylglycerols are not the structural component of biological membranes.[2]

Diet associated with non vegetarians (meat eaters) also offers some benefits such as protein-rich and caloric dense nutrients. It is also a rich source of vitamin B complex, especially B_{12} which is not available in plant foods. The occurrence of cardiovascular diseases, obesity, high blood pressure and high blood cholesterol levels is found to be greater among non-vegetarians owing to the high concentration of saturated fatty acids in animal food.[3]

Vegetarian diet contains the richest dietary antioxidants. Studies over the years have revealed that plants are a rich source of phyto-nutrients, vitamins C, E and carotenes as well as micronutrients such as selenium, Iron, copper, zinc and manganese which are co-factors for optimum catalytic activity of enzymes.[3]

Vegetarian have been broadly classified into three diet types, these are-Restricted or total vegetarians with no animal product in their food (they are also called vegans). Lacto-vegetarians which include only milk and dairy product in their diet and lacto-ovo vegetarians which also allows the inclusion of egg.[3]

Yadav et al. (2013)[4] and Verma et al. (2015)[5] have found no significant difference in TG level between vegetarians and non-vegetarians. Similarly, Pan et al.(1993)[6] and Huijbregts et al. (1980)[7] also have found no significant difference in TG level between

vegetarians and non-vegetarians. On the contrary, Jhala et al. (1998)[8] and Gandhi et al. (2014)[9] have found higher TG level among non-vegetarians. Similarly, Nduka et al. (2011)[3], De Biase et al. (2005)[10] and Famodu et al. (1998)[11] also have found higher TG level among non-vegetarians than vegetarians. In contrast, Dourado et al. (2011)[12] and Lin CK et al. (2010)[13] have found lower TG level among non-vegetarians than vegetarians.

So the findings of the researches are contradicting to each other and not conclusive. Moreover limited information is available regarding influence of lacto-vagetarian diet on lipid profile which is the usual dietary habit of vegetarians of our country.

Methods

The cross-sectional comparative study was carried out in the department of Physiology and department of Biochemistry of Rajshahi Medical College between the period of July 2014 to June 2015. The protocol of this study was approved by Institutional Review Board (IRB) and Ethical Review Committee (ERC) of Rajshahi Medical College. Fifty healthy adult male and female subjects, aged 18-45 years were selected among medical students, doctors, stuff and their relatives. Purposive sampling technique was applied to select each study lacto-vegetarian subject. After careful matching of age, gender and BMI, non-vegetarian subjects were selected for each lacto-vegetarian. Subject having history of hyperlipidaemia, hypertention, any vascular disease, diabetes mellitus, any endocrine disease, chronic illness, alcoholics, smoking, taking antihyperlipidaemic drugs or oral contraceptive pills were excluded from this study.

After proper counseling the aim, objectives, benefit, risk and procedure of the study were explained in details to the subjects. After taking informed consent, complete history taking and physical examination were done and record in a preformed data sheet. Following an overnight fasting (10-12 hours), 3 ml of venous blood sample were drawn into test tube (from the anticubital space of the forearm) by venepuncture after taking all aseptic precautions. After coagulation serum separated by centrifugation at 3000 rpm for 10 minutes. Then serum was used for estimation of triglyceride level by colorimeter. The results were expressed in mmol/L. Collected data were analyzed by using SPSS (Statistical Package for Social Sciences) computer software programme and test to significance were calculated by using unpaired t-test. P value at or below 0.05 was taken as level of significance.

Results

Comparison of background characteristics between vegetarian and non-vegetarian healthy adults were shown in Table-1. There were no statistically significant difference of age (years), weight (kg), height (meter), BMI (kg/m^2), Waist/Hip ratio, Waist/Height ratio, pulse (beats/min), systolic blood pressure (mm of Hg) and diastolic blood pressure (mm of Hg) between the two groups.

Table-1: Background characteristics of the study subjects (n=50)

Parameter	Vegetarian (n-25) (mean±SD)	Non Vegetarian (n-25) (mean±SD)	P-value
Age	33.68±9.05	33.92±9.04	>0.05
Height	1.60±0.07	1.61±0.06	>0.05
Weight	62.76±9.34	63.72±9.79	>0.05
BMI	24.39±3.65	24.40±3.54	>0.05
Waist/Hip ratio	0.86±0.05	0.86±0.05	0.05
Waist/Height ratio	0.51±0.06	0.51±0.06	>0.05
Pulse	79.68±4.71	76.60±4.22	>0.05
Systolic BP	120.0±9.46	114.8±7.56	>0.05
Diastolic BP	76.2±5.05	74.2±5.71	>0.05

The mean triglyceride concentration in healthy adult vegetarian group was 1.26±0.43 mmol/L. It was slightly higher (1.33±0.41mmol/L) in non vegetarians than vegetarians , but not significantly (Table 2).

Table 2: Fasting serum triglyceride concentration in healthy adult vegetarian group and non-vegetarian group (n=50).

Parameter	Vegetarian (n-25) mean±SD(95% CI)	Non Vegetarian (n-25) mean±SD (95% CI)	P-value
Triglyceride (mmol/L)	1.26±0.43 (0.76-2.4)	1.33±0.41 (0.8-2.7)	>0.05

Discussion

Persistent high lipid level is usually associated with different diseases like atherosclerosis, myocardial infarction, cerebro-vascular disease, peripheral vascular disease etc. Hyperlipidemia may cause heart disease and majority of non-communicable diseases are heart related. So, many possible fatal diseases can be avoided by maintaining normal blood lipid levels. It is observed that vegetarians have lower incidence of heart disease, hypertension, diabetes mellitus and cancer.[10]

We have found no significant difference of triglyceride level between vegetarians and non-vegetarians. This finding is compatible with Vishwabharathi *et al.* (2013)[14], Yadav *et al.* (2013)[4],

Verma *et al.*(2015)[5] and Lee*et al.*(2000).[15] It may be due to the fact that total energy intake was same in both groups. Moreover carbohydrate was the main food consumed by the both groups which may mis-interpret the benificial effect of vegan diet on lipid profile.

Additional longitudinal studies on larger sample size should be done to comment about this finding. On the other hand, Jhala *et al.* (1998)[8] have observed higher TG level in non-vegans. The sample size of their study was multiple times greater than this present study which may be reason of the difference. Pan et al. (1993)[6] underwent a study on Buddhist vegetarians, who lives on carbohydrate, did not find no difference in lipid profile which is consistent with the present study. Similarly Huijbregts et al. (1980)[7] have opined that high carbohydrate consumption is the cause of failure to reduce TG level among vegetarians which correlates with the present study finding.

Moreover, Gandhi *et al.* (2014)[9] have opined that vegetarians had lower TG level than non-vegans. However they have included only strict vegans in vegetarian group. On the contrary, this study had included lacto-vegans in vegetarian group which may be the reason of the conflicting finding. In addition, Nduka et al. (2011)[3] and Famodu et al (1998)[11] have found higher TG level among non-vegetarians. It may be due to presence of high concentration of saturated fatty acid in animal fat. Moreover De Biase et al. (2005)[10] also have found that TG level decreases as animal products were restricted in diet. It indicates that animal fat intake is an important contributor of TG level in addition to carbohydrate intake.

Interestingly, Dourado et al. (2011)[12] have found that non-vegetarians had lower TG than vegetarians. Higher percentage of carbohydrate intake among vegetarians may be the cause of this finding. Furthermore, Lin CK et al. (2010)[13] were found that the prevalence of hyper-trigiyceridaemia is non-significantly higher among vegetarians. It indicates that the diet of vegetarians might have affected TG level.

One of the strength of our study is we have done careful matching of anthropometric indices in addition to age and gender. However it was a cross-sectional study on smailer sample size. To establish the cause-effect relationship,a cohort study on larger sample should be done.

Conclusion:

This study did not find any significant difference of triglyceride level between vegetarians and non-vegetarians. It indicates that the vegetarians have similar cardio-vascular risk like the non-vegetarians unless influenced by certain modifiable risk factors like high BMI, lack of exercise, smoking, alcohol consumption, increase intake of dietary fat etc.

References:

1. Botham KM. Lipids of Physiological Significance. In: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA, editors. *Harper's Illustrated Biochemistry*, 28th edition. China: McGraw-Hill Companies Inc., 2009: 121.

2. Satyanarayana U, Chakrapani U. *Lipids.* In: ArunabhaSen, editor. *Biochemistry, 3rd* edition. Kolkata: Books and Allied (P) Ltd, 2006: 32.

3. Nduka AG, Opeyemi AL, Adewale OA, Lucky EO. Lipid profile and oxidative stress status in vegetarians. *Pak J Med Sci* 2011; 27(2): 409-13.

4. Yadav D, Gupta M, Mishra S, Sharma P. Reference interval for lipid profile in North Indian population from Rajasthan according to various partitioning criteria. *Clinica Chimica Acta* 2013; 426: 145-51.

5. Verma A, Kapoor S, Kumari P, Gaur RS. Comparison of cardiovascular risk between vegetarian and non-vegetarian adolescents in North Indian population. *Journal of Chemical and Pharmaceutical Research* 2015; 7(2): 646-9.

6. Pan WH, Chin CJ, Sheu CT, Lee MH. Hemostatic factors and blood lipids in young Buddhist vegetarians and omnivores. Am J ClinNutr1993; 58: 354-9.

7. Huijbregts AWM, Schaik AV, Berge-Henegouwen GPV, Werf SDJVD. Serum lipids, biliary lipid composition, and bile acid metabolism in vegetarians as compared to normal controls. *European Journal of Clinical Investigation* 1980; 10: 443-9.

8. Jhala CF, Shah UV, Shah TK, Naik BK, Dafda JD. A study of serum lipid profile part-1: Establishment of normal reference values of serum lipid levels in healthy vegetarian population of Gujarat Indian J Clin Biochem 1998; 13 (1): 1-7.

9. Gandhi P, Agrawal N, Sharma S. A study of vegetarian diet and cholesterol and triglycerides levels. *Indian Journal of Applied Research* 2014; 4(10): 447-9.

10. De Biase SG, Fernandes SFC, Gianini RJ, Duarte JLG. Vegetarian Diet and Cholesterol and Triglycerides Levels. Arq Bras Cardiol 2007; 88 (1): 32-36.

11. Famodu AA, Osilesi O, Makinde YO, Osonuga, OA. Blood Pressure and Blood Lipid Levels Among Vegetarian, Semi-Vegetarian, and Non-Vegetarian Native Africans. Clincal Biochemistry 1998; 31(7): 545-9.

12. Dourado KF, Siqueira FAC, Shinohara NKS. Relation between dietary and circulating lipids in lacto-ovo vegetarians. NutrHosp 2011; 26(5): 959-64.

13. Lin CK, Lin DJ, Yen CH. Comparison of Renal Function and Other Health Outcomes in Vegetarians versus Omnivores in Taiwan. J Health Popular Nutr, 2010; 28(5): 470-5.

14. Viswabharathi N, Manjula SR, Siddhartha K. Evaluation of Oxidant Status and Lipid Profile In Vegetarians and Fish Eaters. IOSR Journal of Pharmacy and Biological Sciences 2013; 7(6): 9-14.

15. Lee HY, Woo J, Chen ZY, Leung SF, Peng XH. Serum fatty acid, lipid profile and dietary intake of Hong Kong Chinese omnivores and vegetarian. European Journal of Clinical Nutrition 2000; 54: 768-73.

Gender differences in anthropometric somatotype of adult santhals in north bengal, Bangladesh

Sumana Sutradhar[a], Shamim Ara[b], S.M. Akram Hosssain[c], Manjuara Khatun[d]

[a]Assistant Professor Department of Anatomy, Barind Medical College, Rajshahi, Bangladesh.

[b]Professor and Head , Department of Anatomy, Dhaka, Medical College, Dhaka, Bangladesh.

[c]Professor and Head , Department of Anatomy, North Bengal Medical College, Sirajganj, Bangladesh.

[d]Associate Professor Department of Anatomy, Islami Bank Medical College, Rajshahi, Bangladesh.

Correspondence to : S Sutradhar Sumonasutradhar81@gmail.com

Cite this as: BMCJ 2016; 2(2):

Abstract

Background: Somatotype gives information on individual physical constitution in an easily comprehensible form. The somatotype is expressed in a three-numerical rating representing three components: endomorphy, mesomorphy and ectomorphy. Somatotype components are influenced by age, sex, race, diet, environmental factors, occupation and physical activity. **Objectives:** The present study was planned to determine the gender differences in anthropometric characteristics and somatotyping of adult Santhal of North Bengal. **Methods:** This cross sectional type of analytical study was conducted among 200 adult male and female Santhals of North Bengal. Personal information and anthropometric measurements were recorded on questionnaire and datasheet following interview and examinations of the participants respectively. Data were analyzed with the help of SPSS version 19.0 for windows and statistical analysis were done by unpaired student's 't' test. **Results**: Endomorphy component was observed higher in female than male ($P<0.001$). Santhal male showed higher value in ectomorphy component than female ($P<0.01$) but in mesomorphy component no significant difference was observed. Somatotype category observed in male was mesomorph-endomorph (3.13-3.31-2.53) and in female was mesomorphic endomorph (3.91-3.35-2.27). **Conclusion:** Among the three components of somatotype, endomorphy component was higher in female than male and ectomorphy component was higher in male but no significant difference was observed in mesomorphy component between male and female Santhals.

Key words: anthropometric somatotype, gender differences, Santhals.

Introduction:

A somatotype is a convenient short hand descriptor of overall physique in terms of body shape and composition independent of body size.[1] In 1967, Heath and Carter devised somatotype method and recognized three basic components of physique. Endomorphy refers to relative fatness, meosomorphy refers to relative musculoskeletal-development and ectomorphy refers to relative linearity of individual physiques.[2] Somatotype is expressed in a three-numerical rating, for example, a 3-5-2 rating is recorded in this manner where 3 indicates endomorphy, 5 indicates mesomorphy and 2 indicates ectomorphy. In 1990, Heath and Carter classified somatotype into thirteen categories: central, balanced endomorph, mesomorphic endomorph, mesomorph-endomorph, endomorphic mesomorph, balanced mesomorph, ectomorphic mesomorph, mesomorph-ectomorph, mesomorphic ectomorph, balanced ectomorph, endomorphic ectomorph, endomorph-ectomorph, ectomorphic endomorph.[3] It is ideal to conduct anthropolgical research on a homogenous population where hereditary aspects of a trait can be examined with less error and contamination. Like any tribal population, Santhal of North Bengal are close knit homogenous population.

