ISSN-0301-035X(Print)
2219-1607(Online)

Bangladesh Medical Journal

Official Organ of Bangladesh Medical Association

Vol. 46 No. 1 January 2017

BMA Executive Committee for The Year 2017-2018

President	:	Dr. Mustafa Jalal Mohiuddin
Secretary General	:	Dr. Md. Ehteshamul Huq Chowdhury
Vice President, Dhaka City	:	Dr. Kanak Kanti Barua
Vice President, Dhaka Division	:	Dr. Jamal Uddin Khalifa
Vice President, Barisal Division	:	Dr. Md. Kamrul Hassan Salim
Vice President, Chittagong Division	:	Dr. Sheikh Mohammed Shafiul Azam
Vice President, Khulna Division	:	Dr. Sk. Baharul Alam
Vice President, Rajshahi Division	:	Dr. Md. Mustafa Alam (Nannu)
Vice President, Rangpur Division	:	Dr. Md. Delwar Hossain
Vice President, Sylhed Division	:	Dr. Murshed Ahmed Chowdhury
Vice President, Mymensing Division	:	Dr. ANM Fazlul Hoq Pathan
Treasurer	:	Dr. Mohd. Zahid Hussain
Joint Secretary General	:	Dr. Kamrul Hasan (Selim)
Organizing Secretary	:	Dr. Md. Tarique Mehedi (parvez)
Scientific Secretary	:	Dr. Shahryar Nabi (Shakil)
Office Secretary	:	Dr. Md. Sk. Shahid Ullah
Publicity & Public Relation Secretary	:	Dr. Md. Mahbubur Rahman (Babu)
Social Welfare Secretary	:	Dr. Sohel Mahmud
Cultural & Entertainment Secretary	:	Dr. Purabi Rani Debnath
Library & Publication Secretary	:	Dr. Kazi Shafiqul Halim
International Affair Secretary	:	Dr. Md. Abul Hashem Khan

Members

Dr. Mohammed Salim
Dr. Md. Abdul Aziz
Dr. Md. Moniruzzaman Bhuiyan
Dr. Mohammad Mustaq Hossain
Dr. Mohammad Jamal Uddun Chowdhury
Dr. Md. Shafiqur Rahman
Dr. Md. Sharfuddin Ahmed
Dr. Qazi Shaidul Alam
Dr. Md. Jahangir Alam
Dr. Md. Abu Raihan
Dr. M. Nazrul Islam
Dr. Zahrul Huq Sachchu
Dr. Md. Abu Yusuf Fakir
Dr. Ehsanul Kabir Joglul
Dr. Md. Zulfikar Ali (Lenin)
Dr. Uttam Kumar Barua
Dr. Chitta Ranjan Das
Dr. Md. Jabed
Dr. Hasanur Rahman
Dr. Md. Badrul Alam
Dr. Hossain Mohammad Mustafijur Rahman
Dr. Mohammad Harun-Ar-Rashid
Dr. Mahmud Hassan
Dr. M. Iqbal Arslan
Dr. Sayed Atiqul Huq
Dr. Rokeya Sultana
Dr. Bodiuzzaman Bhuyian (Dablu)
Dr. Kamrul Hasan Khan
Dr. Momenul Huq
Dr. Md. Shahidullah Sikder
Dr. Pabitra Kumar Debnath

Information for Authors

Submission of manuscripts

Papers are accepted for publication with an understanding that they are submitted solely to the Bangladesh Medical Journal and are subject to peer review and editorial revision. Statement and opinions expressed in the papers, communications and letters herein are those of author(s) and not necessarily of the editors or publishers. Three hard copies along with a soft copy should be sent to the executive editor of Bangladesh Medical Journal, BMA Bhaban, 15/2, Topkhana Road, Dhaka-1000.

Bangladesh Medical Journal publishes the following:

Full papers, review articles, letters to the editors, debate and opinion papers, editorials, on being a doctor, medical news, medical jokes/poem.

Letters to the editor – letters are invited that discuss, criticize or develop themes on national or international issues related to doctors, medical science or medical profession. Clinical observations, original research presented in a research letter format or case reports or series may be included in letters to the editors. Comments on papers published in Bangladesh Medical Journal are also encouraged. Acceptance will be at the discretion of the editorial board, and editorial changes may be required. Wherever possible, letters from responding authors will be included in the same issue.

Form of full papers submitted for publication:

Full papers should be no more than 4000 words. The onus of preparing a paper in a form suitable for sending to press lies with the author. Authors are advised to consult a current issue in order to make themselves familiar with the journal regarding typographical and other conventions, layout of tables etc. Authors are encouraged to consult the latest guidelines produced by the International Committee of Medical Journal Editors (ICMJE), which contains a lot of useful generic information about preparing scientific papers (http://www.icmje.org/manuscript_a.html)

Manuscripts should be typed on one side of white good quality A4 size paper, with wide margins of at least 2cm and using double space throughout, the preferred font being Garamond size 12. Words at the end of lines should not be hyphenated unless hyphens are to be printed. Page numbering is required. Spelling should generally be that of the Concise Oxford Dictionary, 11th ed. Oxford: Clarendon press. Each component of the manuscript should begin on a new page in the sequence of title page, abstract, text, reference, tables and legends for illustration.

The title page should include the title of the paper, name of the author(s), and name of the departments(s) to which the work should be attributed. The first six authors of a work should be named, followed by "et al." if there are more than six. The unstructured abstract of 150 words should follow the title page. It should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect size and their statistical significance, if possible), and principal conclusion.

The text should be presented in the form of Introduction, Methods, Results & Discussion.

References:

These should be given in the text using the Vancouver system. They should be numbered consecutively in the order in which they first appear in the text using superscript. If a reference is cited more than once the same number should be used each time. References cited only in tables and figures and not in the text should be numbered in sequence from the last number used in the text and in the order of mention of the individual tables and figures in the text. At the end of the paper, on a page(s) separate from the text, references should be listed in numerical order. The journal adheres closely to the Vancouver style of references (see http:// www.nlm. nih.gov/bsd/uniform_ requirements. html, updated 2013).

Sample references are given below –

1. Standard Journal Article

List the first six authors followed by et al:

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7

As an option, if a journal carries continuous pagination throughout a volume (as many medical journals do) the month and issue number may be omitted:

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002; 347:284-7

More than six authors:

Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6

Optional addition of a database's unique identifier for the citation:

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7. PubMed PMID: 12140307

Organization as author:

Diabetes Prevention Program Research Group.

Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5):679-86
No author given:
21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184

Volume with supplement:
Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42 Suppl 2:S93-9.

Issue with supplement:
Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.
Article published electronically ahead of the print version:
Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

2. Books and Other Monographs
Personal author(s):
Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

3. Other Published Material
Newspaper article:
Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12;Sect. A:2 (col. 4).
Dictionary and similar references:
Dorland's illustrated medical dictionary. 29th ed. Philadelphia: W.B. Saunders; 2000. Filamin; p. 675.

4. Unpublished Material
In press or Forthcoming:
Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. Proc Natl Acad Sci U S A. Forthcoming 2002.

5. Journal Article on the Internet
Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.annals.org/ cgi/reprint/ 145/1/62.pdf

Tables
Table should have brief title for each, should be numbered consecutively using Roman numerals and be cited in the text in consecutive order. Internal horizontal and vertical rules should not be used.

Illustration
All drawings should be made with black Indian ink on white paper. Photographs and photomicrographs should be supplied as glossy black and white prints unmoundted. All photographs, graphs and diagrams should be referred to as figures numbered consecutively in the text in Arabic numerals.

Abbreviation
Except for units of measurement, abbreviations are discouraged. Consult scientific style and forma. The CBE manual for authors, editor and publishers (Sixth edition New York: Cambridge University Press, 1994) for lists of standard abbreviation. The first time an abbreviation appears, it should be preceded by the words for which it stands.

Drug names
Generic name should generally be used. When proprietary brands are used in research, include the brand name in parentheses in the methods section.

Permission
Materials taken from other source must be accompanied by a written statement from both author and publishers giving permission to the journal for reproduction. Obtain permission in writing from at least one author of papers that is still in press, unpublished data and personal communications.

The editor of Bangladesh Medical Journal reserves the customary right to style and if necessary shortens the material accepted for publication and to determine the priority and time of publication. Editor assumes that the manuscript submited by the author is based on honest observations. It is not a task of the editor to investigate scientific fraud paper.

Original Article

Effect of Infrared Radiation (IRR) on Patients with Bell's Palsy

*Banu HB[1], Rahman S[2], Hossain S[3],Nessa j[4], Khan EH[5],Mahmood K[6], Rahman DML[7],Ahmed M[8]

Abstract

This prospective study was conducted to determine the effect of Infrared Radiation on the patients presented with Bell's palsy attended at the Department of Physical Medicine and Rehabilitation, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh from January 2012 to June 2012. By dividing in equal two groups 'A' and 'B' (30 patients in each group) a total of sixty (60) patients with Bell's palsy were included in this study according to the selection criteria. Group-A patients were received Infrared Radiation (IRR) including Proprioceptive Neuromuscular Fascilitation (PNF) exercise, Drugs (Prednisolone & Acyclovir) and Counseling for their recovery, where Group- B didn't receive IRR but received rest of management. In Group- A, 25(83.33%) patients recovered completely and among them 12 (40%) patients recovered early (within 2 months). In Group- B, 23(76.67%) patients recovered completely, among them 7 (23.33%) patient recovered early. The difference was statistically significant. The outcome of early recovery is better with the patients treated with combined effect of IRR, PNF exercise and drugs compared with combined effect of PNF, exercise & drugs. The patients who attended with facial nerve paralysis House-Brackmann (HB) Grade IV to VI during initial presentation have reduced chance of full recovery of facial nerve paralysis.

Key Words: Infrared Radiation, Bell's palsy, PNF exercise

Authors:

1. *Dr. Hashina Bilkish Banu, Assistant Professor, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College. Email: rahminrahmin333@gmail.com

2. Professor . Sohely Rahman, Head of Department of Physical Medicine and Rehabilitation, Dhaka Medical College.

3. Dr. Shahadat Hossain, Associate Professor and Head, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College.

4. Dr. Jebunnesa, Associate Professor, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College.

5. Dr. Ehsanul Haque Khan, Associate Professor, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College.

6. Dr. Khurshid Mahmood, Associate Professor and Head, Department of Physical Medicine and Rehabilitation, National Institute of Neuroscience.

7. Dr. D M Lutfur Rahman, Assistant Professor, Department of Radiology and Imaging, Mugda Medical College.

8. Dr. Monjur Ahmed, , Assistant Professor, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College.

* Corresponding Author

INTRODUCTION:

Idiopathic facial nerve palsy or Bell's palsy is a common condition affecting all ages and both sexes.1 This common acute isolated facial palsy is usually due to viral (often Herpes simplex) infection that causes swelling of the nerve in the petrous part of temporal bone and as it traverses the stylomastoid foramen in the skull base.2 Although cause of Bell's palsy is thought to be idiopathic in nature but now-a-days, it is said to be viral in origin.4 There are also some risk factors which may increase the chance of developing Bell's palsy i.e. pregnancy, diabetes, cold or flu, weakened immune system.4,5 In Bell's palsy the nerve become compressed in the facial canal due to swelling and inflammation that is a part of body's reaction to an infectious disease process leading to nerve injury in the form of neuropraxia or axonotmesis.4 Incidence of Bell's palsy is about 20–30/100000/year worldwide.6 In some studies, people with diabetes or hypertension, and pregnant women are more susceptible to peripheral facial paralysis with worse outcome, but this is not seen in all studies.5 The onset of Bell's palsy is acute and about one half of cases attain maximum paralysis in 48 hours and practically all within 3 or 4 days.4 In rare case (1%) it can occur bilaterally - resulting total facial paralysis.7 Most of the Bell's palsy patients recover well. Total recovery is seen in 70–80% of patients overall. With incomplete palsy, the recovery rate is 95–99%, with complete palsy 50–60%.8 Roughly 30% of all patients are left with some sequelae (remaining palsy, hemi-facial spasm, contracture or synkinesis), mainly mild or moderate, but severe in 5% of cases.9 Early treatment (within 3 days after the onset) is necessary for therapy to be effective.4 Steroids have been shown to be effective at

improving recovery by reducing inflammation and antiviral agents may be given to treat viral causes if any.10.11 Antiviral agents are however commonly prescribed due to a theoretical link between Bell's palsy and the Herpes simplex and Varicella zoster virus.11 Vitamins like B1, B6, B12 and Zinc may be given as adjunct therapy which may help with the nerve regeneration.12 Physical therapy is paramount, with the main goal of re-establishing muscle tropism, function and strength to the patients with Bell's palsy.13,14 Infrared radiation is beneficial as it increases circulation and thus reduces oedema. Infrared are those radiation of longer wave length than the red end of the visible spectrum, extending to microwave region, from 770 nm to about 12500 nm.15 The application of infrared produces local vasodilatation of the irradiated part and hence patient get a better circulation which promotes absorption of inflammatory exudates.16 Electrical stimulation therapy (EST) or Transcutaneous electrical nerve stimulation (TENS) may be applied in late case usually after 21 days.17 To increase the strength of facial muscles proprioceptive neuromuscular facilitation exercise and therapeutic massage of facial muscle to reduce oedema is necessary.18 Another treatment used for residual paralysis following Bell's palsy is neuromuscular retraining (NMR). Modalities such as surface EMG, biofeedback and mirror exercises provide sensory information to assist with recovery.19

MATERIALS AND METHODS:

A randomized controlled trial was conducted on 60 patients by random sampling technique with idiopathic facial nerve paralysis (Bell's palsy) who had attended Dhaka Medical College Hospital from January 2012 to June 2012. Patients of both sexes of 13-40 years features of lower motor neuron type of facial palsy with a duration of 1- 30 days was included in this study. Any associated condition e.g. Diabetes mellitus, Hypertension, Pregnancy and Impairment of taste sensation, Hyperacusis patients were excluded from the study. The severity of idiopathic facial nerve paralysis is graded based on House-Brackmann Grading Scale (HBGS). This grading system is formally adopted as the universal standard reporting facial nerve dysfunction after recommendation by Facial Nerve Disorders Committee of the American Academy of Otolaryngology-Head and Neck Surgery in 1985. The factors are analyzed statistically for their role in affecting the outcome of treatment of idiopathic facial nerve paralysis by using a chi-square test of significance.

Grouping of sample:

(i) Group A:

30 patients were received – Infrared Radiation (IRR) 15 minutes for 15 days+ Proprioceptive Neuromuscular Fascilitation (PNF) exercise + Drugs (Prednisolone & Acyclovir) + Counseling.

(ii) Group B:

30 patients were received – Proprioceptive Neuromuscular Fascilitation (PNF) exercise + Drugs (Prednisolone & Acyclovir) + Counseling.

DATA COLLECTION PROCEDURE:

Sixty Cases of Bell's palsy were identified according to inclusion and exclusion criteria. Each subject was allocated randomly into two groups. Group A was given IRR 15 minutes for 15 days + PNF exercise + Drugs (Prednisolone & Acyclovir) + counseling and Group B was given PNF exercise + Drugs (Prednisolone & Acyclovir) + counseling. All the patients were treated with a combination of steroid and acyclovir. The dosage for acyclovir was 2000 mg/day in divided doses for five days and prednisolone was 1mg/kg for first seven days. All the cases were followed every 15 days interval up to first 3 months and the data was recorded. Study parameters were assessed on the basis of House-Brackmann facial grading scale. Baseline clinical data and relevant investigation was done prior to grouping.

Results:

Table- 1: Demographic characteristics among the patients:

Characteristics	Group A	Group B
Age (mean±SD)	29.1±7.07 years	28.6±6.65 years
Duration (mean±SD)	08.53±6.65 days	09.73±5.36 days
Sex		
Male	19 (63.3%)	13 (43.3%)
Female	11 (36.7%)	17 (56.7%)
Marital status		
Married	20 (66.7%)	20 (66.7%)
Unmarried	10 (33.3%)	10 (33.3%)

Occupation		
Business	6 (10.0%)	03 (05%)
House wife	7 (23.3%)	10 (33.3%)
Service	8 (26.7%)	09 (30%)
Student	9 (30.0%)	08 (26.7%)
Side affected of face		
Left	15 (50%)	14 (46.7%)
Right	15(50%)	16 (53.3%)

Table- 1 shows that the mean age in group A was 29.1±7.07 years and group B was 28.6±6.65 years. Mean duration was found 8.53±6.65 and 9.73±5 days; Sixty five and hirty six days in group A and B respectively. Male were found 32 (53.3%) and female were 28 (46.7%) among them 40 (66.7%) were married and 20 (33.3%) unmarried. Occupation as housewife, students and service holders were found 17 (28.3%) patient in each where business holders were 09 (15%). Right side of face affected 31 (51.7%) patients and 29 (48.3%) were affected in left side.

Table- 2: Frequency distribution of improvement score after getting treatment in group A

Scale reading	No. of patients in follow –up						
Grade	Day 1	1st FU	2nd FU	3rd FU	4tFU	5th FU	6thFU
1 -	-	4	4	13	14	25	
II 5	12	10	14	11	14	3	
III 9	3	10	10	4	-	-	
IV 10	12	4	1	1	2	2	
V 5	2	1	1	1	-	-	
VI 1	1	1	-	-	-	-	
Total	30	30	30	30	30	30	30

Table- 2 shows that in group A after three months follow-up all patients were responded to treatment, 25 (83.33%) patients fully recovered and 5 (16.67%) patient's partially recovered. Early recovery (within 2 months) was observed in 13 (43.33%) cases.

Table- 3: Frequency distribution of improvement score after getting treatment in group B

Scale reading	No. of patients in follow –up						
Grade	Day 1	1st FU	2nd FU	3rd FU	4th FU	5th FU	6th FU
I -	-	-	1	7	9	23	
II 7	7	14	15	18	19	6	
III 10	10	10	9	3	1	-	
IV 8	8	4	3	1	-	-	
V 4	4	1	1	1	1	1	
VI 1	1	1	1	-	-	-	
Total	30	30	30	30	30	30	30

Table- 3 shows that in group B after three months follow-up all patients were responded to treatment, 23 (80%) patients fully recovered and 7 (20%) patient's partially recovered. Early recovery (within 2 months) was observed in 7 (20%) cases.

Table- 4: Outcome of treatment after 3 months of follow up by comparison between initial grading with outcome grading in the number of patients.

Initial Grade (NO)	Outcome Grade (No)						
	Grade I	Grade II	Grade III	Grade IV	Grade V	Grade VI	Total
Grade II	12						12
Grade III	19						19
Grade IV	13	5					18
Grade V	4	2	2	1			9
Grade VI				1	1		2
Total48	7	2	2	1			60

Table- 4 shows after three months follow-up, forty eight (80%) patients fully recovered, twelve (20%) patient's partially recovered. In the group that totally recovered, 12 patients were from HB Grade II, 19 patients were from HB Grade III, 13 patients were from HB Grade IV and 4 patients was from HB Grade V. In the group that partially recovered, 5 patients were from HB Grade IV, 5 patients were from HB Grade V and 2 patients were from HB Grade VI.

Table-5: Outcome of treatment after 3 months of follow up by comparison between group A and Group B

Group	After three months follow-up	
	Complete recovery	IIncomplete recovery
A	25(83.33%)	5(16.77%)
B	23(76.67%)	7(23.33%)

Table- 5 shows after three months follow-up, in Group A- 25(83.33%) patients out of 30 shows complete recovery and 5 (16.77%) patient shows incomplete recovery. In Group B, 23(76.67%) patients out of 30 shows complete recovery, among them 7 (23.33%) patient shows incomplete recovery.

DISCUSSION:

Sixty patients were diagnosed to have idiopathic facial nerve paralysis (Bell's palsy) in Dhaka Medical College Hospital from January 2012 to June 2012. The average age at diagnosis was 29 years with a range from 13 years to 40 years. Thirty two (53.33%) patients were male and twenty eight (46.67%) patients were female. Thirty-one (51.67%) patients had right sided facial nerve paralysis and twenty nine (48.33%) patients had left sided facial nerve paralysis. The age and sex distribution in this study were comparable with the study done by Sittel C et al in 2000.20

The patients presented in the Department of Physical Medicine and Rehabilitation, Dhaka Medical College Hospital within 1 to 30 days with the average of eight days from the day they noticed the first symptom.

All the patients diagnosed to have idiopathic facial nerve paralysis (Bell's palsy) were graded based on House-Brackmann Grading Scale during initial presentation21. Twelve (20%) patients had House-Brackmann (HB) Grade II, nineteen (31.67%) patients Grade III, eighteen (30%) patients Grade IV, nine (15%) patients Grade V and two (3.33%) patient Grade VI facial nerve paralysis at the day of first visit.

After three months follow-up, forty eight (80%) patients fully recovered, twelve (20%) patient's partially recovered. In the group that totally recovered, 12 patients were from HB Grade II, 19 patients were from HB Grade III, 13 patients were from HB Grade IV and 4 patients was from HB Grade V. In the group that partially recovered, 5 patients were from HB Grade IV, 5 patients were from HB Grade V and 2 patients were from HB Grade VI.

There was no correlation between the laterality of facial nerve palsy with total recovery of facial nerve palsy. 14 (23.33%) out of 60 patients who presented within three days to the hospital fully recovered while 34 (56.67%) patients presented later then three days had fully recovered from Bell's palsy.

Thirty one (100%) out of 31 patients with HB Grade II and III facial nerve paralysis fully recovered while 17 (62.96%) out of 27 patients with HB Grade IV to VI fully recovered. Patients with HB Grade II and III facial nerve paralysis had a better chance of full recovery compared to patients with

HB Grade IV and VI. Literature review quoted the percentage of full recovery of idiopathic facial nerve paralysis was between 70% to 95% depending on the grading system and treatment given by different caretakers. Peitersen showed 71% of patients regained normal function of facial muscles after an idiopathic paresis meanwhile Hato N et al showed 92.5% of patients had full recovery of facial nerve paralysis in their study8, 22. In our study, 80% of patients with different grading of facial nerve paralysis regained normal function of facial nerve.

In Group A, 25(83.33%) patients out of 30 shows complete recovery and 12 (40%) patient shows early recovery (within 2 months). In Group B, 23(76.67%) patients out of 30 shows complete recovery, among them 7 (23.33%) patient shows early recovery (within 2 months).

The study clearly shows that virtually all patients with clinically incomplete paralysis have excellent recovery of facial function independent of the treatment. The effect of Infrared Radiation on Bell's palsy is questionable. On the other hand, in this study, patients receiving the Infra Red Radiation in addition to PNF exercises and drugs show early recovery (43.33%) compared to patients receiving PNF exercises and drugs (20%).From this study it can be said that Infrared Radiation may have some effect on early recovery of Bell's palsy.

CONCLUSION:

In conclusion, the available evidence from randomized controlled trials is not yet strong enough to become integrated into clinical practice. Further clinical investigation and research with a larger population of patients is necessary before a more specific diagnostic and treatment regimen of this type can be recommended. In conclusion, additional research is needed to conclusively determine when, how, and if IRR is of benefit to patients recovering from Bell's palsy.

LIMITATIONS:

This study has some limitations. Because of small sample size, it was not possible to analyze if the exercises, associated either with or without IRR were effective. Use of photography or video to blind the outcome assessor was not done though it may reduce biasness. Recovery at defined times such as three, six and twelve months of treatment is easier to measure accurately than the time to recovery. Therefore, it requires longer follow-up.

REFERENCES:

1. Nicki R Colledge, Brain R.Walker Stuart H. Neurological disease in Davidson's Principles and Practice of Medicine. Churchill Livingstone. 2010; 21(26):1228.

2. Parveen Kumar, Michael Clark. Cranial nerves in Clinical Medicine. Elavier Saunder 2005; 6 (21):1187.

3. Richard S. Snell. The cranial nerve nuclei and their central connections and distribution. In Clinical Neuroanatomy. Lippincott William and Wilkins. 2010; 7(11)344-345.

4. Dan L.Longo, Anthony S.Fauci, Dennis L. Kasper, Stephen L.Hauser. Trigeminal Neuralgia, Bell's palsy and other cranial nerve disorders in Harrison's Principles of internal Medicine. Mc Graw Hill company.2012; 18(376):3362-3363.

5. Brandenburg NA, Annegers JF. Incidence and risk factors for Bell's palsy in Laredo, Texas: 1974-1982. Neuroepidemiology 1993; 12:313-25.

6. Morris A M, Deeks SL, Hill MD, Balliet R, Shinn JB, Bach-y-Rita, et al. Annualized incidence and spectrum of illness from an outbreak investigation of Bell's palsy. Neuroepidemiology 2002; 21 (5): 255–61.

7. Ahmed A. When is facial paralysis is Bell's palsy? Current diagnosis and treatment. Cleve Clin J Med 2002; 72 (5): 398-401, 405.

8. Peitersen E. Bell's Palsy: The spontaneous course of 2500 peripheral facial nerve palsies of different etiologies. Acta Oto-Laryngologica. Supplementum 2002; 549:4–30.

9. Beurskens CH, Heymans PG. Physiotherapy in patients with facial nerve paresis: description of outcomes. Am J Otolaryngol 2004; 25:394-400.

10. Ramsay MJ, DerSimonian R, Holtel MR, Burgess LP. Corticosteroid treatment for idiopathic facial nerve paralysis: A meta-analysis. Laryngoscope 2000; 110: 335-41.

11. Sullivan FM, Swan IR, Donnan PT, Morrison JM, Smith BH, McKinstry B, et al. Early treatment with prednisolone or acyclovir in Bell's palsy. New England Journal of Medicine 2007; 357(16): 1598–607.

12. Yagi N, Ishikawa Y, Fukazawa T. The effect of steroid and CH3 vitamin B12 on peripheral facial paralysis. Otologia Fukuoaka 1981; 74:1613.

13. Mosforth J, Taverner D. Physiotherapy for Bell's palsy. British Medical Journal 1958; 2(5097):675–7.

14. Brach JS, VanSwearingen JM. Physical therapy for facial paralysis: a tailored treatment approach. Physical Therapy 1999; 79(4): 397–404.

15. Randall L. Braddom. Physical Medicine and Rehabilitation. Saunders Elsvier.2007; 3(21):463.

16. Frederic J.Kottke, Justus F Lehman. Diathermy and superficial heat, laser, and cold therapy in Krusen's Handbook of Physical Medicine and Rehabilitation. W.B Saunders company.1990; 4(13): 285.

17. Quinn R, Cramp F. The efficacy of electrotherapy for Bell's palsy: a systematic review. Phys Ther Rev 2003; 8:151-64.

18. Diels JH, Combs D. Neuromuscular retraining for facial paralysis. Otolaryngol Clin North Am 1997; 30:727-43.

19. Ross B, Nedzelski J, Mclean J. Efficacy of feedback training in longstanding facial paresis. Laryngoscope 1991; 101(7 Pt 1):744–50.

20. Sittel C, Sittel A, Guntinas-Lichius o, Eckel HE, Stennert E. Bell's palsy: A 10-year experience with antiphlogistic-rheologic infusion therapy. Am J Otol 2000;21:425-32.

21. House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg 1985; 93(2):146–7.

22. Hato N,Yamada H, Kohno H, Matsumoto S, Honda N, Gyo k, et al. Valacyclovir and prednisolone treatment for Bell's palsy: a multicenter, randomized, placebo-controlled study. Otol Neurotol. 2007 Apr. 28(3):408-13.

Original Article

Carbetocin and Oxytocin in the Active Management of Third Stage of Labor after Vaginal Birth of Baby

*Barua HR [1], Barua RR [2], Barua S[3], Barua AK [4], Begum K[5]

Abstract

Postpartum hemorrhage (PPH) is one of the major contributors to maternal mortality and morbidity worldwide. Active management of the third stage of labor has been proven to be effective in the prevention of PPH. Carbetocin; a long-acting Oxytocin agonist appears to be a promising agent for the prevention of PPH. In this study Carbetocin is used for the active management of third stage of labor to prevent PPH. Two hundred pregnant women from July 2015 to December 2015 at Rangamati Medical College Hospital, Rangamati, Bangladesh were included in this study. The patients were divided into two groups: Group- 1 (100 women) were received 100µg Carbetocin intravenously and group- 2 (100 women) received 10 IU Oxytocin intramuscularly and both doses were single. These uterotonics were injected at anterior shoulder after the delivery of the baby. Significant difference was observed between the Carbetocin and Oxytocin receiving groups regarding amount of blood loss (335.70 ± 117.71 versus 375.12 ± 145.30), PPH (3 % versus 12%), need of use of other uterotonics (18% versus 30%) and the difference in hemoglobin percent before and after delivery (0.58 ± 0.34 versus 0.97± 0.52). All these parameters were lower in Carbetocin group except hemoglobin level which is higher in group- 2 during 24 hours after delivery. Moreover, blood transfusion was not indicated in group- 1. In conclusion, Carbetocin is superior to Oxytocin in prevention of post partum hemorrhage at the third stage of vaginal delivery with minimal homodynamic changes and side effects.