According to Bangladesh population census 1991, there are about 2,02,744 Santhals in Bangladesh and most of them resides in Rajshahi division. They also inhabit in a wide area of West Bengal, Bihar, Orissa and Chhota Nagpur of India.[4] The Santhal belong to the Proto-Australoid race and retain an aboriginal language, known as Santhali. Primary occupation of the Santhal is agriculture. Both men and women take part in agricultural activities. Santhal village is the most important socio-economic and political unit. Every village has a 'Panchayet' to maintain law order. The Santhals are divided into 12 totemic class. These are: 1) Hansda, 2) Marndi, 3) Soren, 4) Hembrom, 5) Tudu, 6) kisku, 7) Murmu, 8) Baske, 9) Besra, 10) Pauria, 11) Chore and 12) Bedea.[5] Almost all the study examining the gender differences in body size shows that males are significantly heavier and taller than the females, they possess broader shoulders and have bigger bone widths and circumferences than the female.[6] A good number of researches were carried out with Santhal of West Bengal, India showing different aspects of anthropological variations.

Considering the importance of understanding variation in body physique, the present study aims to study gender differences in anthropometric somatotype among male and female adult Santhals particularly on mesomorphic component.

Materials and Methods

This cross-sectional type of analytical study was carried out in the department of anatomy of Dhaka medical college, Dhaka from july 2013 to june 2014. The sample size was 200 adult Santhals (100 male & 100 female) age ranging from 30-49 years. The study subject were selected from three Santhals villages: Sundarpur and Joykrishnapur of Rajshahi districts and Bhabicha of Naogaon districts. Prior permission and informed written consent was taken from the headman of the respective village Panchayet. Personal information and anthropometric measurements were recorded on questionnaire and datasheet following interview and examinations of the participants respectively. With the help of stadiometer, weighing scale, vernier slide caliper, a standardized flexible ribbon tape and a skinfold caliper following ten body measurements were taken: 1. Height (Fig.1.a), 2. Body weight, 3. Skinfold at triceps (Fig.1.b), 4. Skinfold at subscapula, 5. Skinfold at supraspinale, 6. Skinfold at medial calf, 7. Biepicondylar breadth of femur, 8. Biepicondylar breadth of humerus (Fig.1.c), 9. Upper arm circumference & 10. Calf circumference (Fig.1.d). Anthropometric Somatotyping was done incorporating the above ten anthropometric measurements using Heath and Carter's formula: i) **Endomorphy** = - 0.7182 + 0.145(X) - 0.00068 $(X)^2$ + 0.0000014 $(X)^3$. Here, X = (Sum of triceps, subscapular and supraspinale skinfolds) x 170.18 / Body height in cm, ii) **Mesomorphy** = (0.858 x humerus breadth) + (0.601 x femur breadth) + (0.188 x corrected arm girth) + (0.161 x corrected calf girth) - (body height x 0.131) + 4.5, iii) **Ectomorphy** = 0.732 x HWR -28.58 (If HWR ≥40.75), Ectomorphy = 0.463 x HWR -17.63 (If HWR <40.75 but >38.25) & Ectomorphy = 0.1 (If HWR ≤ 38.25). Here, HWR (height – weight ratio) = Height / $\sqrt[3]{}$ Weight.[3] Data were analyzed with the help of SPSS version 19.0 for windows and statistical analysis were done by unpaired student's 't' test.

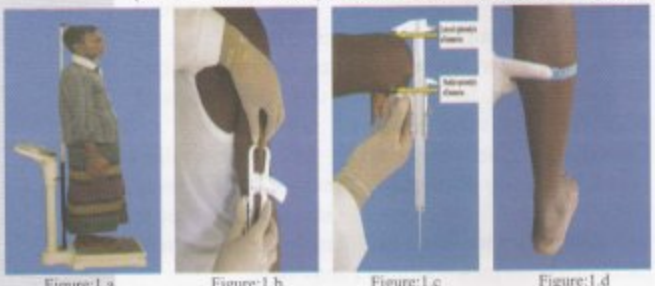

Figure:1.a Figure:1.b Figure:1.c Figure:1.d

Anthropometric mearsurements of different variables.

Results

Results and observations of this study are described below with suitable tables & graphs. In table-1 significant difference in height & weight was observed between male and female (P< 0.001), where height & weight of male was higher than female. Mean height & weight of male was 160.69±3.91cm & 54.54±4.06kg; whereas in female 148.22±6.53cm height & 44.82±5.30kg respectively.

Table 1. Gender differences in different anthropometric measurements between male and female adult Santhals of North Bengal

Anthropometric measurements	Santhal Male(100)	Santhal Female(100)	*P-value*
Height(cm)	160.69±3.91 (144.00-176.00)	148.22±6.53 (140.00-170.00)	0.0001***
Body Weight(kg)	54.54±4.06	44.82±5.30	0.0001***
Skinfold at triceps (mm)	9.60± 1.89	11.07±1.86	0.0001***
Skinfold at subscapula (mm)	10.06±1.92	11.36±2.07	0.0001***
Skinfold at supraspinale (mm)	11.10±1.91	12.94±2.33	0.0001***
Skinfold at medial calf (mm)	8.80±2.33	10.10±2.04	0.0001***
Biepicondylar breadth of humerus (cm)	6.25±0.33	5.94±0.36	0.0001***
Biepicondylar breadth of femur (cm)	7.31±0.60	7.02±0.44	0.0001***
Upper arm circumference (cm)	25.03±1.11	23.18±1.74	0.0001***
Calf circumference (cm)	31.26±1.49	28.96±1.96	0.0001***

* significant at P<0.05, *** significant at P<0.001.

Female had higher value in all skinfolds measurements than male. In female, skinfold measurements at triceps was 11.07±1.86mm, at subscapula was 11.36±2.07mm, at supraspinale was 12.94±2.33mm & at medial calf was 10.10±2.04mm whereas in male all skinfolds measurements shows lower value. Santhal male had higher value in all bone breadths and limb girths measurements than female (P< 0.001). Biepicondylar breadths of humerus & femur was 6.25±0.33 cm & 7.31±0.60cm in male & 5.94±0.36cm & 7.02±0.44 cm in female respectively. Limb girths measurements of upper arm & calf of leg was 25.03±1.11 cm & 31.26±1.49 cm in male and 23.18±1.74 cm & 28.96±1.96 cm in female respectively(Table-1).

Table 2. Gender differences in different anthropometric somatotypes between male and female adult Santhals of North Bengal.

Sex	Endomorphy Mean±SD	Mesomorphy Mean±SD	Ectomorphy Mean±SD
Male (n=100)	3.13±0.57 (2.10-4.30)	3.31±0.65 (2.20-5.30)	2.53±0.63 (1.20-5.40)
Female (n=100)	3.91±0.67 (2.30-5.10)	3.35±0.73 (1.90-6.20)	2.27±0.93 (1.10-4.90)
P value	0.0001***	0.691^{ns}	0.019*

not significant at P>0.05,* significant at P<0.05,*** significant at P<0.001.

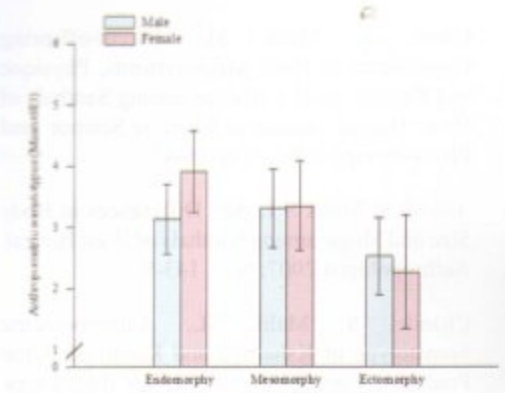

Figure:2 Gender differences in somatotype component of adult Santhals in North Bengal, Bangladesh.

Among the three components of anthropometric somatotype; endomorphy component was more in female than male (P<0.001) but ectomorphy component of somatotype was higher in male than female (P<0.019*). But in mesomorphy component no significant difference was observed between male and female Santhals (Table-2). Somatotype category observed in male was mesomorph-endomorph (3.13-3.31-2.53) and in female was mesomorphic endomorph (3.91-3.35-2.27).

Discussion

The present study was carried out on middle-aged (30-49 years) Santhals and observed females were more endomorphic and males were more ectomorphic than their counterpart. As endomorphy refers to relative fatness based on selected skinfolds measurements and female showed higher value in all skinfold thickness, so female found more endomorphic than male. Ectomorphy component related to height-weight ratio and as Santhal male was taller and heavier than female so male was found more ectomorphic than female. But no significant difference was observed in mesomorphy component as both the population groups requires high level of physical activity for their livelihoods. Results of different variables in this study showed some similarities with the findings of Ghosh and Malik[6] among the Santhals of West Bengal, India. Ghosh and Malik observed females were endomorphic and males were ectomorphic than their counterpart. Both male and female were found mesomorphic. Both Bangladeshi Santhals and Santhals of West Bengal, India belong to Proto-Astraloid race. Most of the Santhals both Bangladeshi and Indian were farmer. So, similarities observed between two groups may be due to same race, same dietary habit, same occupation and physical activity. Gender differences also found in similar type of study conducted by Chandel & Malik (2012) among 1008 adult (18-40 years) Kshatriya and Kurmi of Uttar Pradesh, India. They found Kshatriya and Kurmi male were ectomorphic-mesomorph while Kshatriya and Kurmi female were balanced mesomorph.[7] So, both Kshatriya and Kurmi males have linear and muscular body physique whereas females are muscular in their body physique. The overall high mesomorphic ratings in both the populations can be attributed to the occupation of agriculture and factory works involving high physical activity. Kshatriya and Kurmi were agricultural and factory labourer and Santhals were farmer. Both Kshatriya and Kurmi were agricultural and factory labourer and Santhals were farmer so similarities may be due to same physical activity. According to Chandel and Malik Kshatriya[7] is one of the four castes of Hinduism and Kurmi is a subcaste of Kshatriya caste. So dissimilarities may be due to the racial variation, environmental factor, food habit and selection of different age group. So, Ghosh & Malik[6] and Chandel & Malik[7] revealed sexual dimorphism in anthropometric somatotype of Santhals of West Bengal and Kshatriya & Kurmi of Uttar Pradesh, India, which is consistent with this study.

Conclusion

The anthropometric somatotype, used as a descriptive method of body shape in the present study, revealed a remarkable gender differences in Santhals of North Bengal, Bangladesh. Among the three components of somatotype, endomorphy component was higher in female than male and ectomorphy component was higher in male. But no significant difference was observed in mesomorphy component between male and female Santhals as their occupation requires high level of physical activity.

References

1. Kaur, M. Age Changes in Somatotype Components of Rural and Urban Punjabi Brahmin Females. Journal of Human Ecology 2009; 25(3): 167-73.

2. Heath BH, Carter J E L. A Modified Somatotype Method. American Journal of Physical Anthropology 1967; 27: 57-74.

3. Carter JEL. The Heath – Carter anthropometric somatotype – instruction manual, 2002. Surrey,Canada: Tep and Rosscraft. www.somatotype.org/Heath-CarterManual.pdf. Last accessed on October 1, 2013.

4. Hasan M. Livelihoods of the Santals. 1st edition. Dhaka, Bangladesh: Center for Applied Social studies, 2006..

5. Ghosh S, Malik SL. Parent-offspring Correlations in Body Measurements, Physique and Physiological Variables among Santhals of West Bengal. Journal of Exercise Science and Physiotherapy 2007; 3(1): 26-43.

6. Ghosh S, Malik S L. Sex Differences in Body Size and Shape among Santhals of West Bengal. Anthropologist 2007; 9(2): 143-9.

7. Chandel S, Malik SL. Anthropometric Somatotype of Kshatriya and Kurmi of Uttar Pradesh : Population and Gender differences. Human Biology Review 2012; 1(1): 1-15.

Excessive vaginal discharge of reproductive age : common causative agents

Mst. Sultana Aktar[a], Md. Abdullah Siddique[b], Md. Shah Alam[c], Tapas Kumar Paul[a], Seema Saha[a], Md.Golam Maula[d], Rezowana Sharmin[e], Gopa Sarker[f]

Abstract

Background: Excessive vaginal discharge is a common health hazard of reproductive age women in South Asia including Bangladesh. It may be a physiologic or a pathological manifestation. A pathological vaginal discharge may be infective or non-infective. **Objective:** To find out the prevalence of infective vaginal discharge with their common causative agents in reproductive age. **Methods:** This was a cross-sectional descriptive type of study conducted at Out Patient Department of Obstretrics and Gynaecology, Rajshahi Medical College Hospital. The sample size was 245. Three vaginal swabs from each patient were collected to identify the causative pathogens by wet mount preparation of Gram staining and culture in different culture media. Descriptive analytic techniques were done using SPSS for window in computer. **Result:** A total of 245 patients, 142 (57.9%) were infective. Bacterial vaginosis was the most common (67, 27.3%) microbiological cause. Both bacterial vaginosis and cadidiasis were predominant in the age group 25 -35 years and trichomoniasis was common in younger women than older. **Conclusion:** Before prescribing antibiotics in patients having complain of excessive vaginal discharge, physicians should be confirmed the etiological agents by proper laboratory investigation.

Key words: vaginal discharge, reproductive age, bacterial vaginosis, candidiasis, trichomoniasis

[a] Lecturer, Department of Microbiology, Rajshahi Medical College, Rajshahi, Bangladesh.