Key words: Carbetocin, Oxytocin, Active management of third stage of labor, Postpartum Hemorrhage.

1. *Dr. Hena Rani Barua, Senior Consultant, Obstetric and Gynecology, Rangamati Medical College Hospital, Rangamati, Bangladesh. Email: baruarita @yahoo.com
2. Dr. Rita Rani Barua, Associate Professor, Pathology, Dr. Sirajul Islam Medical College, Dhaka, Bangladesh.
3. Dr. Sushanta Barua, Indoor Medical Officer, Neuromedicine, Dhaka Medical College, Dhaka, Bangladesh.
4. Dr. Ajoy Kishore Barua, Medical Officer, Bandarban Sadar Hospital, Bandarban Hill District, Bangladesh.
5. Dr. Kohinoor Begum, Professor, Obstetric and Gynecology, Popular Medical College, Dhaka, Bangladesh.

* Corresponding Author.

INTRODUCTION:

Post-partum hemorrhage (PPH) is the leading cause of maternal death worldwide; with an estimated mortality rate of 1,40,000 per year or one maternal death in every 4 minutes[1]. PPH occurs in 5% of all deliveries and is responsible for 28% of maternal mortality in Bangladesh[2-3]. The majority of these deaths occur within 4 hours of delivery which indicates that these are a consequence of the third stage of labour4-5. Fatal PPH results in several morbidities like severe iron deficiency anemia, Sheehan's syndrome, coagulopathy, poor lactation and organ damage with associated hypotension, shock and risk of hysterectomy6.

PPH is defined as blood loss more than 500 ml after vaginal delivery and more than 1000 ml after caesarean section that occurs within the first 24 hours7. Blood loss 500 -1000 ml is called minor PPH and >1000ml is major PPH. Many patients known to be high risk for developing PPH such as two or more caesarean sections, multiple pregnancy, placenta praevia, abruptio placenta, fetal macrosomia, history of PPH, anemia, age > 40 years , uterine myoma, polyhydromnios8.

Uterine atony is the major cause of hemorrhage at the third stage of labour and at the early postpartum period. Therefore; active management is more effective than expectant management of the third stage of labor. Third stage of labor is that period following the delivery of baby till placental delivery9-10.

PPH can be prevented by administration of uterotonic drugs. Intramuscular Oxytocin (10 IU) usually prevent PPH in low risk vaginal and caesarean delivery or intravenous infusion (20-40 IU in 1000ml 5% Dextrose, 150ml/h) having 3 -5 minutes half life 11-12. Carbetocin is an alternate long acting synthetic uterotonic with a half life of 40 minutes and uterine contractions occur in less than 2 minutes after intravenous administration of optimal dosage of 100 µg 13. Carbetocin is more effective to control maternal mortality rate preventing PPH. However, a little is known about the effect and advantage of the use of Carbetocin in the management of third stage of vaginal delivery. Therefore, a case- control study using carbetocin and oxytocin was conducted at Rangamati Medical College Hospital to prevent PPH.

METHODS:

This study was conducted on 200 pregnant women attending the Obstetrics and Gynecology department, Rangamati Medical College Hospital from July 2015 to December 2015. The work was approved by local ethical committee and informed consent was taken from the patients regarding its importance, expected value and outcome. All participants were 37 - 40 weeks of gestation with at least two risk factors for developing atonic PPH. Risk factors included were primi gravida > 36 years, history of prolonged labor > 12 hours, multiple pregnancy, PPH, BMI >35 and estimated fetal weight more than 4 kg. Participants with pre-eclampsia, placenta praevia, cardiac, renal, liver diseases, bleeding disorders, epilepsy and known hypersensitivity to carbetocin or oxytocin were excluded from the study group.

All the patients were subjected to full history taking, general, per abdominal and obstetric examination. Ultrasound scan, complete blood count, liver function test and coagulation profile were also done. Firstly we recruited one hundred women of group1 who received a single dose of 100µg I/V carbetocin (case group I) followed by another one hundred women of group 2 who received a single dose of 10 IU I/M oxytocin. Both drugs were administered following delivery of the anterior shoulder of the baby in singleton pregnancy and delivery of the anterior shoulder of second twin in multiple pregnancies.

All the participants were follow- up upto 24 hrs. The uterine tone and amount of blood loss were noted and the need for further uterotonics was checked for two minutes after giving the drugs. Blood loss was estimated by usual method of by counting the number of pads. Blood loss 500 -1000 ml was considered as minor PPH and blood loss >1000ml was considered as major PPH. Hemoglobin level was assessed 24 hrs after delivery.

Systolic and diastolic blood pressure was measured immediately after delivery and 30 and 60 minutes after delivery of the baby. Possible side effects like nausea, vomiting, flushing, tachycardia, shivering, dizziness, headache, palpitation, dyspnea and itching were recorded.

Data was statistically analyzed and described in terms of mean ± standard deviation (±SD), frequencies and in percentage when appropriate. Comparison of numerical variables between the study groups was done using independent t-test. For comparing categorical data, Chi-square (χ^2) test was performed. P-values less than 0.05 were considered statistically significant. All statistical calculations were done using complete program SPSS.

RESULTS:

Table- I. Distribution of population by the characteristics of the patients

	Carbetocin (n =100)	Oxytocin (n = 100)	P- value
Age (years)	30.80 ± 6.52	30.78 ± 6.42	
BMI (kg/m²)	27.62 ± 4.52	26.20 ± 4.52	
Gestational age (weeks)	39.42 ± 1.25	39.30 ± 1.35	
Gravidity	2.48 ± 1.11	2.35 ± 1.04	
Parity	2.56 ± 1.15	2.48 ± 1.25	
Duration of 1st stage of labor (hrs)	12.40 ± 3.60	12.45 ± 3.45	NS
Duration 2nd stage of labor (min)	81.78 ± 20.25	82.65 ± 18.62	
Duration of 3rd stage of labor (min)	4.55 ± 2.25	4.53 ± 2.08	
(min)			

* Data are presented as mean ± SD. NS; Not significant

Two hundred pregnant women were classified into two groups: group 1 included one hundred patients who received carbetocin and group 2 included another one hundred patients who received oxytocin. Baseline characteristics of the patients were summarized in Table 1. There was no significant difference between the groups in age, body mass index, gravity, parity and gestational age. Disparity was not observed between the groups regarding the duration of 1st, 2nd and 3rd stages of labor (Table- I).

Table- II. Distribution of population by the amount of bleeding and usage of other uterotonics

	Carbetocin (n =100)	Oxytocin (n = 100)	P- value
Amount of bleeding (ml)	335.70 ± 117.71	375.12 ± 145.30	
PPH (>500 - < 1000 ml)	3%	12%	
PPH (>1000 ml)	0	1%	0.032
Use of other uterotonics	18%	30%	
Needs for blood transfusion	0	2	

* Data are presented as mean ± SD. * Data are presented as number and percent.

Blood loss, PPH, use of other uterotonics, hemoglobin levels before and 24 hrs after delivery were significantly lower in the carbetocin group (Group 1) than oxytocin group (Group 2). There was significant difference between the two groups regarding occurrence of major PPH and the need for blood transfusion (Table II).

Table III. Distribution of population by side effects of drugs

Side effects of drugs	Carbetocin (n =100)	Oxytocin (n = 100)
Dizziness	1(1%)	0
Shivering	0	1(1%)
Flushing	1(1%)	2 (2%)
Nausea	3(3%)	2 (2%)
Vomiting	4 (4%)	2 (2%)
Tachycardia (> 100 b/min)	8 (8%)	2 (2%)
Palpitation	2(2%)	3(3%)
Dyspnea	2(2%)	3(3%)
No side effects	79(79%)	85(85%)

* Data are presented as number and percent.

On carbetocin group there was no major PPH and no need of blood transfusion. Nausea, vomiting, palpitation, shivering, flushing, dizziness, headache, dyspnea and itching were found in both groups except tachycardia which was more in group 2 (Table III)

DISCUSSION:

The result of this study has shown that carbetocin is superior to oxytocin for the prevention of post partum hemorrhage by active management of third stage of labor. This fact can be explained by the known longer half-life of carbetocin compared to oxytocin resulting in a more uterine response in terms of frequency and amplitude of uterine contractions.

In this study, it is found that the amount of blood loss after delivery is significantly lower in women who received carbetocin than those who received oxytocin. We also found that need for additional uterotonics and blood transfusion were lower among carbetocin group. Hemoglobin level before and after delivery was also less in carbetocin group.

Boucher et al.14 have randomized 160 women undergoing vaginal delivery with at least one risk factor for PPH to receive either carbetocin 100 µg I/M or oxytocin 10 IU I/V infusion over two hours. The need for uterine massage and other uterotonics were significantly lower in the carbetocin group, these results are in agreement with our study. But they find no significant difference in the amount of blood loss or the difference in hemoglobin level before and after delivery between the groups. The difference between these results and our study can be explained by the difference in the route and dose of oxytocin.

Attilakos et al;15 has randomized 377 caesarean section patients received either IV carbetocin 100 µg or IV oxytocin 5 IU after the delivery of the baby. The carbetocin group needed significantly less additional uterotonics which concordant with our findings. However; they found no significant difference regarding blood loss or hemoglobin level before and after operation between the two groups.

This disagrees with our results and may be in the difference in the studied population. We studied women with risk factors for atonic PPH undergoing vaginal delivery, but Attilakos et al. studied on caesarean sections with or without risk factor for PPH. Leung et al ;16 compares the efficacy and safety of intramuscular carbetocin with IM syntometrine in preventing primary PPH in a prospective double-blinded, randomized controlled trail. They find IM carbetocin is as effective as IM syntometrine to prevent primary PPH following vaginal delivery. It is less likely to induce hypertension and other side effects. In this study there is no significant difference between the two groups regarding side effects except tachycardia. These results are also supported by other researchers11, 15.

In conclusion carbetocin is a better uterotonic than oxytocin to maintain adequate uterine tone with minimal homodynamic changes and side effects. Therefore, carbetocin should be routinely used in active management of third stage of labor during vaginal delivery to prevent post partum hemorrhage.

REFERENCES:

1. Abuzahr C, Global burden of maternal death and disability. Br Med Bult 2003; 67:1-11.

2. Reynders FC, Senten L. Tjalma W, Jacquemyn Y. Postpartum hemorrhage: Practical approach to a life threatening complication. Clin Exp Obstet 2006; 33:81-4.

3. Subtil D, Somme A, Ardiet E, Mossers D. Postpartum hemorrhage frequency, consequences in terms of health status and risk factor before delivery. J Gynecol Obstet Biol Reprod 2004; 33: 9-16.

4. Ramanathan G, Arulkumaran S, Postpartum hemorrhage. Curr Obstet Gynecol 2006; 16:6-13.

5. Kane TT, el- kaldy AA, Saleh S, Hage M, Stanback J, Potter L. Maternal mortility in Giza, Egypt: Magnitude, causes and prevention. Stud Fam Plann 1992; 23:45-57.

6. Larciprete G, Montaganoli C, Frigo M, Panetta V, Todde C, Zuppani B, et al. Carbetocin versus oxytocin in casearean section with high risk of postpartum hemorrhage. J Prenat Med 2013; 7:12-18.

7. World Health Organization. The world health report 2005: make every mother and child count, Geneva 2005.

8. Royal college of Obstetrician and Gynecologist. Prevention and management of postpartum hemorrhage, Green top guidelines no. 52 minor revisions November 2009 and April 2011.

9. Knight M, Callaghan WM, Berg C, Alexanders, Bourier-Colle MH, Ford JB. Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the Int. postpartum hemorrhage

collaborative group. BMC pregnancy child birth 2009; 9-55.

10. Su LL, Chong YS, Samuel M. Oxytocin agonists for preventing postpartum hemorrhage. Cochrane Database Syst Rev 2012; 15: CD005457.

11. Moertl MG, Friedrich S, Kraschl J. Wadsac KC, Lang U, Schlemboch D. Hemodynamic effects of carbetocin and oxytocin given as intravenous bolus on women undergoing caesarean delivery a randomized trial. BJOG 2011; 118:1349-56.

12. Engstrom T, Barth T, Melin P, Vilhardt H. Oxytocin receptor binding and uterotonic actuality of carbetocin and its metabolites following enzymatic degradation. Eur J Pharmacol 1998; 355:203-10.

13. Sweeney G. Holbrook AM, Levine M, Yip M, Alfredson K, Cappi S. Pharmacokinetics of carbetocin, along oxytocin analogue, in non-pregnant women. Curr Ther Res 1990; 47:528-40.

14. Boucher M, Nimrod CA, Tawagi GF, Meeker TA, Rennicks White RE, Varin J. Comparison of carbetocin and oxytocin for the prevention of postpartum hemorrhage following vaginal delivery: a double-blind randomized trail. J Obstet Gynaecol 2004; 26: 481-88.

15. Attilakos G, Psaroudakis D, Ash J, Bouchanan R, Winter C, Donald F, Hunt LP, Draycott T. Carbetocin versus oxytocin for the prevention of post partum hemorrhage following caesarean section; the result of a double-blind randomized trial . BJOG 2010; 117: 929-36.

16. Leung SW, NgPS, Wong WY, Cheung TH. A randomized trial of carbetocin versus syntometrene in the management of the third stage of labor. BJOG 2006; 113:1459-64.

Original Article

Protective Effect of Terminalia Chebula Extract on Serum Total Protein against Paracetamol Induced Liver Damage in Wister Albino Rats

*Yeasmin T[1],Akhter QS[2], Imtiaz M[3], Noor N[4], Khanam A[5],

Abstract

Terminalia Chebula extract is used for regeneration of hepatic cells and protection of liver against damage due to its active component. This study aims to observe the protective effect of Terminalia Chebula against Paracetamol induced change of serum total protein level in Wister Albino rats. The study was carried out in the Department of Physiology, Dhaka Medical College (DMC) during January 2013 to December 2013. A total number of 44 rats, age ranging from 90 to 120 days, weight between 150 to 200 gm (initial body weight) were selected for the study. After acclimatization for 14 days, they were divided into control groups and experimental groups. Before sacrifice, final body weights of all the rats were measured. Then all the rats were sacrificed on 22nd day and then blood samples were collected. For assessment of liver function, serum total protein level was done by using standard laboratory kits. The mean serum total protein level was significantly (p<0.001) lower in paracetamol treated control group in comparison to those of baseline control group. Serum total protein level of all experimental groups were significantly (P<0.001) higher than Paracetamol treated control group. From the results of this study, it may be concluded that Terminalia Chebula may have some protective effect against Paracetamol induced liver damage in rats.

Keywords: Terminalia chebula, Hepatoprotective, Paracetamol, Protein.

1, *Tania Yeasmin, Assistant Professor, Department of Physiology, TMSS Medical College, Bogra. Email: bappy04@hotmail.com

2, kazi Shamima Akhter, professor & Head, Department of Physiology, Dhaka Medical College, Dhaka.

3, Masud Imtiaz, Associate professor, Department of Physiology, Khulna City Medical College, Khulna.

* Corresponding Author

INTRODUCTION:

Liver is an important organ which plays a vital role in regulating homeostasis within the body by various functions.1 Liver injury or diseases caused by virus, toxic chemicals, environmental pollutants, certain drugs that has been increase for the past few decades.2 Liver diseases are most serious health problem worldwide, with high endemicity in developing countries. About 20,000 deaths occur every year due to liver diseases.3 According to world health organization (WHO) more than 80% of the world's populations rely on modern medicines for their primary health care needs4.The modern or synthetic drugs used in the treatment of liver diseases have been reported to cause serious adverse side effects. It has been reported that alternative natural sources of medicinal plants have less or no side effect.5

Paracetamol (Acetaminophen) is an analgesic and antipyretic drug which is widely used to cure headache, fever, and other pains and is readily available without prescription. Increasing use and easy availability of paracetamol have led to misuse of the drug and may cause a number of serious clinical problems.6 Paracetamol is hepatotoxic when used in excessive doses or when used in therapeutic doses for a prolonged period.7, 8 In medicinal practices, reliable liver protective drugs are not available but herbal plants may play an important role in management of liver disorders. 9

Terminalia chebula has been used in herbal medicine throughout the ancient times in Bangladesh because it is cultivated in many places of Bangladesh. Locally it is called as Haritaki (Combretaceae family). It is also called the king of medicine because it has been widely used in ayurveda, unani, siddha and homeopathy.10 It contains tannin, chebulic acid, glycosides, sugar, triterpenoids, steroids and flavonoids. Due to some active components of terminalia chebula has high medicinal value. Many studies have been reported for biological properties and protective effects of Terminalia chebula on different diseases.11 Different researchers from different countries have been studied the hepatoprotective effects of Terminalia chebula.12 Recently, some investigators observed that Terminalia chebula significantly increased the paracetamol induced elevation of serum total protein in rats.13,14 From the medicinal values, the present study has been designed to investigate the

protective effect of Terminalia chebula on paracetamol induced liver damage in Wister albino rats.

METHODS:

This experimental study was conducted from January'13 to December'13 in the Department of Physiology, Dhaka medical college (DMC), Dhaka. A total number of 44 apparently healthy Wister albino rats, weight between 150 to 200 grams; age ranging from 90 to 120 days was used. The rats were purchased from the animal house of Department of Pharmacy, Jahangir Nagar University, Shavar, Dhaka. The protocol of this study was approved by Institutional Ethics Committee (IEC) of Dhaka Medical College . The rats were kept in metallic case in the animal house of Institute of Nutrition and Food Science, University of Dhaka (DU). Prior conducting the study, rats were kept in a standard laboratory condition on a 12/12 hour light/dark cycle for 14 days acclimatization. All the rats received basal diet for 21 days. Total study period was 35 consecutive days and the work was done in the Institute of Nutrition and Food Science, DU. After selection, all the rats were acclimatized for 14 days. Then the rats were studied for 21 consecutive days. After acclimatization for 14 days, rats were divided into control groups (n=22) and experimental groups (n=22). Control groups again subdivided into BC (base line control group, n=11) and PC (paracetamol treated control group, n=11). Experimental groups were again subdivided in to TCP-PCT (Terminalia chebula pretreated and paracetamol treated group, n=11) and PCP-TCT (paracetamol pretreated and Terminalia chebula treated group, n=11). After grouping, initial body weight of all the rats were measured on 1st day. All groups of rats received basal diet for 21 consecutive days. In addition to basal diet on 21st day, BC received propylene glycol (2ml/kg body weight, orally) and PC received single dose of paracetamol suspension (750mg/kg body weight, orally). In experimental groups, TCP-PCT received Terminalia chebula extract (200 mg / kg body weight, orally) for 21 consecutive days and paracetamol suspension (750mg/kg body weight, orally) on 21st day. Moreover, PCP-TCT received paracetamol suspension (750mg/kg body weight, orally) on the 1st day and Terminalia chebula extract (200 mg/kg body weight orally) for 21 consecutive days.

Powder form paracetamol was purchased from Square pharmaceuticals and 1 gm of paracetamol was dissolved in 9 ml of propylene glycol and form paracetamol suspension. Again, 300 gm Terminalia chebula mixed with 800 ml distilled water for 3 days and form Terminalia chebula extract which stored in freeze at around 40C and was fed to the experimental rats. Before sacrifice, final body weights of all the rats were measured. On the 22nd day, all the rats were anaesthetized with the help of chloroform (30%) and then sacrificed. The blood samples (approximately 5 ml) were collected from the heart direct puncturing by using sterile disposable syringes and taken in separate clean and dry test tubes with proper identification numbers. Then blood was centrifuged at a rate of 4000 rpm for 5 minutes. After that the supernatant serum was separated from the blood, collected in a labeled eppendorf and preserved in a refrigerator at -20^{o}C until analytical measurement of serum for total protein in Department of Pathology, Dhaka Medical College. Data was reported in Mean and SD (Standard deviation). Statistical analysis was done by One-way ANOVA test and Bonferroni test.

RESULTS:

The initial, final and percent(%) changes of body weight of all rats were almost similar and showed no statistically significant difference between BC vs PC, PC vs TCP-PCT, TCP-PCT vs PCP-TCT (Table I).

Table I: Initial, final and Percent (%) change of body weight in different groups of rats (n=44)

Parameters	BC (n=11)	PC (n=11)	TCP-PCT (n=11)	PCP-TCT (n=11)
Initial body wt(g) Day-1	158.18±6.03	156.45±6.35	161.18 ±14.37	157.91 ±9.85
Final body wt(g) Day-22	163.55±5.96	160.82±8.52	164.45 ±14.69	160.82 ±8.52
% change from final (F) weight to initial (I) weight [F-I/I×100]	3.39 ±1.26	2.80±1.8	2.02±1.25	1.84±2.21

Table- I shows the values are Means ± SD. Statistical analysis was done by one way ANOVA test. n = Number of rats. BC = Baseline control group PC = Paracetamol treated control group TCP-PCT =Terminalia chebula pretreated and paracetamol treated group PCP-TCT = Paracetamol pretreated and Terminalia chebula treated group.

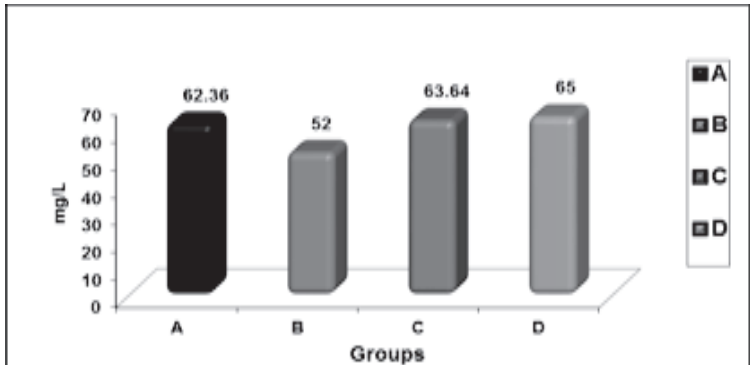
Table I: Initial, final and Percent (%) change of body weight in different groups of rats (n=44)

Parameters	BC (n=11)	PC (n=11)	TCP-PCT (n=11)	PCP-TCT (n=11)
Total protein(mg/L)	62.36±3.44	52.00±2.68***	63.64±6.98¥¥¥	65.00±7.63¶¶¶

Table- II shows the mean serum total protein level was significantly (p<0.001) lower in PC in comparison to that of BC. But this level was significantly (p<0.001) higher in TCP-PCT and PCP-TCT in comparison to that of PC. Again there was no significant difference in this level between TCP-PCT and PCP-TCT Table II.

Values are Means ± SD. Statistical analysis was done by one way ANOVA test and then Bonferroni test. Serum bilirubin (***p<0.001 PC vs BC) (¥¥¥p<0.001 TCP-PCT vs PC) (¶¶¶p<0.001 PCP-TCT vs PC). n = Number of rats BC= Baseline control group PC= Paracetamol treated control group TCP-PCT= Terminalia chebula pretreated and paracetamol treated group PCP-TCT= Paracetamol pretreated and Terminalia chebula treated group.

Figure 1: Mean serum total protein in different groups of rats (n=44)



n = Number of rats
Control group: Without Terminalia chebula- Group A: BC; Group B: PC
Experimental group: With Terminalia chebula- Group C: TCP-PCT; Group D: PCP-TCT

DISCUSSION:

In the present study, serum total protein level was significantly lower in PC in comparison to that of BC, TCP-PCT and PCP-TCT which is comparable to others15, 16, 17 But no significant change was observed by some researchers18. Different studies reported the toxic effect of high dose of paracetamol on hepatocytes and liver functions. It has been suggested that high doses of paracetamol inhibit the synthesis of RNA and protein which finally leads to necrosis of liver cell19.

It has also been suggested that metabolism of excess paracetamol in liver by conjugation with sulphate and glucuronide causes formation of toxic metabolites such as N-acetyl-p-benzoquineimine (NAPQI). This NAPQI imposes oxidative stress by increasing the formation of reactive oxygen species which causes lipid peroxidation and depletion of antioxidant enzymes. This increased oxidative stress leads to destruction of structural and functional organization of cell membrane causing liver cell damage 20. In this study decreased level of serum total protein is suggestive of liver cell damage.

Studies on medicinal plants demonstrated that Terminalia chebula contains some active compounds such as vitamin C, ellagic acid, gallic acid, chebulic acid, bellericanin, β-sitosterol and flavanoids which increase the activities of antioxidant enzymes which in turn obviously protect liver for oxidative damage21. Again Desai et al. noted that Terminalia chebula stimulate protein synthesis, which accelerates the regeneration and production of liver cells thereby contributes hepatoprotective activity11. In this present study, increase level of serum total protein level in TCP-PCT and PCP-TCT rats suggest that supplementation of Terminalia chebula extract provide protection against paracetamol induced liver injury due to its higher content of active component.

CONCLUSION:

From this study, it can be concluded that Terminalia chebula may have some protective effect with increase serum total protein level against paracetamol induced liver damage. Therefore, increasing serum total protein level due to active components of Terminalia chebula.

REFERENCES:

1. Ahsan MR, Islam KM, Bulbul IJ. Hepatoprotective activity of methanol extract of some medicinal plants against carbon tetrachloride-induced hepatotoxicity in rats. Eur J Sci Res. 2009;37(2):302-10.

2. Naglaa H, Hassanen M, Mona H, Ahmed M. Protective effect of fish oil and virgin olive oil on Diethylnitrosamine Toxicity in rats. Int J Nutr food Sci. 2015;4(3):388-96.

3. Kshirsagar AD, Mohite R, Aggrawal AS, Suralkar UR. Hepatoprotective medicinal plants of ayurveda. Asian J Pharm Clin Res. 2011;4(3):1-8.

4. Qadrie ZL, Rajkapoor B, Kavimani S. Hepatoprotective medicinal herbs and animal models for their screening. IJPSR. 2015;6(12):5006-28.

5. Mohammed A, Abubakar SA. Potency of aqueous extract of Azadirachta indica a. juss against lipid peroxidation and liver damage in rats. Int J Mod Biochemistry. 2012;1(1):27-35.

6. Grieco A, Miele L, ForgioneA, Ragazzoni E, Vecchio FM, Gasbarrini G. Mild hepatitis at recommended doses of acetaminophen in patients with evidence of constitutionally enhanced cytochrome P450 system activity. J Clin Pharm Ther. 2008;33:315-20.

7. Rumack BH, Peterson RC, Koch GG, Amara IA. Acetaminophen overdose: 662 cases with evaluation of oral acetylcysteine treatment. Arch Intern Med. 1981;141(3):380-5.

8. Smilstein MJ, Knapp GL, Kulig RW, Rumack BH. Efficacy of oral N-acetylcysteine in the treatment of acetaminophen overdose. N Engl J Med. 1988;319:1557-62.

9. Kumar V, Sharma A, Machawal L, Khan AA. Beneficial roll of herbal hepatoprotectants: A novel approach to prevent hepatotoxicity due to antituberculosis treatment. J Biomed Pharm Res. 2013;2(3):181-s93.

10. Mahesh R, Bhuvana S, Begum VM. Effect of Terminalia chebula aqueous extract on oxidative stress and antioxidant status in the liver and kidney of young and aged rats. Cell Biochem Funct. 2009;27:358-63.

11. Gupta PC. Biological and pharmacological properties of Terminalia chebula Retz (Haritaki). Int J Pharm Pharm Sci. 2012;4:62-8.

12. Desai S, Gite M, Ahmed A, More Y, Gavitre B, Gawali V. Hepatoprotective and antioxidant activity evaluation of PHF08 on carbon tetrachloride induced hepatotoxicity. Der Pharmacia Lett. 2010;2(1):475-81.

13. Sivachandran S, Hariharan P. Hepatoprotective effect of Terminalia chebula on gentamicine induced toxicity in rats. Inter J Vet Sci. 2012;1(1):31-3.

14. Sharma A, Rathore HS. Prevention of acetaminophen induced hepatorenal toxicity in mice with fruits of Terminalia chebula (Myrobalan). Thai J Toxicol. 2010;25(2):144-53.

15. Sandhyak D, Bhaskhar BG, Mahesh GS, Ahmed A. Evaluation of hepatoprotective activity of a polyherbal formulation (PHF-A) by using galactosamine-induced hepatotoxicity in rats. JPBMS. 2010;1(2):1-5.