[b]Professor, Department of Microbiology, Barind Medical College, Rajshahi, Bangladesh.

[c]Professor, Department of Microbiology, Rajshahi Medical College, Rajshahi, Bangladesh.

[d]Associate Professor, Department of Physiology, Barind Medical College, Rajshahi, Bangladesh..

[e]Assistant professor, Department of Microbiology, Barind Medical College, Rajshahi, Bangladesh.

[f]Associate Professor, Obstetrics & Gynaecology Barind Medical College, Rajshahi, Bangladesh.

Correspondence to :
M S Aktar
drsultanaaktar@yahoo.com

Cite this as:
BMCJ 2 016; 2(2):

Introduction

Excessive vaginal discharge is a common complain of sexually active women in gynaecological practice.[1] About 5-10 million women visited the gynaecologyst with the complain of excessive vaginal discharge per year throughout the world.[2] Studies have shown that of women seeking advice in the primary and secondary health care setting, 11% to 38.4% in India, and 34% in Ethiopia with excessive vaginal discharge.[3-7] In Bangladesh, 83% of married women of reproductive age suffered from abnormal vaginal discharge.[8] Vaginal discharge is one of the predisposing factor of pelvic inflammatory diseases, infertility, endometriosis, abortion, preterm labor and delivered of low birth weight baby.[9]

Vaginal discharge may be a normal physiologic occurrence or a pathological manifestation. It is often challenging to distinguish abnormal from normal discharge, both from the patient's and the health care provider's perspective.[10,11] A pathological vaginal discharge may be infectious or noninfectious. The symptom of vaginal discharge was also associated with psychosocial factors of non-infectious etiology.[12] Infectious vaginal discharge is usually related to one of the three conditions, like bacterial vaginosis (BV), vulvovaginal candidiasis (VC), and trichomoniasis.[13,14] Other less common, pathogens include *Neisseria gonorrhea*, *Chlamydia trachomatis*, and Herpes simplex virus.[15] In Asia, bacterial vaginosis was 20-30% and in African & American blacks it was ranging from 45-55%.[16] In India, excessive vaginal discharge cases was 30%, of which bacterial vaginosis was 33%-47%, candidiasis was 20%-40% and trichomoniasis was 8%-10% .[2,17] In Bangladesh, bacterial vaginosis was 29.2%, candidiasis was 53.6% and trichomoniasis was 10.8%.[18] There are some non-infectious causes such as chemical irritation, allergic responses, ectropion endocervical polyp, intra uterine contraceptive device (IUCD), vesicovaginal fistula, rectovaginal fistula, promiscuity, local use of traditional herbal preparations etc.[16,19]

This study was undertaken to find out the prevalence of infective vaginal discharge with their common causative agents among the study population, Which will be helpful for healthcare providers to manage the problem.

Methods

This cross sectional study was conducted at Department of Obstetrics and Gynaecology, Rajshahi Medical College Hospital (RMCH), Rajshahi, Bangladesh. All the female patients of reproductive age (15 – 49 years) having a complain

of excessive vaginal discharge attending at the OPD of Obstetrics and Gynaecology, RMCH constituted the study population. A total number of 245 cases were included in the study after taken their written consent. Three vaginal swabs were taken from each case. A vaginal suspension was prepared with one of the three vaginal swabs and examined under microscope for identification of *Candida* and *Trichomonas*. A thin uniform smear was prepared with the second swab and stained with gram stain for demonstration of *Candida* and clue cells. The last swab inoculated in to blood agar, chocolate agar, MacConkey's agar and Sabouraud's dextrose agar media for the growth of bacteria and *Candida*. The colony morphology, zone of haemolysis, gram stain, catalase, coagulase, oxidase, whiff test, pH determination and IMVic tests were done for identification of bacteria. *Candida albicans* was identified by positive germ tube test. All the laboratory tests and cultures were done in the Department of Microbiology, Rajshahi Medical College, Rajshahi. The cases with complaints of vaginal discharge, but no pathogens were identified, were grouped under non-specific causes. Data were computed and processed using SPSS for window. Descriptive analytic techniques involving frequency distribution, computation of percentage etc. were done.

Result

A total 245 patients with the complain of excessive vaginal discharge were included in the study. The vaginal swabs were collected and tested for identification of causative agents.

Table 1. Microbiological etiology of excessive vaginal discharge among the study subjects.

Aetiology of excessive vaginal discharge	Number of patients n = 245	Percentage
Gardnerella Vaginalis	67	27.3
Candida albicans	55	22.4
Trichomonas vaginalis	20	8.2
Non-specific causes	103	42.0

A total of 245 patients presented with abnormal vaginal discharge were examined. Among them causative agents were identified in 142 (57.9%) cases and non specific causes were 103 (42.0%). *Gardnerella vaginosis* was the most common (67, 27.3%) microbiological cause followed by *Candida albicans* (55, 22.4%) and *Trichomonas vaginalis* (20, 8.2%) (Table 1).

Table 2. Distribution of causative agents according to age.

Age in yrs	Bacteria	Yeast	Protozoa
	G.vaginalis N (%)	*C.albicans* N (%)	*T.vaginalis* N (%)
15-24	7(10.45)	8(14.55)	12(60.0)
25-34	38(56.71)	30(54.55)	5(25.0)
35-45	22(32.84)	17(30.9)	3(15.0)
Total	67(100.0)	55(100.0)	20(100.0)

G.vaginalis and *C.albicans* were more predominant in age group 25-34 years than the other age groups. *T.vaginalis* was more predominant in age group 15-24 years than the others (Table 2).

Discussion

Bacterial vaginosis (BV) (27.3%) is the most common disease found in this study, which is similar to the study conducted by Begum *et al.*[20] in Bangladesh. Koumans *et al.*[21] who had also found a 29.2% prevalence of BV which is consistent with the present study. Whereas Nessa *et al.*[22] in Bangladesh reported 48.1% cases of BV among the sex workers. This high prevalence may be the result of disturbance of vaginal microflora resulting from frequent sexual intercourse and the subsequent frequent washing with water and disinfectant.

Vaginal candidiasis (22.4%) is identified as one of the common microbiological cause of abnormal vaginal discharge in this study. Somia *et al.* (2013)[23] reported a similar result in Pakistan, where their isolation rate was 29.4%. But it was quite high observed in a study of Yusuf *et al.*(2011)[18] in Dhaka, Bangladesh. It may be due to the difference of their study population or seasonal variation.

The frequency of *Trichomonas vaginalis* (20,8.17%), which is the etiological agents of trichomoniasis identified in this study was with the similar rates detected by Nessa *et al.*[22], Rahman *et al.*[24] and Alam *et al.*[25] in Bangladesh.

The high rates of bacterial vaginosis and candidiasis found in this population are of concern. There is evidence that these two infections are associated with adverse pregnancy outcomes, including premature rupture of the membranes, preterm labor, preterm birth, intra-amniotic infection and postpartum endometritis.[26] Kiss *et al.*[27] reported a 46% reduction in the preterm birth rate in a randomized controlled trial of screening (15 and 19 weeks gestation) and treatment of asymptomatic bacterial vaginosis, candidiasis and/ or trichomoniasis in early pregnancy. The present study findings suggest to proper management of the women of reproductive age having a complain of excessive vaginal discharge for prevention of adverse pregnancy outcomes.

The bacterial vaginosis and vaginal candidiasis in the present study are profound at the age of 25 to 34 years. It is consistent with the findings of Yusuf *et al.*(2011)[18] in Bangladesh. Rylander *et al.*[28] and Nwadioha *et al.*[29]also found similar results in Sweden and Nigeria in 2004 and 2010 respectively. The reason for the high isolation rates in this age group may be due to comparatively higher sexual activity than the other age groups.

In this study, *Trichomonas vaginalis* is detected in the highest rate at the age group of 15-24 years It may be the women in this age group usually poor nourished due to growing age and inadequate knowledge about personal hygiene.

Our study possesses a methodological limitation that must be taken into consideration, i.e most common pathogens responsible for excessive vaginal discharge, like bacterial vaginosis (BV), vulvovaginal candidiasis (VC), and trichomoniasis were identified in this study, But less common, pathogens include *Neisseria gonorrhea, Chlamydia trachomatis*, and Herpes simplex were not identified in this study. Due to this limitations, the less common pathogens were not identified. The women having infection of these pathogens were falsely labeled as noninfective. Total prevalence of less common pathogens among the women having excessive vaginal discharge is not more than 5% in Bangladesh.[30,31] That suggests, at least more than 30% of the study subjects were noninfective .

Vaginal discharge is a common presenting symptom observed by general practitioners, gynecologists, and those working in family planning clinics and departments of genitourinary medicine.[32] It can be quite bothersome to the patient. It is present in the vast majority of women during their reproductive age and the distress it causes is usually extremely subjective. Some patients are annoyed by the slightest amount of discharge, while others make no complaints in spite of marked discharge. This subjectivity makes it difficult to evaluate the degree to which the amount and the quality of discharge affect the patient's wellbeing. Therefore the physician must estimate the parameters of the condition's effect and tailor the treatment to the individual.[33] There is strong temptation to prescribe antibiotics solely on the of clinical symptoms, without confirmation through the laboratory tests and cultures.[15] But this approach is not rationale, because a remarkable proportion of the patients complaining excessive vaginal discharge was noninfective, it may result in treatment failures and drug resistant.[15,19] The findings of the present study also agreed with this.

The results of this study have certain implication in clinical practice however. Since the complain of vaginal distress is extremely subjective and a remarkable proportion of the patients complaining vaginal discharge are non infective. So before prescribing antibiotic, physicians should be confirmed about the etiology by proper laboratory test and culture.. Otherwise it put the women at risk for side-effects and promotes antibiotic resistance.

References:

1. Sivaranjini, R. Jaisankar, TJ. Thappa, DM. et al. Spectrum of vaginal discharge in a tertiary care setting. Trop Parasitol 2013; 3(2): 135 - 9.
2. Rekha S, Jyothi S. Comparison of visual, clinical and microbiological diagnosis of symptomatic vaginal discharge in the reproductive age group. Int J Pharm Biomed Res. 2010;1(4):144-8.
3. Valsangkar S, Selvaraju D, Rameswarapu R, Kamutapu S. Impairment of quality of life in symptomatic reproductive tract infection and sexually transmitted infection. J Reprod Infertil. 2014; 15(2): 87–93.
4. Philip PS, Benjamin AI, Sengupta P. Prevalence of symptoms suggestive of reproductive tract infections/sexually transmitted infections in women in an urban area of Ludhiana. Indian J Sex Transm Dis. 2013; 34(2): 83–8.
5. Ray K, Muralidhar S, Bala M, et al. Comparative study of syndromic and etiological diagnosis of reproductive tract infections/sexually transmitted infections in women in Delhi. Int J Infect Dis. 2009; 13(6): 352–9.
6. George R, Thomas K, Thyagarajan SP, et al. Genital syndromes and syndromic management of vaginal discharge in a community setting. Int J STD AIDS 2004; 15(6): 367–70.
7. Moges B, Yismaw G, Kassu A, et al. Sexually transmitted infections based on the syndromic approach in Gondar town, northwest Ethiopia: a retrospective study. BMC Public Health 2013; 13:143.
8. Ministry of Health and Family Welfare. Strengthening RTI/STD services: lessons learned from health and family welfare centres. Dhaka: Population Council, 1998.
9. Schwebke J. Bacterial vaginosis.Curr Infect Dis Rep 2000; 2(1): 14–17.
10. Granato P. Vaginitis: Clinical and laboratory aspects for diagnosis. Clinical Microbiology Newsletter 2010; 32(15):111–6.

11. Mlisana K, Naicker N, Werner L, et al. Symptomatic vaginal discharge is a poor predictor of sexually transmitted infections and genital tract inflammation in high risk women in South Africa. J Infect Dis 2012; 206(1): 6–14.
12. Patel V, Pednekar S, Weiss H, et al. Why do women complain of vaginal discharge? A population survey of infectious and pyschosocial risk factors in a South Asian community. Int J Epidemiol 2005; 34(4):853–62.
13. Blackwell A. Vaginal discharge. Practitioner 1985; 229: 987-95.
14. Levine S, Benson C, Goodman LS, et al. Infectious vulvovaginitis, cervicitis, epididymitis and prostatitis. Disease-a Month 1987; 33(3):124-79.
15. Watson WJ. Vaginal Discharge: An Approach to Diagnosis and Management. Can Fam Physician 1987; 33:1847-52.
16. Sherrard J, Donders G, White D. European (IUSTI/WHO) Guideline on the Management of Vaginal Discharge. Int J STD AIDS 2011; 22(8): 421-9.
17. Masand DL, Patel J, Gupta S. Utility of Microbiological Profile of Symptomatic Vaginal Discharge in Rural Women of Reproductive Age Group, J Clin Diagn Res 2015 Mar; 9(3): 4-7.
18. Yusuf MA, Chowdhury M, Islam KMS, et al. Common microbial etiology of abnormal vaginal discharge among sexually active women in Dhaka, Bangladesh. South East Asia Journal of Public Health 2011; 1:35-9.
19. Mitchell H. Vaginal discharge-causes, diagnosis, and treatment. BMJ 2004; 328:1306-8.
20. Begum N, Muazzam N, Shamsuzzaman SM, IslamMDU, Chowdhury AK, Begum SA. Prevalence of bacterial vaginosis among the PID patients in Bangladesh. Faridpur Med Coll J 2011; 6:10-3.
21. Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the United States, 2001-2004; associations with symptoms, sexual behaviors, and reproductive health. Sex Transm Dis 2007; 34: 864-9.
22. Nessa K, Waris SA, Alam A, et al. Sexually transmitted infections among brothel-based sex workers in Bangladesh: High prevalence of asymptomatic infection. Sex Transm Dis 2005; 32:13-9.
23. Somia G, Hina Q, Jawaid W, Bukhari U, Javed Y. Women facing heavy vaginal discharge (Leucorrhea) by virtue of unhealthy life style. Faculty of pharmacy, Jinnah University for Women, Karachi, Pakistan. IRJP 2013; 4(1).
24. Rahman M, Alam A, Nessa K, et al. Etiology of sexually transmitted infections among street-based female sex workers in Dhaka, Bangladesh. J Clin Microbiol 2000; 38:1244-6.
25. Alam N, Rahman M, Gausia K, et al. Sexually transmitted infections and risk factors among truck stand workers in Dhaka, Bangladesh. Sex Transm Dis 2007; 34: 99-103.
26. Donders GG, Van Calsteren K, Bellen G, et al. Predictive value for preterm birth of abnormal vaginal flora, bacterial vaginosis and aerobic vaginitis during the first trimester of pregnancy. Int J Gynecol Obstet 2009; 116: 1315-24.
27. Kiss H, Petricevic L, Husslein P. Prospective randomized controlled trial of an infection screening programme to reduce the rate of preterm delivery. BMJ 2004; 329: 371.
28. Rylander E, Berglund A, Krassny C, Petrini B. Vulvovaginal candida in a young sexually active population: prevalence and association with oro genital sex and frequent pain at intercourse. Sex Transm infect 2004; 80: 54-7.
29. Nwadioha SI, Egah DZ, Alao OO, Iheanacho E. Risk factors for vaginal candidiasis among women attending primary health care centers of Jos, Nigeria. J Clin Med Res 2010;2:110-3.
30. Hawkes S, Morison L, Foster S, et al. Reproductive tract infections in women in low-income, low prevalence situations: assessment of syndromic management in Matlab, Bangladesh. Lancet 1999; 354:1776-81.
31. Bogaerts J, Ahmed J, Akhter N, Begum N, Van Ranst M, Verhaegen J. Sexually transmitted infections in a basic healthcare clinic in Dhaka, Bangladesh: syndromic management for cervicitis is not justified. Sex Transm Infect 1999; 75:437-8.
32. Adler MW. Vaginal discharge: Diagnosis. BMJ 1983; 287:1529-31.
33. Rioux JE. Challenging case studies in vaginitis. In: Ortho Pharmaceuticals. Profiles in practice. 1980; 14.