16. Doorika P, Ananthi T. Antioxidant and hepatoprotective properties of Terminalia arjuna bark on isoniazid induced toxicity in Albino rats. Asian J Pharm Tech. 2012;2(1):15-8.

17. Elamparithi D, Boominathan M. Comparative study on antimicrobial, hepatoprotective activity of Terminalia chebula different fraction. Int Stand Serial Number. 2012;2(4):16-23.

18. Panunto W, Jaijoy K, Lerdvuthisopon N, Lertprasertsuke N, Jiruntanat N, Soonthornchareonnon N, Sireeratawong S. Acute and chronic toxicity studies of the water extract from dried fruits Terminalia chebula Rezt. in rats. Int J Appl Res Natural Prod. 2011;3(4):36-43.

19. Kon K, Kim JS, Jaeschke H, Lemasters JJ. Mitochondrial permeability transition in acetaminophen-induced necrosis and apoptosis of cultured mouse hepatocytes.J Hepatol. 2004;40:1170-9.

20. Hinson JA, Bucci AR, Irwin LK, Michael SL and Mayeux PR. Effect of inhibitors of nitric oxide synthase on acetaminophen induced hepatotoxicity in mice. Nitric Oxide. 2002;6:160-7.

21. Rasool MK, Sabina EP, Lavanya K, Nithya P. Therapeutic effect of Indian ayurvedic herbal formulation Triphala on acetaminophen-induced hepatotoxicity in mice. J Pharmacol Toxicol. 2007;2(8):725-31.

Original Article

Profile of Patients Attending at the Department of Physical Medicine and Rehabilitation in a Specialized Hospital of Bangladesh

*Chakraborty PK [1], Islam MJ [2], Hossain MS [3], Ahmed M [4], Amin MR [5], Jamal D [6].

Abstract

Physician's documentation has become the critical component in rehabilitation of patients. The scope of Physical Medicine and Rehabilitation (PMR) encompasses more than a single organ system. Attention to the whole person is paramount. The aim of the study was to appraise the disease pattern and demographic information of the patients received outpatient rehabilitation services at the department of PMR, National Institution of Neuroscience and Hospital, Dhaka, Bangladesh. This is a retrospective study carried out for the period of two years July 2013 to June 2015. Total number of patients was 29678, among them 57.02% were male and 42.98% were female. Maximum patients (26.15%) were in age group 41-50 years and in housewife (37.76%) in occupation, where majority (56.33%) of them came from Dhaka city. Regarding disease pattern, 56.32% was neurological, 33.46% was musculoskeletal and 7.25% of patients were suffering from rheumatologic problem. Among leading diseases, largest disease group was stroke (20.02%), 10.48% was non-specific low back pain, 9.92% was Bell's palsy, 5.35% was lumbar spondylosis, 5.13% was carpal tunnel syndrome, 4.11% was prolapsed lumber inter-vertebral disk (PLID), 3.72% was cerebral palsy. Knowledge about the existing disease pattern and health seeking behavior is essential to provide need based health care delivery to any population.

Keywords: Profile, Diseases, National Institution of Neuroscience and Hospital, PMR.

1 *Prasanta Kumar Chakraborty, Assistant Professor, Department of Physical Medicine & Rehabilitation, National Institute of Cancer Research and Hospital, Dhaka, Bangladesh ,

E-mail: pkcborty@gmail.com

2 Md. Shahadat Hossain ,Md. Jahidul Islam ,Associate Professor, Department of Physical Medicine and Rehabilitation, Dhaka Medical College, Dhaka, Bangladesh.

3 Md. Shahadat Hossain ,Vice Principal and Associate Professor, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh.

4 Monzur Ahmed ,Assistant Professor, Department of Physical Medicine and Rehabilitation, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh.

5 Md. Ruhul Amin Assistant Professor, Department of Physical Medicine & Rehabilitation, National Institute of Diseases of the chest and Hospital, Dhaka, Bangladesh.

6 Dilir Jamal, Registrar, Department of Physical Medicine & Rehabilitation, National Institute of Traumatology and Orthopaedic Rehabilitation, Dhaka, Bangladesh.

*Corresponding Author

INTRODUCTION:

Physical medicine and Rehabilitation (PMR) focuses on the restoration of function and the subsequent reintegration of the patient into the community. As with other branches of medicine, the cornerstone of PMR is a meticulous and thorough clinical evaluation of the patient. Consequently, the evaluation must assess not only the disease but also the way the disease affects and is affected by the person's family and social environment, vocational responsibilities and economic state, avocational interests, hopes, and dreams. Traditionally, the in-patient rehabilitation unit or the outpatient physiatry clinic has been the optimal setting for a comprehensive evaluation by the entire rehabilitation team.1 Determining the degree to which a person's life is impacted by a medical condition is complex and in part perplexing. Physicians, and particularly physiatrists, are often burdened with the task of being the key interpreter.2 The experienced physiatrist develops an intuition for how much detail is needed for each patient given a particular presentation and setting. Assessment of some or all of these elements is required for a complete understanding of the patient's state of health and the illness for which he or she is being seen. These elements also form the basis for a treatment plan.3 However, it is believed that the pattern of medical diseases in developing countries is different from that of the developed ones.4

National Institute of Neuro-sciences (NINS) in Bangladesh was established with the vision of making this institute as the center of excellence not only in this country but also for others. It is a matter of pride that the institute has started

functioning from September 2012. There are more than fifteen departments.5 Physical Medicine and Rehabilitation is one of them. This department tries to correlate with other departments in providing facilities, faith and satisfaction to the patients6. The total number of patients at Physical Medicine Department has been increasing day by day. Almost all the patients coming to this department were from different areas of Bangladesh by themselves or referred by physicians from different department of National Institution of Neuroscience and Hospital. In July-2013 to June- 2015 about 29678 patients were treated by PMR department of National Institution of Neuroscience and Hospital.

MATERIALS AND METHODS:

To attain disease profile and demographic information (age, sex, catchment area and occupation), we undertook a retrospective review of the records at Physical Medicine and Rehabilitation department of National Institute of Neuroscience and Hospital, Dhaka over a period of two year from first July 2013 to thirtieth June 2015 and determined the various diagnoses of attending patients. Information was extracted from the patients` hospital records by means of a questionnaire assessing the participants` demographics and diagnoses. The subjects were enrolled on an individual basis, despite the varying number of visits by a given patient during the period of study. After collection of the data in a standardized proforma, all the data were analyzed and presented in simple statistical percentage using Microsoft Excel.

RESULTS:

Table I shows the total number of 29678 patients received Physiatric management during the study period, among them 57.02% (16922) was male and 42.98% (12756) was female; 26.15% (7761) were in age range of 41-50 years. Catchment areas were 56.33% (16718) Dhaka city and 43.67% (12960) outside Dhaka city; where 37.76% (11206) of the studied population were housewives.

Table- I. Socio-demographic characteristics of patients (n=29678)

Characteristics		Number of patients	Percentage (%)
Sex	Male	16922	57.02
	Female	12756	42.98
Age (in years)	0-10 years	795	2.68
	10-20 years	947	3.19
	21-30 years	5110	17.22
	31-40 years	6853	23.09
	41-50 years	7761	26.15
	51-60 years	5375	18.11
	60-70 years	2498	8.42
	Above 70 years	339	1.14
Catchment area (Residency)	Dhaka city	16718	56.33
	Outside Dhaka city	12960	43.67
Occupation of patient	Service holder	6832	23.02
	Retired Service holder	1896	6.39
	Housewife	11206	37.76
	Laborer	1290	4.35
	Farmer	2120	7.14
	Businessman	1935	6.52
	Student	1707	5.75
	Unemployed	1366	4.60
	Others	1326	4.47

Figure-1 shows the psychiatric services provided in the department, 56.32% were neurological, 33.46% were musculoskeletal and 7.25% patients were rheumatologic condition.

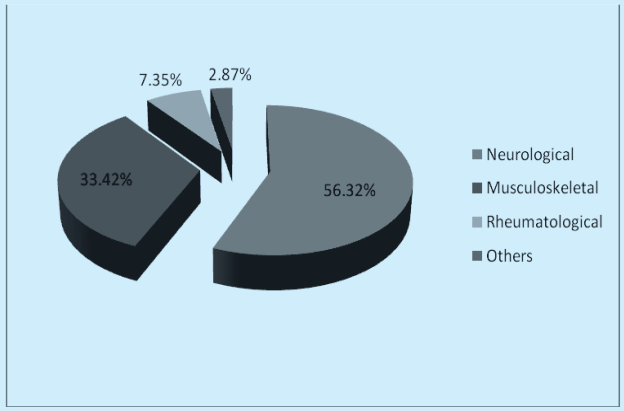


Figure-1: Physiatric services provided to the patients

Table- II emphasizes the results related to the 29678 patients' profile of Neurological diseases. Ischemic stroke was 29.03% encounted highest among neurological diseases. Next come Bell's palsy was 17.62%.

Table-II: Neurological diseases:

Serial Number	Disease	Number of patients	Percentage (%) for whole patients(n=29678)	Percentage (%) for Neurological diseases(n=16715)
1	Ischaemic Stroke	4852	16.35	29.03
2	Bell's palsy	2945	9.92	17.62
3	Carpal Tunnel Syndrome	1523	5.13	9.11
4	Cerebral Palsy	1105	3.72	6.61
5	Hemorrhagic Stroke	1087	3.66	6.50
6	Guillain Barre Syndrome	764	2.57	4.57
7	Myopathy	712	2.40	4.26
8	Motor Neuron Disease	502	1.69	3.00
9	Parkinson's Disease	465	1.57	2.78
10	Transverse Myelitis	357	1.20	2.14
11	Nerve injury	156	0.53	0.93
12	Brachial plexopathy	155	0.52	0.93
13	Seizure disorder	28	0.09	0.17
14	Others	2064	6.95	12.35
	Total	16715	56.32%	100%

Table- III presents the Musculoskeletal diseases as there Low back pain (non specific) was (31.32%), Lumber spondylosis 15.98%, prolapsed Lumber Inter-vertebral disc was 12.30%, Cervical spondylosis and Osteo-arthritis of knee presented almost the same 10.84% and 10.57% respectively.

Table-III: Musculoskeletal diseases

Serial Number	Disease	Number of patients	Percentage (%) for whole patients(n=29678)	Percentage (%) for Musculoskeletal diseases(n=9930)
1	Low Back Pain (Non-specific)	3110	10.48	31.32
2	Lumbar spondylosis	1587	5.35	15.98
3	Prolapsed Lumber Intervertebral Disc (PLID)	1221	4.11	12.30
4	Cervical Spondylosis	1076	3.63	10.84
5	Osteo-arthritis of Knee joint	1050	3.54	10.57
6	Neck Pain(sprain/strain)	583	1.96	5.87
7	Lumbar radiculopathy	455	1.53	4.58
8	Cervical Radiculopathy	206	0.69	2.07
9	Spondylolisthesis (Lumbar)	203	0.68	2.04
10	Osteoporosis	24	0.08	0.24
11	Others	435	1.47	4.38
	Total	9930	33.46%	100%

Table- IV describes the Rheumatological diseases. Adhesive Capsulitis / Periarthrosis of shoulder joint was found 36.41%, then represented planter fascitis 15.73%, polyarthritis was 14.12%, spondylo-arthitis was 11.83% and tennis elbow was 10.22% and the rest percentages were minimum.

Table-IV: Rheumatological diseases:

Serial Number	Disease	Number of patients	Percentage (%) for whole patients (n=29678)	Percentage(%) for Rheumatological diseases(n=2181)
1	Adhesive Capsulitis/Periarthrosis of shoulder joint	794	2.68	36.41
2	Plantar Fasciitis	343	1.16	15.73
3	Polyarthritis/ Rheumatoid Arthritis	308	1.04	14.12
4	Spondyloarthropathy/Ankylosing Spondylitis	258	0.87	11.83
5	Tennis Elbow	223	0.75	10.22
6	De Quervain's Tenosynovitis	129	0.43	5.91
7	Juvenile Idiopathic Arthritis	17	0.06	0.78
8	Others	109	0.37	5.00
	Total	2181	7.35%	100%

DISCUSSION:

A uniform data system (UDS) for Medical Rehabilitation is maintained in USA and published annually. No such system exists in Bangladesh.6 In this study it has been tried to find out the age, sex, occupation, residency and disease pattern of the patients attending the dept. of Physical Medicine & Rehabilitation, National Institution of Neuro-science and Hospital.

In this study, 57.02% of patients were male and 42.98% were female. Alamoudi OS et al4 in their study showed that male was 54%. Nafiza A et al7 showed 63.4% patients were males and 36.6% were females with a male to female ratio of 1.7:1.Chowdhury RN et al8 presented their study with the male patients (63.3%) predominated with a sex ratio was almost 2:1.

Occupations of patients were housewives (37.76%), labourer (4.35%), serviceman (23.02%), farmer (7.14%), businessman (6.52%), students (5.75%). Nafiza A et al7 showed 32 .25% House wife, 30.40% Businessman, 26.6% Farmer, 10.75% Student.

This study showed 5.87% of patients were less than 20 years of age, 17.22% were 21-30 years, 23.09% were 31-40 years, 26.15% were 41-50 years, 18.11% were 51-60 years and 9.56% were above 60 years of age. Chowdhury RN et al8 showed 8.1% of patients were under 20 years of age, 16.7% were 21-30 years, 15.5% were 31-40 years, 26% were 41-50 years, 18.5% were 51-60 years and 15.2% were above 60 years of age.

In our study, among whole patients (29678), 56.32% were neurological diseases. Among the neurological diseases(16715), majority of patients had stroke 35.53% [Ischaemic stroke (29.03%) and Hemorrhagic stroke(6.5%)], Bell's palsy(17.62), carpal tunnel syndrome(9.11%), Cerebral palsy(6.61%), GBS(4.57%), Myopathy(4.26%), MND(3%), PD(2.78%), TM(2.14%). Patten of neurologic diseases conducted by Chowdhury RN et al8 showed stroke was the most common (47.7%), PN(3.9%), MND(3.3%), GBS(0.9%) etc. Mohammad QD9 in his study stated that the incidence of stroke is increasing in this country in comparison to developed country.

In this study, Among whole patients (29678), 33.46% were musculoskeletal diseases. Among the musculoskeletal diseases (9930), majority of patients had non-specific LBP (31.32%) and others were lumbar Spondylosis (15.98%), PLID (12.30%), cervical Spondylosis (10.84%), OA knee (10.57%). Neck pain (sprain/strain) (5.87%), lumbar radiculopathy(Lumbago-sciatica) (4.58%), cervical radiculopathy (2.07%), Spondylolisthesis (Lumber) - (2.04%), osteoporosis(0.24%). Ahmed B et al10 showed that main causes of back pain were muscle strain (39.65%), nonspecific LBP (22.41%), prolapsed lumbar intervertebral disc (17.24%), lumbar Spondylosis (13.79%) and sciatica (6.91%). In a study done by Shahadat M11, 68.1% patients were diagnosed as nonspecific LBP, 19.8% were lumbar spondylosis, 4.4% patients were unilateral sacralisation, 4.4% were PLID and 2.2% were spondylolisthesis. Hasan SA et al12 documented non-specific low back pain (59.95%) as most common disease in his study.

In our study, Among whole patients (29678), 7.25% were Rheumatological diseases. Among the Rheumatological diseases, most of the patients were suffering from Adhesive Capsulitis/Periarthrosis of shoulder joint(36.41%) and others were Plantar Fasciitis(15.73%), Polyarthritis/ Rheumatoid Arthritis(14.12%), Spondyloarthropathy / Ankylosing Spondylitis(11.83%), Tennis Elbow(10.22%), De Quervain's Tenosynovitis(5.91%), Juvenile Idiopathic Arthritis(0.78%). In a rheumatological study done by Hasan SA et al12 showed that among the soft tissue rheumatism Adhesive Capsulitis(25.33%), Plantar Fasciitis(3.65%), Tennis elbow(2.77%), Tendinitis/ enosynovitis(3.46%), Juvenile Idiopathic Arthritis(0.78%). Hasan SA et al12 also showed that among inflammatory arthritis Rheumatoid Arthritis were 36.06%, Spondyloarthropathy/Ankylosing Spondylitis were 28.89% and Juvenile Idiopathic

Arthritis(0.78%)/Juvenile AS were 9.80%.

Most of the patients were coming from Dhaka city (56.33%) and from outside Dhaka city it was 43.67%. Probably this situation may be due to frequent use of bus for movement and journey. Masud MH et al13 showed that urban patients were 75.36% and rural patients were 24.63%. On the other hand, for the metropolitan area patients feel easy to reach in the hospital. Shakoor MA et al14 showed in their study that most of the patients (65.7%) used bus for movement and journey.

From the above discussion, it is clearly demonstrated that the findings of the study performed in Physical Medicine department of National Institution of Neuro-science and Hospital is consistent with the findings of different institutes of Bangladesh.

CONCLUSION:

A majority of patients who receive Physiatric management in NINSH are middle aged and have stroke, low back pain (non specific) and Bell's palsy. This study throws some light on the pattern of diseases treated in the PMR department. There should be a large scale multi-centered study need to perform in our country and a uniform data system should be constructed for Medical rehabilitation in Bangladesh.

LIMITATION:

This study was done in a small population and secondary data (Record review) were taken.

ACKNOWLEDGEMENT:

Dr. Md. Khurshid Mahmood, Associate Professor and Head, Department of PMR; Professor M Badrul Alam, Joint Director and Professor Quazi Deen Mohammmad, Director of National Institution of Neuro-science and Hospital, Dhaka. Fellow colleagues, medical technologist and our family members.

DISCLOSURE:

Self financing, Conflict of interest is none declared and Ethical approval was not required.

REFERENCE:

1. Ganter BK, Erickson RP, Butters MA, Takata JH, Noll SF. Principle of evaluation and management. In: Delisa JA, editor, Physical Medicine and Rehabilitation-principle and practice. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 3-5.

2. Weiss L, Isaacson AC. General principles. In: Weiss LD, Weiss JM, Pobre T, editors, Oxford American handbook of Physical Medicine and Rehabilitation, 1st ed, New York: Oxford University Press; 2010. p.13.

3. O'Dell MW, Lin CD, Panagos A. The Physiatric history and physical examination. In: Braddom RL, editor, Physical Medicine and Rehabilitation, 4TH ed, Philadelphia: Elsevier; 2011, p.3.

4. Alamoudi OS, Attar SM, Ghabrah TM, Al-Qassimi MA. Pattern of Common Diseases in Hospitalized Patients at an University Hospital in Saudi Arabia: A Study of 5594 Patients. JKAU: Med. Sci. 2009; 16(4):3-12.

5. Mohammad QD. Establishment of National Institute of Neuroscience and Hospital, Bangladesh perspective [editorial]. J Natl Inst Neurosci Bangladesh. 2015; 1(1):1.

6. Hossain MS, Chakraborty PK, Rahman S, Islam MJ, Amin MR, Saha RK, Khan MH, Yasmin N. Diseases pattern in the department of Physical Medicine & Rehabilitation in a tertiary level hospital. Bangladesh Med J. 2014 Sep; 43(3):130-133.

7. Nafiza A, Islam MZ, Farjana S. Pattern of Skin Diseases: Experience from a Rural Community of Bangladesh. Bangladesh Med J. 2012; 41(1):50-52.

8. Chowdhury RN, Hasibul Hasan ATM, Rahman YU, Khan SI, Hussain AR and Ahsan S. Pattern of neurological disease seen among patients admitted in tertiary care hospital. BMC Research Notes 2014, 7:202

9. Mohammad QD. Management of stroke - Bangladesh perspective. Bangladesh Med J. 2013 Jan; 42(1):34-37.

10. Ahmed B, Alam S, Rashid I, Rahman N, Rahman A, Uddin T, Azad GN. Effects of Transcutaneous Electrical Nerve Stimulation (TENS) on patients with Acute Low Back Pain. JAFMC. 2011 December; 7(2):29-32.

11. Shahadat M. A Comparative Study of the Effects of UST and SWD on the patients with chronic low back pain [Dissertation]. Dhaka: BCPS; 2005.

12. Hasan SA, Rahim MA, Bakar Siddiq MA, Hossain MS, Taslim A, Paul S, et al. Study of spectrum of rheumatic diseases in the department of Physical Medicine & Rehabilitation, Chittagong Medical College Hospital, Bangladesh. JCMCTA. 2009; 20(1): 6-11.

13. Masud MH, Rahman MZ, Parveen S, Rana MA, Chowdhury MS, Rahman MA, et al. Demographic and Clinical Profile of Patients with Irritable Bowel Syndrome Attending in Gastroenterology Out Patient Department of BSMMU. Comilla BMA Med J. 2012 July; 27(2):15-18.

14. Shakoor MA, Islam MA, Ullah MA, Ahmed MM, Hasan SA. Clinical profile of the patients with chronic low back pain-A study of 102 cases. JCMCTA. 2007; 18(2): 16-20.

Original Article

Effect of Dyslipidaemia on Arrhythmia in Diabetic Patients

*Hoque SJ[1], Rahman A[2], Miah MB[3] , Alam MZ[4], Irfan SMR[5], Safdar AMB[6]

Abstract

Dyslipidaemia is an important risk factor for cardiovascular morbidity and mortality. This cross-sectional study aims to find out the effect of dyslipidaemia on arrhythmia in diabetic patients. A total of sixty (60) diabetic patients, 31 were male and 29 were female, mean age was 59.58±11.38 (range 40 to 84) years with arrhythmia were selected at the department of Cardiology at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder(BIRDEM) General Hospital, Dhaka over a period of six months from January to July 2014. All the patients were accomplished with 24 hours Holter ECG monitoring, among them 40 were dyslipidaemia with mean age 60.7±13.1years and 20 were without dyslipidaemia with mean age 58±10.3 years (p-value was 0.424). Mean pulse, systolic and diastolic blood pressure were 78±15 (range 55-98) beats/min, 132±20 (range 90-180) mm of Hg and 79±8 (range 60-100) mm of Hg respectively. Mean maximum and minimum heart rate were 114±22 and 57±14 beats respectively. Mean cholesterol level was 222.58±55.51 mg/dl, mean triglyceride 241.26±98.81 mg/dl, LDL 135.53±35.61 mg/dl and HDL 41.46 ±15.46 mg/dl. Mean supraventricular beats in 24 hours was 12031± 4201 with dyslipidaemia and 8522± 2099 without dyslipidaemia which was statistically significant. Mean ventricular beats in 24 hours was 13472 ± 4872 with dyslipidaemia and 8754 ± 2689 without dyslipidaemia which was also statistically significant. Arrhythmia was found more common among diabetic patients having dyslipidaemia than without dyslipidaemia.

Key Words: arrhythmia, diabetes mellitus, 24 hours holter monitoring, ischaemic heart disease (IHD).

1. *Dr. Shabnam Jahan Hoque, Junior Consultant, Department of Cardiology, BIRDEM General Hospital & Ibrahim Medical College, Email: sjahanhoque@yahoo.com

2. Dr. Aparna Rahman, Senior Medical Officer, Dept. of Cardiology, BIRDEM General Hospital & Ibrahim Medical College.

3. Dr. Md. Babul Miah , Senior Medical Officer, Dept. of Cardiology, BIRDEM General Hospital & Ibrahim Medical College.

4. Dr. Md. Zahid Alam, Associate Professor, Dept. of Cardiology, BIRDEM General Hospital & Ibrahim Medical College.

5. Dr. SM Rezaul Irfan, Junior Consultant, Dept. of Cardiology, BIRDEM General Hospital & Ibrahim Medical College.

6. Dr. AMB Safdar, Associate Professor, Dept. of Cardiology, BIRDEM General Hospital & Ibrahim Medical College.

*Corresponding Author:

INTRODUCTION:

Dyslipidaemia is one of the important modifiable risk factor for cardiovascular disease morbidity and mortality.1 Cardiovascular disease remains the single most common cause of death in developed nations.2,3 Sudden death from cardiac causes is estimated to account for approximately 50 percent of all deaths.2,3 The majority of such sudden deaths are caused by acute ventricular tachyarrhythmias , which may occur in persons without known cardiac disease or in association with structural heart disease.2-4 Lipid-lowering interventions have been shown to reduce coronary events and all-cause mortality.5-7 It is possible that some of the beneficial effects of lipid-lowering therapy can be attributed to the reduction of ventricular arrhythmias and sudden death.5,7

Holter monitoring technologies and loop recorders allow prolonged monitoring of heart rhythm for periods from a few days to several months, making it possible to detect infrequent arrhythmias in patients of all ages.8 Cardiac rhythm monitoring has an established diagnostic and prognostic role in different circumstances: syncope, palpitations and monitoring of patients with known or suspected episodes of atrial fibrillation (AF), e.g. those with stroke of uncertain aetiology (cryptogenic stroke).9-11

There might be an association between dyslipidaemia and arrhythmia. However, no data are available regarding the direct relationship between dyslipidaemia and arrhythmia, especially in the clinical setting of acute coronary syndrome. One recently completed study showed that hypercholesterolemia could induce proarrhythmic neural and electrophysiologic remodeling in myocardium.12 This remodeling induced by hypercholesterolemia is characterized by heterogeneous nerve sprouting and sympathetic hyperinnervation, which may contribute to the

dispersion of repolarization during sympathetic activation. In addition, hypercholesterolemia apparently can directly remodel membrane currents. The alteration in membrane current is associated with prolonged actionpotential duration, longer QTc intervals, and increased repolarization dispersion. The purpose of this study was to observe any association of dyslipidaemia with arrhythmia.

METHODOLOGY:

This cross-sectional study was carried out in the department of Cardiology at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder (BIRDEM) General Hospital, Dhaka, Bangladesh from January to July 2014. Purposive sampling was done among 60 adult diabetic patients, age >18 years of either sex having Diabetes mellitus along with arrhythmia were included in this study. Non-diabetic patients, patients with electrolyte imbalance and those who were not willing to participate in the study were excluded. After enrollment all patients were evaluated clinically by taking history and physical examination. After taking informed consent, data were collected regarding smoking history, history of Hypertension, IHD. Pulse, systolic and diastolic pressure were recorded in all cases. Among all cases 24 hours holter ECG monitoring was done. After collection of blood, fasting blood glucose, HbA1c, lipid profile (serum cholesterol, Triglyceride, HDL, LDL) were measured and recorded accordingly. Dyslipidaemia was considered according to ATP III guideline with Serum Total cholesterol > 200 mg/dl, TG >150 mg/dl, LDL >100 mg/dl, HDL <40 mg/dl (male) and <50 mg/dl (female). Ethical permission was approved by appropriate authority. Data were analyzed using SPSS version 17.0 and p value <0.05 was considered as significant.

RESULTS:

Among the total 60 cases, mean age was 59.58±11.38 (range 40-84) years. Eighty percent of the study population were 50 years and above. Among the study population, 26.67% were smoker. Common co-morbidities were hypertension 83.30%, Ishemic heart diseases 86.6% and dyslipidaemia in 66.7% (40) patients. Among the total 60 cases 36.67% subjects were found in adequate glycemic control and 63.33% were not in adequate glycemic control. Mean pulse, systolic and diastolic blood pressure were 78±15 (range 55-98) beats/min, 132±20 (range 90-180) mm of Hg and 79±8 (range 60-100) mm of Hg respectively. Various types of arrhythmia were observed. Ventricular ectopy, supraventricular ectopy, atrial fibrillation and sinus pause were present in 100%, 71.67%, 8.33% and 5% cases respectively. In case of ventricular ectopics 40.0% subjects had single PVC's, 20.0% had triplets, 16.67% had couplets, 15.0% had trigeminy, 13.33% had bigeminy, 13.33% had ventricular run and 06.65 % had late VE's (Table II). In case of supraventricular ectopic 43.33% had single PAC's, 33.33% had atrial run, 25% had atrial pairs, 18.33% had bigeminy, 15.00% had late beats, 13.33% had trigeminy and 11.67% had drob beats (Table-III). Mean age was found 60.7±13.1 years and 58.0±10.3 years in groups with and without dyslipidaemia respectively (Table-IV). Twenty three (57.5%) patients were male in dyslipidaemia group and 8(40.0%) in group without dyslipidaemia (Table-V) which were not statistically significant (p>0.05). Mean cholesterol, TG, HDL and LDL were not statistically significant (p>0.05) between male and female groups (Table-VI). Significant difference was found in mean total ventricular beats and mean supraventricular beats between groups with and without dyslipidaemia (Table-VII &VIII).