Chemotherapy in combination with Trastuzumab is better than chemotherapy alone in HER2 positive breast cancer patients

Md Dayem Uddin[a], Ipshita Zerin[b], Md Shafayat Habib[c], Arif Hosen[d], Julekha Khatun[e]

Abstract

Background: Breast cancer is the most common cancer in women worldwide. It is also the principal cause of death from cancer among women globally. Despite the high incidence rates, majority of the diagnosed breast cancer patients are still alive 5 years after their diagnosis, which is due to proper detection and treatment. **Objective:** To evaluate the survival gains of trastuzumab with standard chemotherapy in patients with HER2+ metastatic breast cancer. **Methods:** This multicenter Randomized Control Trial (RCT) study had conducted in the different hospitals and clinics in Rajshahi city since January 2013 to December 2015. A total of 130 women having HER2 positive breast cancer in the stage II and stage III, 52 in TAC (Taxotere, Doxorubicin and Cyclophosphamide), 61 in TAH (Taxotere, Doxorubicin, Herceptin/ Trastuzumab) and 17 women in placebo arm, were allocated randomly. Data on background characteristics and treatment outcomes including survival status of the intervention groups were collected by a preformed data collection sheet. Kaplan-Meier curves were constructed for the survival distribution of the different intervention groups. The log rank test was applied to compare the survival distribution among the intervention groups. **Results:** The overall median survival of the study subjects was 25.57 months. The median survival for the TAC, TAH and placebo were 23.33, 28.51 and 20.40 months respectively. Using TAH provided 5.18 months more survival over TAC. The survival distributions among the intervention groups was statistically significant ($p = 0.011$). **Conclusion:** Combination of traditional standard chemotherapy and trastuzumab - which is associated with fewer side effects, is an appealing better care for the breast cancer patients of stage II and stage III with HER2 positive than the traditional standard chemotherapy regimens alone.

Key Words: Trastuzumab, Breast Cancer, HER2 Positive.

[a] Professor and Head, Department of Clinical Oncology, Barind Medical College, Rajshahi, Bangladesh.

[b] MS Fellow in Electrical Power Engineering, Faculty of Engineering, University of Putra, Malaysia.

[c] Radiotherapist, Department of Radiation Oncology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

[d]Resident, Department of Radiation Oncology, Rajshahi Medical College Hospital, Bangladesh.

[e]Medical officer, Department of Radiation Oncology, Rajshahi Medical College Hospital, Bangladesh.

Correspondence to : MD Uddin professordayem@yahoo.com

Cite this as: BMCJ 2 016; 2(2):

Introduction

Breast cancer (BC) is the most common cancer worldwide with an estimated 1.67 million new cases diagnosed in 2012 (25% of all cancers). BC is the fifth cause of death from cancer overall (522,000 deaths) and it is the most frequent cause of cancer death in women in less developed regions. In the developed countries, it is the second cause of cancer death (198,000 deaths 15.4%), after lung cancer. In developed countries 6% to 10% of women will have metastatic disease when diagnosed with BC; in developing countries this percentage can reach 60%. Depending on initial stage, tumor biology, and type of treatment scheme received, 30% to 50% of women with early BC will relapse. The amplification of the human epidermal growth factor receptor 2 (HER2) is observed in 25% to 30% of all BCs. Patients with BC with over expression of HER2 have, originally, a poorer prognosis and shorter overall survival (OS). The development of effective HER2 targeted drugs is considered a major breakthrough in BC therapy. Trastuzumab was the first anti-HER2 drug approved for treatment of HER2 positive (HER2+) metastatic BC, either alone or in combination with chemotherapy. This anti-HER2 monoclonal antibody was associated with a significantly longer time to disease progression, higher response rate, longer response duration, and improved overall survival. During the last decade, HER2 targeted therapeutic approaches continued to evolve with a positive impact on the survival of the women with HER2+ metastatic BC.[1,2]

Trastuzumab is a recombinant humanized monoclonal antibody that selectively targets the extra-cellular domain of the HER2 receptor. It was approved by the FDA in September 1998 as the first targeted therapy for HER2 positive metastatic breast cancer, and has since led to significant improvements in the overall prognosis for patients with HER2 positive metastatic disease.[3,4] Trastuzumab, a monoclonal antibody that targets HER2, has significantly improved disease-free and overall survival when combined with chemotherapy for patients with breast cancers treated in both the adjuvant and metastatic settings.[5,6] The use of trastuzumab with or without chemotherapy is the

backbone of systemic treatment of HER2 positive breast cancer. The incorporation of trastuzumab into the treatment of HER2 positive breast cancer was based on a groundbreaking Phase III trial in which 469 women with HER2 positive metastatic breast cancer (MBC) were randomized to receive standard chemotherapy with or without trastuzumab.[7]

This study aimed to evaluate the combine effect of trastuzumab and low-intensity chemotherapy on patients' survival in comparison with traditional standard chemotherapy regimens in patients with HER2+ metastatic Breast Cancer.

Methods

This multicenter Experimental – Randomized Control Clinical Trial study had conducted in the department of Radiation Oncology, Rajshahi Medical College Hospital (RMCH) and other private hospitals and clinics in Rajshahi city since January 2013 to December 2015. Patients with HER2 positive breast cancer having stage II and stage III attended at these hospitals and clinics during the study period were the study population. Total 130 women, 52 in TAC, 61 in TAH and 17 women in placebo arm were enrolled randomly in this study. In TAC arm: 52 women were randomly allocated to the TAC (Taxotere, Doxorubicin and Cyclophosphamide) arm. TAC arm consists of Taxotere (75 mg/m^2, day 1), as 1 hour infusion preceded by Doxorubicin (50 mg/m^2, day 1) and Cyclophosphamide (500 mg/m^2, day 1), both given as an intravenous bolus. This TAC protocol runs for 6 cycles in every 3 weeks. In TAH arm: 61 women were randomly allocated to the TAH (Taxotere, Doxorubicin, Herceptin/ Trastuzumab) arm. TAH arm consists of Taxotere (75 mg/m^2, day 1), Doxorubicin (50 mg/m^2, day 1) and Herceptin/ Trastuzumab (8mg/kg for 1st cycle and 6mg/kg from 2nd cycle, day 1), In this arm other combined therapy will run till 6 cycles and Herceptin will run up to 12 cycles in every 3 weeks. In Placebo arm: 17 patients were allocated to placebo arm. The patients having cardiovascular disease were excluded from the study. After selection, every patient was followed at the interval of 3 months up to 36 months (3 years), if survived. Before selection the women, informed written consent was taken from each of them. Data on back ground characteristics and treatment outcomes of the intervention groups were collected by a pre formed data collection sheet.

Data were computed and processed using SPSS for window. Descriptive analytic techniques involving frequency distribution, computation of percentage etc. were done. Kaplan-Meier curves were constructed for the survival distribution of the different intervention groups. The log rank test was applied to compare the survival distribution among the intervention groups.

Results

TAC arm had a total of 52 patients, TAH arm had a total of 61 patients and Placebo arm had a total of 17 patients. A total of 130 patients, 77 (59.2%) patients belonged to the 36-50 years age group, 21 (16.2%) patients were in the age group of 25-35 years and the rest 32 (24.6%) were above 50 years. In between age 25-35 years, 10 patients received TAC, 8 patients received TAH and 3 patients received placebo. In between age 36-50 years, 33 patients received TAC, 31 patients received TAH and 13 patients received placebo. Age above 50 years, 9 patients received TAC, 22 patients received TAH and 1 patient received placebo.

In this study, most of patients belong to the middle class family. Among 130 patients, 68 (52.3%) patients belong to that group, 45 (34.6%) patients belong to upper- middle class and 17 (13.1%) patients belong to the Lower-Middle class. Most of the patients were found to have the tobacco addiction along with betel leaf. Among 130 patients 89 (68.5%) patients took tobacco and 41(31.5%) patients did not have any addiction to tobacco. Most of the study subjects, 97 (75.0%) patients did not experience any radiation therapy in their lifetime and the rest 33 (25.0%) patients had the history of getting radiation therapy in their early age for any kind of cancers or other diseases. Among 130 patients 78 (60.0%) did not get any Hormone Replacement Therapy (HRT). 52 (40.0%) patients experienced HRT in their lifetime. Among 130 patients 74 (57.0%) patients were used to take oral contraceptive as their contraception. 56 (43.0%) patients took other contraception method not oral contraceptive. Among 130 patients 51(39.3%) patients had ER-/PR-, 19 (14.6%) patients had ER+/PR-, 45 (34.6%) patients had ER+/PR+, 15 (11.5%) patients had ER-/PR+ receptor status.

Among 130 patients only 23(17.7%) patients used to breastfeed their children and remaining 107 (82.3%) patients did not. Among 130 patients 75 (57.7%)

patients maintained their conjugal life and remaining 55(42.3%) patients did not have normal conjugal life. More than forty one percent (54, 41.5%) of the patients had menopause and rest (76, 58.5%) of the patients did not experience it. Hypertension was found among the 42.3% (55) of the patients and the rest 75(57.3%) were normotensive. Diabetes Mellitus (DM) with or without hypertension was also found in many patients. A total of 130 patients, 97(74.6%) patients had comorbidity and the rest 33(25.4%) did not have any comorbidity. If the circumstances surrounding a patient's death were not available, the cause of death was classified as unknown, even if the patient had developed recurrent breast cancer or a second malignancy. The other efficacy end point examined was disease free survival (DFS), defined as the time from enrollment to documentation of the first of any of these events: local, regional, or distant recurrence of breast cancer; a contra lateral breast cancer; a second primary cancer; or death as a result of any cause.

Table 1 Median survival among different intervention groups

Drug	Median Survival (months)
TAC	23.33
TAH	28.51
Placebo	20.40
Overall	25.57

Women assigned to the Trastuzumab had a significantly increased Overall Survival (OS) relative to those randomly assigned to the control group when the stratification factors are taken into account (stratified HR, 0.70; 95% CI, 0.59–0.83; *P*=.011). The median survival for the TAC and TAH was 23.33 and 28.51 months respectively (Table 1).

From the Kaplan-Meier curves we can see that the median survival of placebo group was 20.40 months. On the other hand, the TAC group, the overall survival is 23.33 months (Table 1) and among 52 patients the percent of incidence is 62.3% (35). There were a significant number of death incidents between 4-12 months and a highly significant number of death incident occurred between 22-34 months and most of the incident had occurred between in this time.

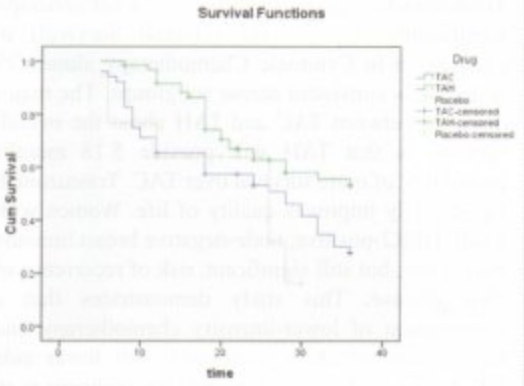

Figure-1 Kaplan Meier curves for different groups associated with patient survival

On the contrary, for TAH, the overall survival is 28.51 months and among 61 patients the percent of incidence is 41% (25) which showed better efficacy of using this combination. Moreover, from the Kaplan-Meier curve it gave an eye evident that though there is a couple of incidence between 8-16 and 18-23 but it had a more steady period from 24-36 months with an interval of only 3 incidence. So, in the comparison, the major outcome between TAC and TAH about the overall survival, the evidence of this study was using TAH would provide (28.511-23.33) = 5.181 months, probability of more survival over TAC.

The log rank test was applied to compare the survival distribution among the intervention groups. The survival distributions among the intervention groups was statistically significant (p = 0.011).

Discussion

Globally, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females. In developing countries like Bangladesh and in India, the breast cancer is also becoming the most common Cancer among women for the last few years.[8] The drug trastuzumab is a monoclonal antibody and works by targeting breast cancer cells that over express the HER2 protein. By binding to the protein receptors on these cells, trastuzumab interrupts the growth signal, thereby slowing and stopping the growth and helps not to spread the tumours. Approximately 20% to 25% of breast cancers over express the HER2 protein[9]

Trastuzumab and Cytotoxic Chemotherapy significantly improve OS (Overall Survival) in comparison to Cytotoxic Chemotherapy alone. OS benefit was consistent across subgroups. The major outcome between TAC and TAH about the overall survival is that TAH will provide 5.18 months probability of more survival over TAC. Trastuzumab significantly improves quality of life. Women with small, HER2-positive, node-negative breast tumours have a low, but still significant, risk of recurrence of their disease. This study demonstrates that a combination of lower-intensity chemotherapy and trastuzumab which is associated with fewer side effects than traditional chemotherapy regimens is an appealing standard of care for this group of patients.

In the study, we wanted to know if a combination of Herceptin and just chemotherapy with doxorubicin and taxane, would offer benefits to women diagnosed with small HER2 positive breast cancers that hadn't spread to the lymph nodes and had a low risk of recurrence. It was evident that overall survival was better in women who got Trastuzumab plus chemotherapy compared to women who got only chemotherapy. Disease-free survival was better in women who got Trastuzumab plus chemotherapy compared to women who got only chemotherapy.

We found only 17% patients who are obese in our study. Carcinogens found in tobacco smoke pass through the alveolar membrane and into the blood stream, by means of which they may be transported to the breast via plasma lipoproteins. Those potential breast carcinogens in tobacco smoke can be taken up and metabolized in humans. In our study, among 130 patients 89 patients took tobacco and 41 patients did not have any addiction to tobacco.[10]

A review of 54 studies in 1996 found that women have a slightly higher risk of breast cancer while they are taking birth control pills that contain both estrogen and progestin and during the 10 years after they stop taking the pills.[11] The present study findings goes in favour of it.

Exposure to ionizing radiation is the longest-established and most firmly established environmental cause of human breast cancer in both women and men. Ionizing radiation can increase the risk for breast cancer through a number of different mechanisms, including direct mutagenesis (causing changes in the structure of DNA), genomic instability (increasing the rate of changes in chromosomes, therefore increasing the likelihood of future mutations).[12] In this study among 130 patients 51 patients had ER-/PR-, 19 patients had ER+/PR-, 45 patients had ER+/PR+, 15 patients had ER-/PR+.

The Kaplan-Meier survival curve is defined as the probability of surviving in a given length of time while considering time in many small intervals. There are three assumptions used in this analysis. Firstly, at any time patients who are censored have the same survival prospects as those who continue to be followed. Secondly, the survival probabilities are the same for subjects recruited early and late in the study. Thirdly, the event happens at the time specified.[13] Patients randomly assigned to the Trastuzumab had a significantly increased OS relative to those randomly assigned to the control group when the stratification factors are taken into account (stratified HR, 0.70; 95% CI, 0.59–0.83; *P*=.011). The median survival for the TAC and TAH was 23.33 and 28.51 respectively. The absolute decreases in distant recurrence were 7.2 percentage points after two years and 14.9 percentage points after three years, although the latter value had a wide confidence interval (10.1 to 19.5 percentage points). Among eligible patients who continued treatment after doxorubicin and cyclophosphamide and who were HER2 positive on central testing, the relative reduction in the mortality rate associated with trastuzumab was 38 percent (P=0.01). The primary concern regarding the safety of trastuzumab is the increased risk of cardiac dysfunction. In the study, the cumulative three-year incidence of congestive heart failure increased by about 3 percentage points with the addition of trastuzumab. Most episodes occurred during trastuzumab treatment, but additional follow-up will be needed to define the long-term cardiotoxicity of trastuzumab. Clearly, appropriate selection and careful cardiac monitoring of patients are essential. Trastuzumab did not increase the overall frequency or severity of non-cardiac adverse effects associated with the chemotherapy regimens, but we did see rare cases of interstitial pneumonitis in patients receiving trastuzumab during or shortly after the docetaxel phase of treatment. Two cases were fatal. Possible explanations have included the left breast is slightly larger than the right, breast feeding preferentially on the right breast protects from cancer, and that right handed women check the left breast for lumps more often. However, these explanations have been countered by findings that different quadrants of the

breast have different laterality ratios, men also have asymmetric occurrence of breast tumours, and this asymmetry is present in both invasive and in situ tumours. Left breast is slightly larger than right breast so it naturally contains more breast tissue. More breast tissue is present to be at risk for the development of a cancer more frequently than the smaller breast.

The comparison of the overall survival between TAC and TAH intervention group in this study suggests that TAH will provide more than 5 months probability of additional survival over TAC. So, the addition of Trastuzumab with cytotoxic chemotherapy to HER2 breast cancer patient gives better result in comparison to traditional chemotherapy alone considering both response rate and overall survival.

This study demonstrates that a combination of low-intensity chemotherapy and trastuzumab - which is associated with fewer side effects than traditional chemotherapy regimens, is an appealing standard of care for the breast cancer patients of stage II and stage III with HER2 positive. Trastuzumab combined with cytotoxic agents such as taxanes, vinorelbine, gemcitabine, and capecitabine has been shown to produce superior response rates, TTP, and overall survival times in patients with MBC, and triplet combinations have the potential to offer additional benefit. Trials of trastuzumab treatment beyond disease progression and retreatment after neoadjuvant relapse are also under way, and it is hope that data from those trials will provide further guidance for clinical practice. The number of trastuzumab-based treatment options in clinical practice is steadily increasing with each new clinical trial. Trastuzumab has become the foundation of care in HER2 positive disease, and ongoing studies seek to provide further improvements in outcomes, broaden potential treatment approaches, and provide further information about the optimal use in clinical practice. Moreover, trastuzumab can be combined with a wide range of chemotherapy regimens while adding little to the toxicity profile of chemotherapy. Cardiac events can occur during trastuzumab treatment but are generally reversible and manageable. It is evident that overall survival was better in women who got trastuzumab plus chemotherapy compared to women who got only chemotherapy. Disease-free survival was better in women who got trastuzumab plus chemotherapy compared to women who got only chemotherapy.

References:

1. Mendes D, Alves C, Afonso N, Cardoso F, Coelho JLP, Costa L. Management of Metastatic HER2-Positive Breast Cancer: Where Are We and Where Do We Go From Here? Cancer Network. http://www.cancernetwork . Last accessed March 15, 2016.

2. Bullock K, Blackwell K. Clinical efficacy of taxane trastuzumab combination regimens for HER-2-positive metastatic breast cancer. Oncologist 2008;5:515-25.

3. Jeyakumar A, Younis T. Trastuzumab for HER2-Positive Metastatic Breast Cancer: Clinical and Economic Considerations. Clinical Medicine Insights: Oncology 2012;6: 179-87.

4. Gianni L, Dafni U, Gelber RD. Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: A 4-year follow-up of a randomised controlled trial. Lancet Oncol 2011;12:236-44.

5. Khoury T, Kanehira K, Wang D, et al. (2010) Breast carcinoma with amplified HER2: a gene expression signature specific for trastuzumab resistance and poor prognosis. *Modern Pathology* 2010; **23:**1364-1378.

6. Andersson M, Lidbrink E, Bjerre K. Phase III randomized study comparing docetaxel plus trastuzumab with vinorelbine plus trastuzumab as first-line therapy of metastatic or locally advanced human epidermal growth factor receptor 2–positive breast cancer: the hernata study. J ClinOncol 2011;29:264–71.

7. Callahan R, Hurvitz S. HER2-Positive Breast Cancer: Current Management of Early, Advanced, and Recurrent Disease 2011; 23(1):37-43.

8. Burstein H. Adjuvant medical therapy for HER2-positive breast cancer. Up-to-date. 2016. http://www.nature.com/modpathol/journal/v23/n10/full/modpathol2010125a.html. Last accessed October 11, 2016.

9. Dybdal N, Leiberman G, Anderson S, McCune B, Bajamonde A, Cohen RL. Determination of HER2 gene amplification by fluorescence in situ hybridization and concordance with the clinical trials immunohistochemical assay in women with metastatic breast cancer evaluated for treatment with trastuzumab. Breast Cancer Res Treat 2005, 93(1), 3-11.

10. Verde, Catalina Santiago, Luis Miguel Chicharro, et al. (2016) Effect of Genetic Polymorphisms and Long-Term Tobacco Exposure on the Risk of Breast Cancer. Int. J. Mol. Sci 2016;17:726.

11. Pritchard KI. (2001) Hormone Replacement in Women with a History of Breast Cancer. The Oncologist 2001;6:353-62.

12. Preston DL, Kitahara CM, Freedman DM, et al. (2016) Breast cancer risk and protracted low-to-moderate dose occupational radiation exposure in the US Radiologic Technologists Cohort. B Jnl of Can 2016;115:1105-12.

13. Goel MK, Khanna P, Kishore J. Understanding survival analysis: Kaplan-Meier estimate. Int J Ayurveda 2010; 1(4): 274–8.

Effect of Vitamin A on Lung Function Test in patient with Chronic Bronchial Asthma

M Obaidulla Ibne Ali[a], Nur-E-Atia[b], Tohorul Islam[c], Gopal Chandra Sarker[d]

[a]Associate professor, Department of Physiology, Rajshahi Medical College, Rajshahi, Bangladesh.

[b]Junior Consultant, Mohanpur, Rajshahi, Bangladesh.

[c]Junior Consultant, Chapai Nawabganj Bangladesh.

[d]Professor, Department of Physiology, Barind Medical College, Rajshahi, Bangladesh.

Correspondence to : MOI Ali
Drbachchu1966@gmail.com

Cite this as:
BMCJ 2016; 2(2):

Abstract

Background: Decreased antioxidant levels in the lungs is a feature of chronic bronchial asthma. Anti-oxidant therapy positively correlates with lung function in asthmatic patients. **Objective:** To observe the changes of lung function in patients with chronic bronchial asthma both before and after supplementation of vitamin A. **Methods:** This was a randomized controlled trial carried out in the department of physiology, Rajshahi Medical College, Rajshahi. Adult patients suffering from chronic bronchial asthma were the reference population. Sixty experimental subjects aged 20 to 45years were selected from the Asthma center of Rajshahi Medical College Hospital by necessary inclusion and exclusion criteria. They were divided into two equal groups, study and control by randomization. Pulmonary function parameters such as FVC, FEV1, FEV1/FVC% and PEFR were measured before and three month after supplementation of vitamin A in study subjects and placebo in controls. Paired t-test was applied to observe the difference of lung function parameters between pre and post intervention of the two groups. **Results:** The mean FVC, FEV1, FEV1/FVC% and PEFR following vitamin A were not changed significantly than the pre supplementation values in patients with chronic bronchial asthma. **Conclusion:** No significant improvement of pulmonary functions occur after supplementation of vitamin A in chronic bronchial asthma patients.

Key words: antioxidant, Pulmonary function, chronic bronchial asthma

Introduction

Respiratory disease is a major cause of death and disability in many countries.The etiology of most of non-infectious lung disease remains elusive despite a major increase in research on the respiratory system.[1] Morbidity and mortality of chronic bronchial asthma are increasing but its fundamental cause is still unknown despite intensive research. In chronic asthma inflammation may be accompanied by intensive air flow limitation.[2]

There are evidences that endogenous oxidants produced by hypersensitive inflammatory cells destroy airway epithelium which slough into bronchial lumen and thus aggravates asthma.[3] Free radicals are always being produced in our body. However, body operates several mechanisms for termination of these free radical, which are injurious to the body. Antioxidants neutralize free radicals and participate in protective mechanism.[3]

Antioxidants and vitamin A may delay or prevent direct oxidation of oxidizeable substrates or scavenge oxidant free radicals and neutralize the Physiologic oxidant burden created by both exogenous and endogenous free radicals. They either block the initiation of free radical formation of inactivate (scavenge) free radicals and minimize radical induce damage. Thus good antioxidant status of vitamin E, ascorbic acid, glutathions and vitamin A of the body is necessary to prevent ourselves from free radical mediated tissue injury.[4]

Acute asthmatic attacks impair the anti-oxidant defense system. When oxidant overwhelm anti-oxidants, tissue injury and disease results. Decreased level of anti-oxidants in the lungs is a feature of chronic bronchial asthma and that there is a marked decrease of these levels during acute asthmatic attacks. These observations highlight the positive correlation between anti-oxidant therapy in asthmatic patients. They documented that decline in the concentration of antioxidants super oxide dismutase and glutathione in lung fluid from asthmatic patients ten minutes after exposure to grass or ragweed allergens.[5]

Some researcher have studied lung function after supplementation of antioxidant vitamins and observed improvement of lung function following

such supplementation. Very few research have been done in our country and a little published data are available about the effect of vitamin A on lung function test in chronic asthmatic patients.

Aim and Objectives

To study of lung function test in chronic asthmatic patients before and after supplementation of vitamin A.

Inclusions criteria

Established cases of male patients with chronic bronchial asthma were taken.

Exclusions criteria

Subject suffering from pulmonary tuberculosis, bronchial neoplasm, heart failure, diabetes mellitus and renal failure were excluded from the study.

Materials and Methods

This randomized controlled trial has been designed to observed the effect of vitamin A supplementation among the patients with chronic bronchial asthma in the department of physiology of Rajshahi Medical College between the period of July2003 to June 2004.The protocol of this study was approved by Institutional Review Board (IRB) and Ethical Review committee (ERC) of Rajshahi Medical College.

Sixty apparently healthy males suffering from chronic bronchial asthma aged 20 to 45years were selected from the Asthma center of Rajshahi Medical College Hospital with their consent after explanation in details the aim, objectives. benefit, risk and procedure of the study to them considering all inclusion and exclusion criteria. The 60 study subjects were divided into two groups, study and control groups by randomization. The study and control groups were supplemented with oral vitamin A 10,000 IU (Cap. Retenol forte, Drug International Ltd. Bangladesh) and placebo once daily for 3 months respectively.