Table- I: Baseline biochemical parameters of the study population (n=60)

Parameters	Mean± SD	Minimum-Maximum
FBG (mmol/l)	19.32±10.2	5.5-35.3
Hb A1c (%)	12.34±5.8	6.7-18.4
Cholesterol (mg/dl)	222.58±55.51	99-345
Triglyceride (mg/dl)	241.26±98.81	113-540
HDL (mg/dl)	41.46±15.46	19-68
LDL (mg/dl)	135.53±35.61	111-189

Table- I represents distribution by the bio-medical parameters where fasting blood glucose was within 5.5 to 35.3 mmol/l, Hb A1C was within 6.7-18.4(%). Mean cholesterol was 222.58±55.51 mg/dl, triglygeride was 241.26 ± 98.81mg/dl, High density lipoprotien and low density lipoprotien was 41.46 ± 15.46 mg/dl and 135.53 ± 15.46 mg/dl respectively.

Table- II: Findings of different type of ventricular ectopics in all cases on 24 hours Holter monitoring (n=60)

Events	Number	Percentage
Single PVC's	24	40.00
Triplets	12	20.00
Couplets	10	16.67
Trigeminy	09	15.00
Bigeminy	08	13.33
Ventricular run	08	13.33
Late VE's	04	06.65
Mean ± SD total ventricular beats in 24 hours (Maximum Minimum)	3019 ± 889 (19336-15)	

Table- III: Findings of diferrent type of supraventricular ectopy in 43 cases on 24 hours holter monitoring (n=60)

Events	Number	Percentage
Single PAC's	26	43.33
Atrial run	20	33.33
Atrial pairs	15	25.00
Bigeminy	11	18.33
Late	09	15.00
Trigeminy	08	13.33
Drop	07	11.67
Mean ± SD total supraventricular beats in 24 hours (Maximum Minimum)	4508 ± 1505 (20840-23)	

Table- IV shows association between age and dislipidaemia, the highest no of dyslidaemia was 14 which were found in age group 61-70 years whereas the highest (11) patients of without dyslipidaemia was found in age group 51-60 years. The mean of dyslipidaemia and without dyslipidaemia patients were 60.7±13.1 and 58±10.3 respectively where p-value was 0.424

Table IV: Association between age and dyslipidaemia (n=60)

Age (years)	Dyslipidaemia (n=40)	Without dyslipidaemia (n=20)	p value
	n (%)	n (%)	
<50	9 (22.5)	3 (15.0)	
51-60	13 (32.5)	11 (55.0)	
61-70	14 (35.0)	4 (20.0)	
>70	4 (10.0)	2 (10.0)	
Mean±SD	60.7±13.1	58.0±10.3	0.424
Range (min-max)	40-84	42-81	

P value was calculated using from unpaired t-test

Table- IV shows association between age and dislipidaemia, the highest no of dyslidaemia was 14 which were found in age group 61-70 years whereas the highest (11) patients of without dyslipidaemia was found in age group 51-60 years. The mean of dyslipidaemia and without dyslipidaemia patients were 60.7±13.1 and 58±10.3 respectively where p-value was 0.424

Table V: Association between gender and dyslipidaemia (n=60)

Sex	Dyslipidaemia (n=40)	Without dyslipidaemia (n=20)	p value
	n (%)	n (%)	
Male	23 (57.5)	8 (40.0)	0.200
Female	17 (42.5)	12 (60.0)	

p value was extracted using chi square test

Table V shows association between gender and dyslipidaemia. Dyslipidaemic male was 57% and female was 42.5% whereas absent of dyslipidaemia in male was 40% and female was 60%. This was statistically significant.

Table VI: Association between lipid profile with sex (n=60)

Lipid profile	Male (n=31)	Female (n=29)	p value
	Mean±SD	Mean±SD	
Cholesterol (mg/dl)	211.1±48.9	231.3±59.2	0.154
Triglyceride (mg/dl)	218.9±89.6	254.9±98.7	0.144
HDL (mg/dl)	38.1±16.2	42.1±13.1	0.299
LDL (mg/dl)	124.5±27.8	138.6±36.4	0.096

P value reached from unpaired t-test

Table- VI shows distribution by association between lipid profiles with sex. Mean cholesterol in male was 211.1± 48.9 mg/dl where in female it was 231.3±59.2, mean triglyceride was in male 218.9±89.6mg/dl but in female 254.9±98.7mg/dl then mean HDL represented in male 38.1±16.2% mg/dl and in female that was 42.1±13.1mg/dl followed by mean LDL in male was 124.5±27.8mg/dl but in that was in female 138.6±36.4mg/dl. Table represented that women were more vulnerable than men.

Table VII: Comparison of mean total ventricular beats in subjects with and without dyslipidaemia (n=60)

	Dyslipidaemia (n=40)	Without dyslipidaemia (n=40)	p value
	Mean±SD	Mean±SD	
Total ventricular beats in 24 hours	13472±4872	8754±2689	0.001*

*=significant
p value reached from unpaired t-test

Table- VII showing total ventricular beats in 24 hours among dyslipidaemia group which is significantly more in number in comparison to group without dyslipidemia showing significant role of dyslipidemia causing arrhythmia.

Table VIII: Comparison of mean total supraventricular beats in subjects with and without dyslipidaemia (n=60)

	Dyslipidaemia (n=40)	Without dyslipidaemia (n=40)	p value
	Mean±SD	Mean±SD	
Total supraventricular beats in 24 hours	12031±4201	8522±2099	0.001*

*=significant
P value reached from unpaired t-test

Table showing Total supraventricular beats in 24 hours among dyslipidemia group which is significantly more in number in comparison to group without dyslipidemia showing significant role of dyslipidemia causing arrhythmia

DISCUSSION:

Total number of patients was 60 with male predominance and mean age was 59.58±11.38 years. Common co-morbidities in this study were hypertension, IHD and dyslipidaemia. Gunalp et al. found hypertension, IHD and stroke as co-morbid conditions.13 The study subjects had mean pulse 78±15 (55-98) beat/minute and mean maximum and minimum heart rate were 114±22 and 57±14 beats respectively. Ewing et al. found in his study that maximum heart rate was 114±10 beats/ min and minimum rate was 66±9 beats /min in 24 hours Holter ECG findings in diabetic subjects with arrhythmia.14 Brownlee et al. Observed that diabetic subjects with arrhythmic had maximum heart rate was 118±15 beats/min and minimum heart rate was 79±10 beats /min.15 Fasting Blood Glucose(FBG) and HbA1c% level were 19.32 mmol/l and 12.34% respectively. Stamler et al. observed that mean±SD RBS and HbA1C% levels were 20.29±8.61 mmol/l and 10.48±4.11 respectively.16 Jocoby et al. seen that mean±SD RBS and HbA1C% levels were 18.29±7.55 mmol/l and 11.37±5.92 respectively.17 Mean cholesterol level was 222.58±55.51 mg/dl, mean triglyceride 241.26±98.81 mg/dl, LDL 135.53±35.61 mg/dl and HDL 41.46 ±15.46 mg/dl in our study. Gomez et al. found almost similar lipid profile reports.18

Regarding ventricular ectopics, it was seen that 40% had single PVC's, 20% had triplets, 16.67% had couplets and 13.33% had ventricular run in our study. In case of supraventricular ectopics, it was seen that 43.33% subjects had Single PAC's, 33.33% atrial run, 25% had atrial pairs. James et al. in a similar study found that mean total supraventricular beats in 24 hours was 3705 whereas, PAC's was observed in 41% subjects and atrial run in 16% cases.19 Regarding supraventricular events, another study by Binici et al. revealed that mean total supraventricular beats in 24 hours was 3929 whereas, PAC's was observed in 70% subjects and atrial run was observed in 42% patients.20 Regarding ventricular events Adabaq et al.21 found mean total ventricular beats in 24 hours was 3256 and single PVC's were noted in 42% subjects in their study. It was seen that statistically significant difference in mean ventricular beats and supraventricular beats in 24 hours between controlled diabetes and those with uncontrolled diabetes.

Present study revealed that male were higher in dyslipidaemia group compared to groups without dyslipidaemia but that difference was not statistically significant (p>0.05). The mean cholesterol, TG, HDL and LDL were also not statistically significant (p>0.05) between male and female patients. O'Meara et al. study showed higher prevalence of dyslipidemia among men than women.22 Different study also agreed with our observation. They showed the mean values of LDL cholesterol, HDL cholesterol, and triglycerides was not statistically significant between male and female patients.23-24 Badea et al. the mean values ± SD of serum lipids and fasting blood glucose is noticed that the mean values of serum TG were slightly elevated. Total Cholesterol levels were close to the limits specified by guidelines for diabetic patients and for patients with cardiovascular diseases, with no significant differences between males and females.25 Mean values of HDL-C were decreased. HDL-C levels were found to be higher in females (37.22 ± 10.75) com¬pared with males (35.36 ± 7.70), with statistical signifi¬cance (p=0.00081).26 Few studies have shown that postmenopausal women present with a significant increase of TC, LDL-C and TG values, but insignificant decrease of HDL-C.27-28 On the other hand, a comparative study of plasma lipid profile tests in healthy young population showed that TC and LDL-C levels were significantly increased in men. The same study showed that HDL-C levels were significantly decreased in men compared with BMI and age matched women.

Present study revealed that significant difference was seen in mean ventricular beats 13472 ± 4872, 8754 ± 2689 in 24 hours between groups with and without dyslipidaemia. Significant difference was also seen in mean supraventricular beats 12031 ± 4201, 8522 ± 2099 in 24 hours between groups with and without dyslipidaemia. Liu et al. comparison of lipid profiles between patients with VT/VF and controls revealed that patients experiencing VT/VF had higher levels of TC, LDL-C and triglyceride at 3 months after MI, and a higher level of LDL-C at admission.29

CONCLUSIONS:

Arrhythmia is more common among diabetic patients having dyslipidaemia than those without dyslipidaemia. Dyslipidaemia may play an important role in arrhythmogenesis in diabetic case. Therefore dyslipidaemia should be controlled adequately to combat arrhythmia and IHD in diabetic cases.

REFERENCES:

1. M.J. Field, L. Burnett, D.R. Sullivan, P.Stewart Clinical biochemistry and metabolism, In: Brian R. Walker, Nicki R. Colledge, Stuart H. Ralston, Ian D. Penman (eds.) Davidson's Principles & Practice of Medicine 22nd edition Edinburgh, Churchill Livingstone Elsevier; 2014, p. 452 - 3.

2. Myerburg RJ, Kessler KM, Castellanos A. Sudden cardiac death: epidemiology, transient risk, and intervention assessment. Ann Intern Med 1993;119:1187-97.

3. Myerburg RJ, Interian A Jr, Mitrani RM, Kessler KM, Castellanos A. Frequency of sudden cardiac death and profiles of risk. Am J Cardiol 1997; 80:10F-19F.

4. Zipes DP, Wellens HJJ. Sudden cardiac death. Circulation 1998;98: 2334-51.

5. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998;339:1349–57.

6. LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282:2340–6.

7. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383–9.

8. Galli A, Ambrosini F, Lombardi F. Holter Monitoring and Loop Recorders: From Research to Clinical Practice. Arrhythmia & Electrophysiology Review 2016;5(2):136–43.

9. Zimetbaum P, Goldman A. Ambulatory arrhythmia monitoring: choosing the right device. Circulation. 2010;122:1629–36.

10. Brignole M, Vardas P, Hoffman E, Huikuri H, Moya A, Ricci R, et al. Indications for the use of diagnostic implantable and external ECG loop recorders. Europace 2009;11:671–87.

11. Giada F, Bertaglia E, Reimers B, Noventa D, Raviele A. Current and emerging indications for implantable cardiac monitors. Pacing Clin Electrophysiol 2012;35:1169–78.

12. Liu YB, Wu CC, Lu LS, Su MJ, Lin CW, Lin SF, et al. Sympathetic nerve sprouting, electrical remodeling, and increased vulnerability to ventricular fibrillation in hypercholesterolemic rabbits. Circ Res 2003;92:1145–52.

13. Gunalp M, Atalar E, Coskun F, Yilmaz A, Aksoyek S, Aksu NM, Sivri B. Holter monitoring for 24 hours in patients with thromboembolic stroke and sinus rhythm diagnosed in the emergency department. Adv Ther. 2006;23(6):854-60.

14. Ewing DG, Borsey DQ, Travis P, Bellavere F, Neilson JJM, Clarke BF. Abnormalities of Ambulatory 24-hour Heart Rate in Diabetes Mellitus Diabetes 1983; 32: 101.

15. Brownlee M, The pathobiology of diabetic complications: A unifying mechanism, Diabetes, 2005; 54:1615–25.

16. Stamler J, Vaccaro O, Neaton JD, Wentworth D, Multiple Risk Factor Intervention Trial Research Group. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the multiple risk factor intervention trial. Diabetes Care 1993; 16:434–44.

17. Jacoby RM, Nesto RW. Acute myocardial infarction in the diabetic patient: pathophystology, clinical course and prognosis. J Am Coll Cardiol 1992; 20:736–44.

18. Gomez MJ, Roldan I, Díez JL, García K, Sanmiguel D, Salvador A et al. Predictive value of differential pulse pressure in the diagnosis of silent myocardial ischemia in patients with type-2 diabetes. Rev Esp Cardiol. 2007; 60(5): 543.

19. James J.H, Kumar S, Thomas L, Thomas S. Supraventricular ectopy and recurrence of atrial fibrillation after electrical cardioversion. Europace 2006; 8: 341.

20. Binici Z, Intzilakis T, Nielsen OW, Kober L, Sajadieh A, Excessive Supraventricular Ectopic Activity and Increased Risk of Atrial Fibrillation and Stroke. Circulation. 2010; 121: 1904-11.

21. Adabag A, Susan A, Kuskowski MA, Zenovich AG, Maron BJ, Spectrum and prognostic significance of arrhythmias on ambulatory Holter electrocardiogram in hypertrophic Cardiomyopathy. Am Coll Cardiol. 2005; 45(5):697-704.

22. O'Meara JG, Kardia SL, Armon JJ, Brown CA, Boerwinkle E, Turner ST. Ethnic and sex differences in the prevalence, treatment, and control of dyslipidemia among hypertensive adults in the GENOA study. Arch Intern Med. 2004;164(12):1313-8.