Complete history taking and physical examination of both the groups were done and record in a preformed date sheet before and after the intervention. Pulmonary function parameters such as FVC, FEV_1, FEV, /FVC % and PEFR were measured by digital spirometer on standing position of all patients of both the groups. Collected data ware analyzed in computer by using SPSS version 16.0. Paired t-test was applied to observe the difference of lung function parameters between pre and post intervention of the two groups.

Results

Table 1. Measured and predicted value of FVC with percent deviation before and after supplementation with vitamin A.

Group	Measured value (L) Mean± SE	Predicted value (L) Mean ± SE	Percent deviation from predicted value (%)
Group-A n =30			
BS (A_1)	2.46 ± 0.11	4.38 ± 0.06	-43
AS (A_2)	2.46 ± 0.11	4.38 ± 0.06	-43
P value	>0.05	>0.05	
Group-B n=30			
BS (B_1)	2.30 ± 0.33	4.49 ± 0.08	-48
AS (B_2)	2.30 ± 0.37	4.49 ± 0.08	-38
P value	>0.05	>0.05	

BF = Before supplementation, AF = After supplementation

Percentage deviation of FVC from predictive value in group B before supplementation was 48% less, Which after supplementation came down to 38% less from predicted value (Table 1).

Table 2. Measured and predicted value of FEV_1 before and after supplementation with vitamin A.

Group	Measured value (L) Mean± SE	Predicted value (L) Mean ± SE	Percent deviation from predicted value (%)
Group-A n=30			
BS (A_1)	1.46 ± 0.09	3.70 ± 0.05	-60
AS (A_2)	1.46 ± 0.09	3.70 ± 0.05	-60
P value	>0.05	>0.05	
Group-B n=30			
BS (B_1)	1.46 ± 0.04	3.72 ± 0.05	-64
AS (B_2)	1.46 ± 0.05	3.72 ± 0.05	-52
P value	>0.05	>0.05	

BF = Before supplementation, AF = After supplementation

The mean measured value of group B (before supplementation) was 1.46 ± 0.04, which was 1.46 ± 0.05 after supplementation, percentage deviation of FEV_1 from predicted value in Group B before supplementation was 64% less, which after supplementation came down to 52% less from predicted value (Table 2).

Table 3. Measured and predicted value of FEV_1/FVC% with percent deviation from predicted values before and after supplementation with vitamin A.

Group	Measured value (L) Mean± SE	Predicted value (L) Mean ± SE	Percent deviation from predicted value (%)
Group-A n=30			
BS (A_1)	59 ± 0.01	84 ± 0.25	-30
AS (A_2)	59 ± 0.01	84 ± 0.25	-30
P value	>0.05	>0.05	
Group-B n=30			
BS (B_1)	63 ± 0.7	83 ± 0.18	-22
AS (B_2)	63 ± 0.8	83 ± 0.18	-19
P value	>0.05	>0.05	

BF = Before supplementation, AF = After supplementation

The mean measured value of group B (before supplementation) was 63%, which was 63% after supplementation. Percentage deviation of FEV_1/FVC% from predicted value in Group B before supplementation was 22% less, which after supplementation came down to 19% less from predicted value (Table 3).

Table 4. Measured and predicted value of PEER before and after supplementation with vitamin A.

Group	Measured value (L) Mean± SE	Predicted value (L) Mean ± SE	Percent deviation from predicted value (%)
Group-A n=30			
BS (A_1)	285 ± 16.72	604 ± 2.49	-52
AS (A_2)	287 ± 16.98	604 ± 2.49	-52
P value	>0.05	>0.05	
Group-B n=30			
BS (B_1)	242 ± 17.19	613 ± 3.14	-60
AS (B_2)	259 ± 8.24	613 ± 3.14	-58
P value	>0.05	>0.05	

BF = Before supplementation, AF = After supplementation

The mean measured value of group B (before supplementation) was 242 ± 17.19, which increased to 259 ± 8.24 after supplementation.

Percentage deviation of PEER from predicted value in Group B before supplementation was 60% less, which after supplementation came down to 58% less from predicted value (Table 4).

Discussion

Present study has been done to observe the changes in lung function among patients with chronic bronchial asthma, both before and three months after supplementation of vitamin A. lung functions were assessed by measuring FVC,FEV_1,FEV_1/FVC% and PEER. Previous studies reported that the pulmonary function parameters such as FVC, FEV_1, FEV_1/FVC% and PEER in patients with chronic bronchial asthma are always lower in comparison to healthy subjects.[6,7]

When subjects in this study were supplemented with vit-A, no significant change in mean FVC,$FEV_1$$FEV_1$/FVC% & PEFR were obseved. Though mean PEFR in this group was slightly increased following vit-A supplementation, the change was not statistically significant. No significant change of the above parameter was seen after vit-A supplementation when compared to control subjects measured at the end of the study. It is consistent with the findings of McKeever et al.[8]

C.Bodner *et. al.* (1999)[9] also found significant correlation between the amount of dietary intake of antioxidant vitamins and their plasma levels. Dietary intake values were significantly correlated with plasma level for vitamin C (r=0.42, P<0.001), vitamin E (r=0.34, P<0.001 and ß-carotene (r=0.26, P_s<0.01) but not for vitamin A. Findings of this study explain why no improvement of lung function occurred in this study subjects who were supplemented only with-vitamin A.

The lower pulmonary volume and capacities in asthmatic subjects of the present study were most likely due to bronchoconstriction by air pollutants as most subjects of this study were from urban area, where pollution is supposed to higher than that of rural area. So improvement of pulmonary function values were not significantly increase after supplementation of vitamin A.

Present study reveals that lower pulmonary functions occurs in patients with chronic bronchial asthma and no improvement of these lower pulmonary functions occur after supplementation of vitamin A.

Limitation of this study is the small sample size and study was done in only northern part of Bangladesh, so it is difficult to draw a definite conclusion. Further study to be done in different areas with large sample size and follow up study with other antioxidants and vitamin for long duration.

References

1. Menzel DB. Antioxidant in lung Disease, Deprtment of Community and Environmental Medicine, University of California lvine, College of Medicine, Irvine, California, 1998; 323-36.
2. Holgate ST, Frew A. Respiratory Disease. In: Parveen K, Michael C, editors. Kumar & Clark Clinical Medicine, 5th edition. Edinburgh London: Saunders, 2002; 874.
3. Hatch GE. U.S. Environmental Protection Agency, Asthma, Inhaled oxidant and antioxidants. American Journal of Clinical Nutrition 1995; 61(suppl): 625s-30s.
4. Chaudhury Sk. Concise Medical Physiology 4th edition New Central Book Agancy (P) Ltd. Calcatta, 2002; 349.
5. Kumar V, Abbas AK, Fausto N (editors): Robbins and Corton Pathologic Basis of Disease 7th edition Saunders. Thomas Press India Ltd. 2004;17.
6. Crompton GK, Haslett C, Chilvers ER. Disease of the respiratory system. In; Haslett C et al. (editors): Davidson's Proncipal and Practice of Medicine. 18th edition Churchill Livingstone, Edinburgh London New York 1999;326-34.
7. Spiro SG, Roberts GM. Lung function test. Medicine International 1991;4(14):3661-8.
8. McKeever TM, Scrivener S, Broadfield E, Jones j, Britton j, Lewis SA. American journal of Respiratory and Critical care Medicine 2002;165(9): 1299-1303.
9. C Bodner, D Godden, K Brown et al. Antioxidant intake and adult-onset wheeze: a case–control study. Aberdeen WHEASE Study Group. Eur Respir J, 13 (1999), 22–30

Alzhiemers Disease: An important cause of dementia

Md. Muazzem Hossain[a], Nasrin Jahan Shammi[b], Kazi Wali Ahmed[c], Rezowana Sharmin[d]

Abstract

Dementia is not a disease but symptom. Alzheimer disease is the most common form, a degenerative disorder of brain that leads to memory loss. Dementia has become a concern worldwide as the global population is ageing. There is no way to definitively diagnosed Alzheimer disease without performing an autopsy. But associated diagnostic parameters like CT scan, MRI, PET, CSF and Plasma based protein biomarker are also helpful. Rivastigmine, Donepezil, Mementine etc. are used for treatment. There is no cure for Alzheimer disease, however promising research and development for early detection and treatment is underway.

[a] Professor, Department of Anatomy, Barind Medical College, Rajshahi, Bangladesh.

[b] Associate professor, Department of Pharmacology, Barind Medical College, Rajshahi, Bangladesh.

[c] Professor, Department of Pharmacology, Barind Medical College, Rajshahi, Bangladesh.

[d] Assistant Professor, Department of Microbiology, Barind Medical College, Rajshahi

Correspondence to : M M Hossain @yahoo.com

Cite this as: BMCJ 2 016; 2(2):

Introduction

Dementia is a symptom that can be caused by a number of progressive illnesses. It is the main cause of dependency in older people. There were 46.8 million people living with dementia worldwide in 2015, increasing to 74.7 million by 2030 and 131.5 million by 2050.[1] More than 60% people with dementia live in developing countries.[2] Approximately 5% of people between the age of 65 and 74 have Alzheimer disease.[3] Alzheimer disease is clinically characterized by a progressive cognitive impairment including impaired judgment, decision making, ability to perform activities of daily living, ability to learn and remember new information and orientation, often accompanied in later stages by psychobehavioral disturbances as well as language impairment (speaking, reading, writing). Life expectancy of the population with this disease is reduced[4]. The mean life expectancy following diagnosis is approximately seven years. Fewer than 3% of patients live more than fourteen years. Alzheimer disease is predicted to affect 1 in 85 people globally by 2050[5]. At present it causes upto 100,000 deaths annually[6]. Alzhiemer disease carries significant implication for patient, their families and our society. The article emphasizes clinical and neurological aspect of Alzheimer disease specially dementia.

Pattern of Alzhiemer disease

Alzheimer disease (AD) is the cause of irreversible dementia. There are two main form of Alzhiemer disease, genetic based early onset familial Alzhiemers disease and a more prevalent age-dependent form called sporadic Alzhiemers disease. Familial Alzhiemer disease affects people younger than 65 and the remainder of Alzhiemer disease cases occur in adults aged 65 and older as sporadic Alzhiemers disease[2]. The familial form is due to mutation in 3 gene: amyloid precursor protein (APP) gene on chromosome 21, presenilin 1 gene (PSEN1) and presenilin2 gene (PSEN2), located on chromosome 1&14[7].

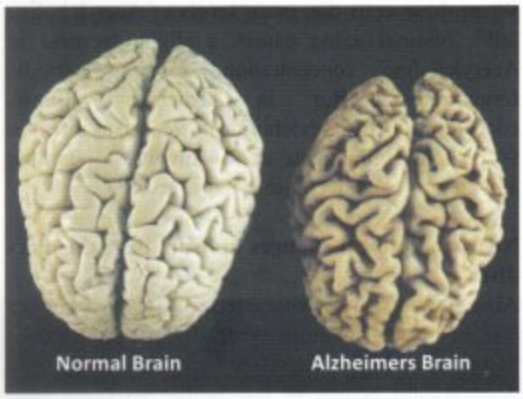

Figure:1 Healthy Brain versus Alzheimer's Brain

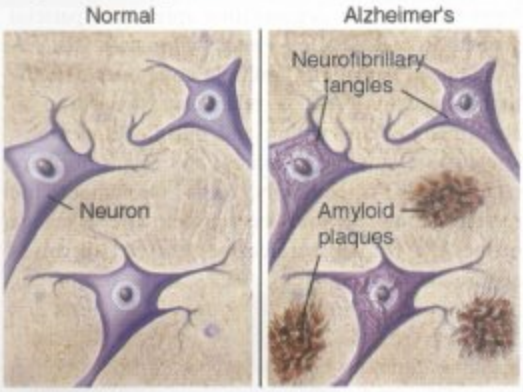

Figure 2: Neurological changes in Alzheimer's dtsease

Risk factors for Alzhiemers disease

Alzhiemers disease is a multifactorial disease with no single cause known and several modifiable and non-modifiable risk factors are associated with its development and progression. Established risk

factors trigger neuronal dysfunction[8]. In particular ageing, family history (3-5 fold increase risk when a first degree relatives is affected), apolipoprotein E4, head injury, depression, hypertension, type-2 diabetes, hypercholesterolemia, obesity, atrial fibrillation, presence of cerebral emboli and low physical and cognitive activity can significantly contribute to the development and progression of Alzhiemers disease[9].

Pharmacological cause of dementia in Alzhiemer disease

In Alzhiemers disease, the learning and memory centres in the medial temporal lobes are susceptible to damage. Small groups of cells known as basal forebrain produce a chemical called Acetylcholine (Ach) that is important for learning and memory. When these cells die, brain levels of Acetylcholine fall[10]. Normal aging causes a slight decrease in Acetylcholine concentration, causing periodic forgetfulness. But in Alzheimer disease, concentration of Acetylcholine decreased as much as 90 percent[10]. Glutamate is also involve in learning and memory and decrease in same level[11].

Neuroanatomical changes in brain in Alzhiemers disease

Alzheimer disease is characterized by a progressive loss of cortical neurons, specially pyramidal cells that mediate higher cognitive function[12]. AD-related degeneration begins in the medial temporal lobe predominantly in entorhinal cortex and hippocampus. The degeneration spreads to parietal areas, frontal cortex and ultimately causes pronounced damage to multiple components of the limbic system[13]. AD is related to deposition of abnormal proteins within and outside of neurons, known as amyloid plaques and neurofibrillary tangles (NFT). Normally, cells throughout life release soluble amyloid –beta protein after cleavage of the APP (a cell surface receptor). AD involves abnormal cleavage of APP that results in precipitation of Amyloid-beta into beta sheets and formation of senile plaques, which consists of insoluble amyloid-beta protein. It is believed that microglia and astrocytes then mount an inflammatory response to clear the amyloid aggregates and this inflammation causes destruction of adjacent neuron[14]. Every brain cells contain long fibres that holding brain cell in its proper shape and helping transport of nutrients within cell. In AD these fibres begin to twist and tangle. The brain cell loses its shape (Fig:1) and unable to transport nutrients properly, it eventually dies[15](Fig:2).

Diagnosis

The gold standard for the diagnosis of AD is an autopsy based pathological evaluation. Because amyloid plaque and NFT are only found through biopsy. However mini mental state examination (MMSE) , Alzhiemers disease assessment scale (ADAS) and physical examination allow physician to make an accurate diagnosis of AD in 90% cases[16]. Blood test for hormonal imbalance, vitamin deficiency and urine analysis for UTI is also performed. Several neuroimaging and other biomarkers approach are being used to study AD and exclude brain tumour, cerebrovascular attack, traumatic brain injury, infection. Biomarkers are needed to identify high risk patients for early treatment as well as for monitoring disease progression and response to treatment. Fluid markers (CSF and plasma based protein marker), computed tomography (CT scan), magnetic resonance imaging (MRI), positron emission tomography (PET) are widely used. PET utilizes 18-Flurodeoxy glucose, which measures regional brain metabolism.The earliest sign of AD detectable on an FDG-PET scan is the hypometabolism of the posterior cingulated cortex and precuneus[17]. It helps in distinguishing different forms of dementia, especially AD bersus frontotemporal dementia[18]. PIB-PET(Pittsbrugh compound B) has been developed for directly and clearly imaging beta-amyloid deposits in vivo using a tracer that binds selectively to the A-beta deposits[19]. In AD patients show marked enlargement of lateral ventricle, medial temporal lobe atrophy involving the hippocampus and entorhinal cortex[20]. It differentiates progression from minimal cognitive impairment to AD-dementia.

Treatment of Alzhiemer disease

Alzhiemers disease includes instigation of pharmacological symptomatic treatments and initiation of psychological support and co-morbid conditions.

Pharmacotherapy

The FDA approved two types of medication for this purpose. These medications help to control the symptom but do not slow down the progression or reverse the course of disease itself[21]. At present, the mainstay of Alzeimer's disease is drugs that target neurotransmitter system in brain. The first groups are cholinesterase inhibitors: rivastigmine, galantamine,

donepezil. Mementine is another FDA-approved medication for use in moderate to severe AD[22]. Rivastigmine prevent breakdown of acetylcholine and increase Ach concentration in brain. Mementine regulates the activity of glutamate in brain. Overstimulation of nerves by glutamate is the cause of neuron degeneration in AD[23]. Glutamate binds to N-methyl-D-aspartate(NMDA) receptors on the surface of brain cells. Mementine acts by blocking of NMDA receptors and therefore protecting the nerves from excessive glutamate stimulation[24].

Psycotherapy

In addition to cognitive decline, Alzhiemer disease can cause severe behavioral and psychiatric symptoms. These symptoms include anxiety, sleeplessness, agitation, hallucinations and delusions. Antipsychotic drugs consistently reduce agitated behaviour, concern have been expressed recently over the safety of both the older (haloperidol) and second generation antipsychotics (quetiapine, risperidone, olanzapine).

Immunotherapy

βA has been reduced by injecting AD patients with a synthetic form of beta-A called AN 1792.Some people respond to immunization with a slowly progression of disease even after 4-6 years[25]. Other studies have found a clearing of beta-A without any cognitive benefit[26].

Conclusion

Dementia due to Alzhiemers disease is a critical public health issue in the world with a significant health, social and financial burden on society. Although the diagnosis of AD is often missed or delayed, people with dementia need special care which should be started early in the disease and evolve constantly over time requiring advanced planning, monitoring, coordination. Creating awareness is the first priority. Training healthcare workers on dementia and try to identify "caregivers" with expertise to takecare of patients. It is imperative that the correct course of treatment be implemented to delay further brain deterioration and slow the onset of symptoms. New approaches are needed to ensures patients access to essential resources and further research work should aim to improve diagnostic and therapeutic effectiveness for the benefit of future generation.

References:

1. Worid Alzheimer's report 2015: The Global Impact of Dementia. The Global Voice on Dementia. https://www.alz.co.uk/research/world-report-2015. Last accessed on February 22, 2017.
2. Alzheimer's disease international statistics. Available at: http://www.alz.co.UK/research/statistics.htnril. Accessed Feb.4, 2017.
3. Alzheimer's association 2010. Available at: http://alz.org. Accessed Feb.4, 2017.
4. Katzman R. Education and prebalence of dementia and Alzhiemers disease. Neurology 1993; 43: 13.
5. Brookmeyer R, Zohnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. Alzhiemers and Dementia 2007; 3(3): 186-91.
6. Saxena U. Bioenergetics breakdown in Alzheimer's disease: tagets for new therapies. Int J Physiol Pathophysiol Pharmacol 2011; 3(2): 133- 9.
7. Piaceri I, Nacmias B, Sorbi S. Genetics of familial and sporadic Alzheimer's disease. Biosci 2013; 5:167-77
8. Saxena U. Alzhiemers disease amyloid hypothesis at crossroads: where do we go from here? Expert opinion Therapeutics.Targets 2010; 14(12): 1273-77.
9. Struble RG , Ala T, Patrylo PR et al. Is brain amyloid production a cause or a result of dementia of Alzhiemers type? J Alzhiemers Disease 2010; 22(2): 393-9.
10. Zimmerberg B. Synaptic Transmission: A Four Step Process. Multimedia Neuroscience. Education Project, Williams College Neuroscience. 1998.
11. Selkoe DJ. Alzheimer's disease is a synaptic failure. Science 2002; 298: 789-91.
12. Gosche KM. Hippocampal volume as an index of Alzheimer's neuropathology: Findings from the Nun study. Neurology 2002; 58 :1476-82.

13. Small GW. Neuroimaging and Genetic Assessment for early diagnosis of Alzheimer's disease. J of Clinical Psychiatry 1996; 57: 9-13.

14. Mellon EA, Pilkinton DT, Clark CM, et al. Sodium MR imaging detection of mild Alzheimer disease: preliminary study. Am J Neuroradiol. 2009; 30(5): 978-84.

15. "What is a PET scan? How does a PET scan work?" Medical News Today: Health News-June 22, 2009.

16. American Health Assistance Foundation: Alzheimer's disease, Macular Degeneration and Glucoma. http://www.ahaf.org. Last accessed on July 10, 2016.

17. Minoshima S, Giordani B, Berent S et al. Metabolic reduction in posterior cingulated cortex in very early Alzhiemers disease. Neurol 1997; 42: 85-94.

18. Mosconi L, Tsui WH, Herholz K et al. Multicenter standardized 18F-FDG PET diagnosis of mild cognitive impairment Alzhiemers disease and other dementias. J Nucl Med 2008; 49: 390-8.

19. Obrien JT. Role of imaging techniques in diagnosis of dementia. Br J Radiol 2010; 80: 571-7.

20. Devanand DP, Prathanban G, Khandji A et al. Hippocampal and entorhinal atrophy in mild cognitive impairment: Prediction of Alzhiemer disease. Neurology 2007; 68; 828-36.

21. Holtzman DM, Morris JC, Goate AM. Alzheimer's disease: The challenge of the second century.Sci Transl Med 2011. April 6; 3(77): 77sr1. doi:10.1126/scitranslmed.3002369.

22. Alzheimer's disease fact sheet. Alzheimer's disease education and referral centre. National Institute on Ageing, https://www.nia.nih.gov/alzheimers/publication/alzheimers-disease-fact-sheet#treating. Last accessed on February 22, 2017.

23. Reisberg B, Rachelle D, Albrecht S. Mementine in moderate to severe Alzhiemer sdisease. New England journal of Medicine 2003; 348: 1333-41.

24. Saltiel, Emmanuel. Memantine (Namenda). Medicine Net. 2 Nov. 2003. http://www.medicinenet.com/memantine/article.htm. Last accessed on February, 2017.

25. Vellas B, Black R, Thal LJ et al. Long term follow-up of patients immunized with AN 1792: reduced functional decline in antibody responders. Curr Alzhiemer Res 2009; 6;144-51.

Villous adenoma of the urinary bladder: A case report

Arefa Sultana[a], Shah Md Badruddoza[b]

[a]Assistant Professor Department of pathology, Rajshahi Medical College, Rajshahi, Bangladesh.

[b]Professor, Department of Pathology, Rajshahi Medical College, Rajshahi, Bangladesh.

Correspondence to : A Sultana dr.bithi.raj@gmail.com

Cite this as: BMCJ 2016; 2(2):

Abstract

A 48-years old women presented with gross haematuria that had lasted for one week. There were no lower urinary tract symptoms and flank pain. On cystoscopy, a smooth surfaced bladder mass with a single stalk was found. After transurethral resection of the tumour in the bladder, histopathology confirmed that the tumour was a villous adenoma.

Introduction:

Villous adenoma of the urinary tract one a well recognized but uncommon entity. Several case reports and a number of studies detailing the pathologic features and prognosis of villous adenomas in the urethra, bladder and urachus have been published. [1-4] There have been only 10 cases reported of a villous adenoma of the urinary tract in the medical published work[5]. However histogenesis and malignant potential of these tumours remain controversial. Villous adenomas are found most frequently in men. Patients ranged from 33to 79years of age with a mean age of 57years.

Case report:

A 48years old women presented with gross haematuria that had lasted for one week. There were no lower urinary tract symptoms and flank pain or any cardiovascular, respiratory, gastrointestinal, or neurological symptoms. On physical examination, no abnormality was found and the urinanalysis revealed red blood cells. The urine cytology negative for malignancy and other routine blood test were within normal limits. On ultrasound scan of the bladder suggested the presence of mass in the bladder. On cystoscopy, a smooth surfaced bladder mass with a single stalk was found. After transurethral resection of the tumour in the bladder, histopathology confirmed that the tumour was a villous adenoma with a polypoid growth of the glandular epithelium consisting of small tubular glands, dilated cystic glands and papillary fronds lined by a columnar epithelium with goblet cells (Fig-1).

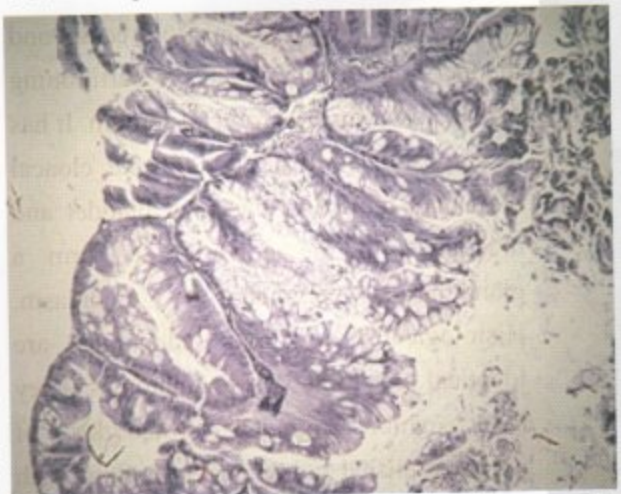

Fig. 1: Histological section showing villous adenoma of the bladder, consisting of papillary fronds covered by columnar epithelium with goblet cells (H&E X 400).

The glandular epithelial cells displayed mild nuclear atypia and nuclear pseudostratification with some mucus cells admixed. The histological diagnosis was correlated with the clinical features, imaging results and other pathological findings, the patient was diagnosed with rare case of villous adenoma of the urinary bladder.

Discussion:

This case illustrates a middle-aged women with villous adenoma without cystitis glandularis or dysplasia. Villous adenomas are found most frequently in men. Patients presented clinically with hematuria, irritative symptomps and occasionally mucusuria. The most frequent site was the bladder dome and the posterior wall; our case was on posterior wall of urinary bladder.

Embryologically, the distal colorectum and bladder both develop from the partitioning of the cloaca by the urorectal septum. It has been postulated that parts of the cloacal rests may remain in the adult bladder and urachus with the potential to form a glandular epithelial neoplasm. Histologically villous adenomas are identical to colonic villous adenomas. They both exhibit rounded projections of pseudostratified columnar epithelium with goblet-type mucin-producing cells and the nuclear atypia is variable.[5] The immunohistochemical profile of these two entities is also similar with positive findings for cytokeratin 20 and carcinoembryonic antigen (CEA), and negative findings for epithelial membrane antigen (EMA) staining in most cases.

The coexistence of glandular metaplasia with invasive adenocarcinoma of the urothelium is a frequent finding. Therefore, it has been suggested that glandular metaplasia (cystitis glandularis), in some cases, might evolve into adenocarcinoma. [6,7] However, at least one study did not confirm that intestinal metaplasia was a strong risk factor for the development of a malignant neoplasm of the urinary bladder.[8] In four cases , among the published case reports there was coexistence of cystitis glandularis with the villous adenoma. However, there is no evidence to suggest that the cystitis glandularis associated with a villous adenoma results in adenocarcinoma of the bladder.

The differential diagnosis of a villous adenoma includes florid cystitis glandularis and a well-differentiated adenocarcinoma. The former does not have the well- formed villous structures that are typical of the villous adenoma. In the latter, the epithelium is pseudostratified, and the nuclei are enlarged, crowded and hyperchromatic, features that are not present in cystitis glandularis.[6]

Once villous adenoma has been diagnosed , it is important to exclude the presence of invasion. In the colon, breaching of the muscularis mucosae is regarded as the point at which a villous adenoma becomes an adenocarcinoma. In the bladder the superficial muscle coat is not as well defined and therefore the presence of invasion is more difficult to assess.

Subjective features, such as the degree of dysplasia and surrounding stromal reaction, must be used.[9]

Patients with isolated villous adenomas in the urinary bladder have an excellent prognosis and surgical resection is curative. However, it is uncertain whether an untreated lesion might eventually develop into an adenocarcinoma.[10] Therefore, close follow up is recommended because of the possibility that this condition might be premalignant. Considering the biologic behaviour and potential and differential diagnosis of villous adenoma, it is important to diagnosis the rare entity accurately, so that effective therapy can be instituted with good prognostic out come.

References:

1. Adegboyega PA, Adesokan A.Tubulovillous adenoma of the urinary bladder. Mod. Pathol. 1999; 12: 735-8.
2. Chaudhuri A, Sandhu DP, Xuereb J. Villous adenoma of the urinary bladder. BJU Int. 1999; 84:177-8.
3. Cheng L, Montironi R, Bostwick DG. Villous adenoma of the urinary tract : a report of 23 cases, including 8 with coexistent adenocarcinoma. Am .J. Surg.Pathol. 1999; 23:764-71.
4. Sung MT, Lin JW, Chen WJ. Villous adenoma of the urinary tract: a report of two cases. Chang Gung Med. J.2000; 23: 291-5.
5. Wooseuk Sung, Byung-Dae Park, Sun Lee and Sung-Goo Chang, Villous adenoma of the bladder.Int. J of Urol.2008; 15:551-3.
6. Tran KP, Epstein JI, Mucinous adenocarcinoma of the urinary bladder type arising from the prostatic urethra. Distinction from mucinous adenocarcinoma of the prostate Am. J.Surg. Pathol. 1996; 20:1346-50.
7. Daroca PJ, Mackenzie F, Reed RJ, Keane JM. Primary adenovillous carcinoma of the bladder. J. Urol. 1976; 115: 41-5.
8. Thraser JB. Rajan RR, Perez LM, Humphrey PA, Anderson EE. Cystitis glandularis. Transition to adenocarcinoma of the urinary bladder. N. C. Med. J 1994; 55: 562-4.

9. Corica FA, Husmann DA, Churchill BM et al.Intestinal metaplasia is not a strong risk factor for bladder cancer: study of 53 cases with long-term follow-up. Urology 1997; 427-31.

10. Channer JL, Williams JL, Henry L. Villous adenoma of the bladder.J clin pathol. 1993; 46: 450-2.

11. Seibel JL, Prasad S, Weiss RE, Bancila E, Epstein Jl. Villous adenoma of the urinary tract: a lesion frequently associated with malignancy. Hum pathol. 2002; 33: 236-41.

Barind Medical College Journal (BMCJ)

Information for Authors

General

1. Articles for publication, original articles, review articles, case reports and other communications from authors should be directed to Prof. Dr. Md. Manzurul Haque, **Editor-in-Chief at the following address:**

BMCJ Division
Barind Medical College
Choto Bongram, Namovodra, Boalia, Rajshahi-6207
Mobile: +8801711815827

2. Manuscripts submitted to ***Barind Medical College JOURNAL (BMCJ)*** should be submitted with the understanding that they have neither been published, nor are, under consideration for publication elsewhere, except in the form of an abstract. Prior abstract publication(s) should be described in the form of a footnote to the title. Articles should contain original data concerning the course (prognosis), cause (etiology), diagnosis, treatment, prevention, or economic analysis of a clinical disorder or an intervention to improve the quality of healthcare. Published manuscripts become the sole property of the Journal and will be copyrighted by Barind Medical College; By submitting a manuscript to the Journal, the author(s) agree(s) to each of these conditions.

3. All submissions should be accompanied by a forwarding letter listing signed by all authors with affiliations and addresses of the authors and identifying the author to receive correspondence and proofs. (A corresponding author's name, address, mobile no., and e-mail address must be specified in the letter).

4. All submissions to BMCJ are subject to peer review. The principal author may be asked for the names and email addresses of potential suggested reviewers familiar with the field. Please ensure preferred reviewers are not from your university or institution with whom you have collaborated. Anyone whom the author does not want to be considered may also be named as a non-preferred reviewer. Ultimately, the final selection of reviewers is at the discretion of the Editor(s) of BMCJ.

5. All authors should be responsible for a significant part of the manuscript. All authors should have taken part in writing, reviewing, and revising the intellectual and technical content of the manuscript. Any author whose name appears on an article assumes responsibility and accountability for the results. The editorial Board does not subscribe to the opinion and views expressed in the article.

6. It is incumbent upon the submitting author/agent **to ensure the accuracy and inclusion of all contributing authors' names and affiliations** upon original submission of the article. Once an article is accepted for publication, changes in authorship while the article is in production – including page proofs – are NOT permitted. Changes in authorship after publication are strictly prohibited.

7. Three paper (hard) copies of the manuscript and a soft copy on a CD-Rom in MS-Word (in Doc. Format) should be sent.

Manuscript Preparation

All manuscripts should be concise and written in English in a readily understandable style.

WORD and DATA LIMITS

Article Type	Maximum Word Limit*	Abstract Word Limit	References	Figures	Tables
Original	6,000	300 (structured)	100	5	5
Review	10,000	400	200	10	8
Case reports	4,000	250	15	2	2
Short communication	2,000	200	15	2	2
Editorials	1000	N/A	10	2	2
Letter to the Editor	500	N/A	5	2	1

**These limits relate to the text of the manuscript; word limits do NOT include the abstract, figure and/or table legends, acknowledgments, disclosures, or references.*

Requirements for text

Prepare all text, double spaced, in Microsoft Word. Do NOT supply a PDF of your manuscript. Provide the order of items as follows:

- Title page
- Abstract (structured)
- Text (*Introduction, Materials and Methods, Results, Discussion and Conclusion(s)*)
- Acknowledgments
- Author Disclosure Statement(s)
- References
- Correspondence address

- Legends
- Tables
- Figures

Requirements for Title Page

The title page of your submission should be prepared in Microsoft Word and MUST be included as part of your main text document (not as a separate file) and should contain the following items:

- The complete title of the article
- **All** contributing authors' full names, complete affiliation(s), including department, institution, city, state, country.
- A brief running title of no more than 50 characters, including spaces
- The corresponding author's complete contact information including address, working fax number, and email address

Requirements for Abstract

- The abstract should be prepared in Microsoft Word
- Abstract should be no more than 300 words
- Abstract should be **structured**, stating the background, methods, results (including the sample size), and conclusions drawn from the study
- The use of the first person should be avoided
- Do not use proprietary or trade names in the title or abstract
- Clearly summarize the results and conclusions of the work
- References are not permitted in the abstract
- 3-5 key words which must being with small letter unless special necessity

Text

In general, the text should be organized under the headings: *Introduction, Materials and Methods, Results, Discussion, Conclusion(s), Acknowledgment(s) Author Disclosure Statements,* and *References*. Use only standard abbreviations, which can be found in the AMA's Manual for Authors & Editors or the Council of Biology Editors Style Manual. At first usage, spell out terms and give abbreviations in parentheses. Thereafter, use only abbreviations. It is not necessary to spell out standard units of measure, even at first usage. Use generic names for drugs if possible.

Acknowledgments

The author should acknowledge only those people and their institutions that have made significant contributions to the study.

Disclosure Statement

Immediately following the *Acknowledgments* section, include a section entitled, *Author Disclosure Statement*. In this portion of the article, authors must disclose any commercial associations that might create a conflict of interest in connection with submitted manuscripts. This statement should include appropriate information for EACH author, thereby representing that competing financial interests of all authors have been appropriately disclosed according to the policy of the Journal. It is important that all conflicts of interest, whether they are actual or potential, be disclosed. This information will remain confidential while the article is being reviewed and will not influence the editorial decision. Please see the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals at www.icmje.org/recommendations/browse/roles-and-responsibilities/author-responsibilities-conflicts-of-interest.html for further guidance. If no conflicts exist, the authors must state "No competing financial interests exist."

References

References must be prepared double spaced and **numbered consecutively as they are cited in the text using superscript numbers.** Do not include reference numbers in parentheses or brackets. References appearing for the first time in tables and figures must be numbered in sequence with those cited in the text where the table or figure is mentioned. **Use journal abbreviations as provided by Medline.** List all authors when there are six or fewer. When there are more than six authors, list the first three, followed by et al. Personal communications or unpublished data are not used as references.

Sample references:

- ***Journal article with up to six authors:*** Preyde M, Hatton-Bauer J, unningham C, Panjwani D. Evaluation of an informational pamphlet on distress and erceptions of supportive care for men with prostate cancer. J Men's Health 2012;9:160–167.
- ***Journal article with more than six authors:*** Sandhu NP, Brid Mac Bride M, Dilaveri CA, et al. Male breast cancer. J Mens Health 2012;9:146–153.
- ***Book:*** Klabunde RE. Cardiovascular Physiology Concepts. Phildadelphia, PA: Lippincott Williams & Wilkins, 2011.
- ***Chapter in a book:*** Certo CM, De Turk WE, Cahalin LP. History of Cardiopulmonary Rehabilitation In: De Turk WE, Cahalin LP, editors. Cardiovascular and pulmonary physical therapy, second

edition: an evidence-based approach. New York, NY: McGraw Hill-Medical, 2010. p. 3-15.

• ***Websites:*** *Please follow this structure for website references, including capitalization and punctuation:* List author/organization name (if available). Article title. List website address. Last accessed on (include last date the site was accessed.)

• ***Conference Proceedings****: Please follow this structure for Conference Proceeding references, including capitalization and punctuation:* List all Authors' (or) Editors' names (last name first, followed by first and middle initials). Conference title. Date of conference. Location of conference. City of publisher: Publisher; Year of publication. Complete number of pages in proceedings book.

Correspondence Address

Following the references, provide the name, postal mailing address, and valid email address of the corresponding author. If accepted, this information will be published and made available to the public.

Legends

Supply a single, separate page/file containing all figure legends. Provide a double-spaced legend for each supplied figure. Legends should be numbered consecutively. If applicable, provide explanations in the legend for any abbreviations, arrows, etc. in the figure. If a figure is being reprinted from a copyrighted publication, appropriate credit must be given in the legend.

Tables

Prepare all tables double spaced in one separate page for each in Microsoft Word. Be sure to provide a title for each table. Cite tables in sequence in the text. Explain abbreviations used in the body of the table in footnotes. If a table is being reprinted from a copyrighted publication, appropriate credit must be supplied in a footnote.

Figures

Cite figures consecutively in the manuscript within parentheses: [*Example:* These keratotic areas can be confused with condyloma (Fig. 2A).]

PREPARATION OF FIGURE FILES

• Figures should be numbered in the order cited in the text.

• Figures should not show the name of a patient or a manufacturer.

• Name figure files using only alphanumeric characters. Do not use symbols, dots, or dashes.

• File names should be formatted with first author's last name and the figure number. (Ex: SmithFig1)

• **Do not embed any figures or tables in the main text.**

• Publication of color figures is encouraged, but the cost for color printing must be subsidized by the author(s). Contact the Publisher for an estimate. Please consider these costs when preparing your manuscript for submission.

IMPORTANT

Patient Release Information

If applicable, it is incumbent upon the author(s) to obtain patient release statements of permission to reproduce any identifiable images of patients. The submitting author should provide written confirmation of this critical information. Acceptable forms of consent statements are emails or letters. The Journal does not provide a generic patient release form.

The written consent must contain specific information about the patient's name, age, and if pertinent, conservatorship – as well as stated permission – granting the Journal the rights to publish the photograph within its pages (which should include the name of the Journal and your article title).

INFORMED CONSENT, STUDY ETHICS APPROVAL, AND SUBJECT CONFIDENTIALITY

Patients and Study Participants

All manuscripts must comply with the privacy and confidentiality requirements outlined on the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals website. For more information, visit www.icmje.org/recommendations/browse/roles-and-responsibilities/protection-of-research-participants.html

When articles include reports of studies on human subjects, state in the Methods section that an appropriate institutional review board or ethics committee approved the study. Authors who do not have formal ethics review committees should follow the principles of the Declaration of Helsinki. In the Methods section, state that informed consent was obtained from subjects (specify written or verbal).

The principal author must state that if animals were used experimentally, permission was obtained from the appropriate committee(s), and that the animals were treated humanely and the standards conformed to those of current ethical animal research practices.

In addition, text and photographs should not reveal any identifying information unless it is essential for scientific purposes (in which case, consent should be obtained). Masking the subjects' eyes in photographs is often insufficient to protect their identity.

ETHICAL CONSIDERATIONS IN THE CONDUCT AND REPORTING OF RESEARCH: PROTECTION OF HUMAN SUBJECTS AND ANIMALS IN RESEARCH

Protection of research participants

When reporting experiments on people, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national), or if no formal ethics committee is available, with the Helsinki Declaration as revised in 2008. If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study. When reporting experiments on animals, authors should indicate whether institutional and national standards for the care and use of laboratory animals were followed.

PUBLISHER

The Journal is published by **BMCJ Division, Barind Medical College, Choto Bongram, Namovodra, Boalia, Rajshahi-6207, Mobile: +8801711815827, E-mail: md.anayet_u@yahoo.com**

For speedy relief in Acid Peptic Diseases

acifix®

Rabeprazole 20 mg Tablet

Fixes acid FAST

Faster activation rate due to highest pKa (5.00)[1]

12

times faster onset of action than conventional proton pump inhibitors

Ensures faster relief from Acid peptic diseases

Highest parietal cell concentration[2]

13%

more potent than conventional proton pump inhibitors

Ensures powerful relief from acid peptic diseases

Longest methoxy-propoxy side chain[3]

45%

additional mucus and mucin secretion

Provides more protection against acid and NSAIDs

Non-cytochromic metabolism[1]

Less inter-patient variation in clinical efficacy

Ensures superior efficacy in all patients

Absorption and activation at high pH[1]

Can be taken irrespective of meal

Ensures dosing compliance and adherence to therapy

* *Full prescribing information is available upon request*

References: 1. Annual Review of Genomics and Human Genetics.Sept, 2001. Vol. 2: 9-39 2.www.aciphex.com 3. J. vet. Pharma col. Therap. 27, 455–466, 2004.

BEXIMCO PHARMA here's to Life

BEXIMCO PHARMACEUTICALS LTD.
Dhaka, Bangladesh

Approved by the U.S. FDA
also Certified by

AGES Health Canada

For more information visit: www.beximcopharma.com
PTG- 109714/02-17/55,000 HPL