23. Stern N, Grosskopf I, Shapira I, Kisch E, Isaacov A, Limor R, et al. Risk factor clustering in hypertensive patients: impact of the reports of NCEP-II and second joint task force on coronary prevention on JNC-VI guidelines. J Intern Med. 2000;248:203.

24. Kastarinen MJ, Nissinen AM, Vartiainen EA, Jousilahti PJ, Korhonen HJ, Puska PM, et al. Blood pressure levels and obesity trends in hypertensive and normotensive Finnish population from 1982 to 1997. J Hypertens. 2000;18:255-62.

25. Badea AR, Nedelcu L, Valeanu M, Zdrenghea D. The Relationship between Serum Lipid Fractions and Heart Rate Variability in Diabetic Patients with Statin Therapy. Clujul Med. 2014; 87(3): 152– 8.

26. Liu CC, Kuo TB, Yang CC. Effects of estrogen on gender-related autonomic differences in humans. Am J Physiol Heart Circ Physiol. 2003;285:H2188- 93.

27. Roy A, Kundu D, Mandal T, Bandyopadhyay U, Ghosh E, Ray D. A comparative study of heart rate variability tests and lipid profile in healthy young adult males and females. Niger J Clin Pract. 2013;16(4):424- 8.

28. Fu CH, Yang CC, Lin CL, Kuo TB. Alteration of cardiovascular autonomic functions by vegetarian diets in postmenopausal women is related to LDL cholesterol levels. Chin J Physiol 2008;51:100-105.

29. Liu YB, Wu CC, Lee CM, Chen WJ, Wang TD, Chen PS, et al. Dyslipidemia is associated with ventricular tachyarrhythmia in patients with acute ST-segment elevation myocardial infarction. J Formos Med Assoc. 2006;105(1):17-24.

Original Article

Knowledge and Acceptance of HPV Vaccination among Women Attending at Out Patient Department of Dhaka Medical College Hospital

*Lipi LB [1], Rahman MM[2] , Shaha N[3], Sultana M[4], Ara I[5]

Abstract

Vaccination is a part of primary prevention to prevent cervical cancer. The causative agent of cervical cancer is Human Papilloma Virus (HPV). The purpose of this study was to assess the knowledge and awareness regarding cervical cancer prevention by HPV vaccination and acceptance of vaccination among women attending at outpatient department of Dhaka Medical College Hospital. A qualitative study was undertaken using face to face in depth interviews from July 2015 to December 2015. A total of 229 women were included and their mean age was 34.07±7.92 ranging from 18 to 60 years. Awareness and knowledge about cervical cancer was very poor. Only 22.7% participants were aware of HPV vaccination. Knowledge was high among women coming from high socioeconomic condition which was 31.5% (p=0.03). Participants who were highly educated had more knowledge on vaccination about 66.7% (p=0.001). There was a high acceptance (83.8%) of HPV vaccination among participants. The findings focus on the importance of awareness development on cervical cancer and its risk factors. Continuous screening of cervical cancer for early diagnosis and prompt treatment and publicity of awareness development program by mass-media (television, cable line add etc.), poster, billboard and most importantly through health education could play an important role in cervical cancer prevention.

Key Words: Human Papilloma Virus,vaccination, primary prevention, cervical cancer

1. *Dr. Lutfa Begum Lipi, junior Consultant, Department of obstretics and gynaecology, Dhaka Medical College Hospital, Dhaka. Email:lutfa.ssmc@gmail.com

2. Dr. Mohammed Mizanur Rahman,associate prof , department of Urology, National Institute Of Kidney Diseases And Urology,Dhaka

3. Dr. Nibedita Shaha, Assistant Registrar, Department of obstretics and gynaecology, Dhaka Medical College Hospital, Dhaka.

4. Dr.Meher Sultana, Assistant registrar, Department of obstretics and gynaecology, Dhaka Medical College Hospital, Dhaka.

5. Prof. Iffat Ara, Proffesor , Department of obstretics and gynaecology, Popular Medical College,Dhaka.

*Corresponding Author

INTRODUCTION:

Among the total global cervical cancer 80% occur in developing country.1 Globally– 527 624 new cases - half the global burden is in Asia ,one quarter in Southern Asia.2 In Bangladesh yearly burden of cervical cancer is about 17686 and around 10364 women die from cervical cancer each year. 3 Hospital based data revealed that cervical cancer constitutes 22 -29% of female cancer in Bangladesh.4 Interestingly, the disease is excellently preventable. Cancer prevention is action taken to lower the chance of getting cancer. By preventing cancer, the number of new cases of cancer in a group or population is lowered. Hopefully, this will lower the number of deaths caused by cancer. To prevent new cancers from starting, scientists look at risk factors and protective factors. Anything that increases the chance of developing cancer is called a cancer risk factor; anything that decreases the chance of developing cancer is called a cancer protective factor.

Avoiding risk factors and increasing protective factors may help prevent cancer .Risk factors for cervical cancer are the human papilloma virus infection(HPV) (a common sexually transmitted virus), having sex at an early age, multiple sexual partners, Smoking or using tobacco, using birth control pills for a long time ,weakened immune system- such as those who have human immunodeficiency virus (HIV) infection , been exposed to diethylstilbestrol (DES) before birth. The protective factors that decrease the risk of cervical cancer is HPV vaccination. So vaccination is a part of primary prevention to prevent cervical cancer.

Cervical cancer is almost always caused by human papilloma virus (HPV) infection that spreads through sexual contact.5 There are more than 150 types of human papilloma virus that infect cervix, vagina, vulva, anus and about 30 of these can infect the cervix. Human Papilloma Virus (HPV) type 16 and 18 contributes to over 70% of all cervical cancer cases.6-8

Bangladesh is a developing country with limited resources. The Government of Bangladesh (GOB) has developed wide cervical cancer screening program through Visual Inspection of Cervix with Acetic Acid (VIA).9

The services for cervical and breast cancer screening are currently available as opportunistic screening at 252 facilities including Bangabandhu Sheikh Mujib Medical University (BSMMU), Medical College Hospitals, District Hospitals, Maternal and Child Welfare Centers, Upozilla Health Complexes (UHC), Union Health & Family Welfare Centers (UH&FWC), Urban Primary Health Care centers and Non-Government Organizations (NGO). The trained Family Welfare Visitors (FWVs), Senior Staff Nurses (SSNs) and Doctors offer VIA to detect the pre-cancer or early stages of cervical cancer among women 30 years and above visiting the mentioned centers.10 VIA positive women are referred to BSMMU and various government MCHs for colposcopic evaluation and necessary management. This service is technically and financially supported by GOB, BSMMU and UNFPA.10,11

However, only three lac women have received screening services during the last five years.12 During evaluation of the 'Cervical Cancer Screening Program of Bangladesh' low coverage of the target population was observed. Lack of awareness about cervical cancer and its prevention, low availability of services may be underlying factors for this low intake of services. In fact, several studies have mentioned that the uptake of screening in developing countries is poor .13 Lack of awareness of cervical cancer has been identified as one of the factors contributing to the high prevalence of this condition in the developing world compared to the developed one.14 Unlike developed countries, cervical cancer prevention program have failed to meet their objectives in developing countries due to financial, social and logistical problems.15

Vaccination against the human papilloma virus in women before sexual activity also prevents cervical cancer.16-19 Vaccines are available that can protect against certain HPV infections. HPV vaccines that have been developed are based on recombinant expression and self assembly of the major capsid protein-1 into virus like practical (VPLs) that resemble the outer capsid of whole virus. The HPV VPLs contain no DNA and are not live attenuated virus. Three vaccines are approved by the FDA to prevent HPV infection: Gardasil, Gardasil 9, and Cervarix. All three vaccines prevent infections with HPV types 16 and 18, two high risk HPV typethat cause about 70% of cervical cancers and an even higher percentage of some of the other HPV-associated cancers. Gardasil also prevents infection with HPV types 6 and 11, which cause 90% of genital warts . Gardasil 9 prevents infection with the same four HPV types plus five additional high-risk HPV types (31, 33, 45, 52, and 58).20,21

To decrease the country wise and global burden of the disease, the community perception regarding disease process, progression, screening and prevention by vaccination have to be assessed first. So this study was designed to find out the knowledge regarding prevention of cervical cancer by HPV vaccination and its acceptance among women attending OPD of a tertiary hospital.

METHODS AND MATERIALS:

The present study was conducted among the outdoor patients of Obstetrics & Gynecology department of Dhaka Medical College Hospital (DMCH), Dhaka from July 2015 to December, 2015. The study period was only 6 months. It was a cross sectional, prospective, observational and single centered study. The aim of the study is to assess the level of awareness among the women attending the OPD of Dhaka Medical College Hospital regarding cervical cancer prevention by vaccination.

The sample was collected from the women attending GOPD of DMCH by random sampling. The sampling was done to select the patient according to the eligibility criteria. Women of reproductive age group who give consent were enrolled in this study. Then the respondents were explained about the study procedure and assurances were given that no benefit or harm would be occurred for being included in this study from their perspective. Sample unit was selected from the study population and data were collected from the selected patient by preformed structured questionnaire, the questionnaire included how HPV could be caught and what it might cause, what they knew about cervical cancer, what they knew about vaccination and acceptance of HPV vaccination. With the demographic details orientation of risk factors, female preponderance cancer, knowledge about cervical carcinoma, vaccination and other prevention procedure as well as source of information's were observed and recorded.

A consent form was prepared. Questionnaire was filled with informed written consent. Expert opinions were taken from specialists of the Department of Gynae & Obstetrics, pathology, virology department of DMCH, Dhaka. All the data were gathered, accumulated, edited, reduced and decorated. All data were checked and edited after collection. Frequency distribution and normal distribution of all continuous variables were calculated and Chart was prepared by spreadsheet of Windows 7. Data were entered into computer and analyzed with the help of SPSS windows version 17. 'P' values <0.05 was considered as statistically significant.

RESULT:

Table- I: Distribution of Patients by clinical characteristics (n=229)

Characteristics	Frequency	Percent
Age in years		
Below 30 years	65	28.4
30-39	94	41.0
Above 40 years	70	30.6
Mean±SD	34.07±7.92	
Para		
1	5	10.9
2	25	54.3
3	9	19.6
4	7	15.2
Mean ±SD	2.36±0.85	
Age of marriage		
<13 years	65	28.8
14 -18 years	94	55.9
>18 years	70	15.3
Mean ±SD	16.12±2.83	
Education		
Illiterate	23	10
primary	118	51.5
secondary	76	33.2
Above secondary	12	5.2
Monthly income (Taka)		
<10,000	156	68.12
>10,000	73	31.88

Figure-1 shows the psychiatric services provided in the department, 56.32% were neurological, 33.46% were musculoskeletal and 7.25% patients were rheumatologic condition.

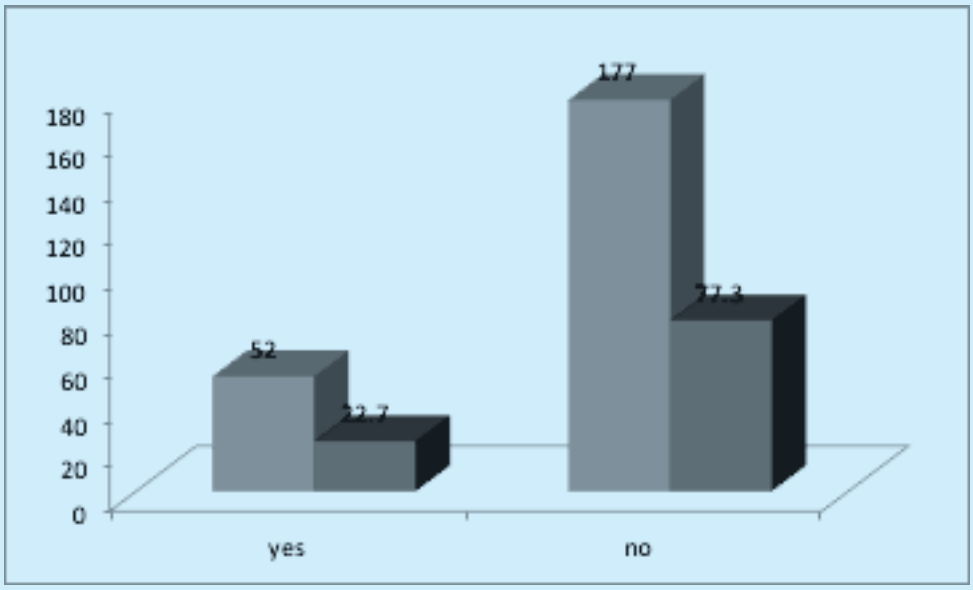


Figure I : knowledge about vaccination (n=229)

Table II: Distribution by the knowledge about cervical cancer and vaccination (n=229)

Questions		no	%
	Had ever heard about HPV	52	22.7
asked to explain how HPV might be caught and what it may cause	Knowledge about how HPV may be caught and what it may cause	40	17.45
	HPV is a sexually transmitted disease	50	21.83
	HPV can cause cervical cancer	22	9.6
	HPV can cause genital warts	2	0.87
	Did not know	170	77.3
asked to explain what they knew about cervical cancer	Knowledge about cervical cancer	58	25.3
	Did not know	171	74.7
	Knowledge about vaccines	52	22.7
	Did not know	170	77.3
asked about vaccines	Acceptance of vaccination against HPV	192	83.8

Table- II shows distribution by the knowledge about cervical cancer and vaccination where 84% respondents accepted usefulness of HPV vaccination and wanted to take it.

Table III: Relationship between age of the respondents and knowledge on vaccine (n=229)

Age	Knowledge on vaccine		X^2	*P*
	Yes	No		
Below 30 years	13 20.0%	52 80.0%	3.071	0.215
30-39	18 19.1%	76 80.9%		
Above 40	21 30.0%	49 70.0%		
Total	52	177		

Table III shows women aged more than 40 years have more knowledge which is about 30 %.

Table IV: Relationship between education & income of the respondents with knowledge on vaccine (n=229)

	Knowledge on vaccine		X^2	*P*
	Yes	No		
Education				
Illiterate	2 8.7%	21 91.3%	3.071	0.215
Up to primary	18 15.3%	100 84.7%		
Above primary	28 36.8%	48 63.2%		
Above secondary	10 83.3%	2 16.7%		
Total	58	171		
Monthly income(Taka)				
<10,000	29 18.6	127 81.4		
>10,000	23 31.5	50 68.5		

Table IV shows relationship between education & income of the respondents with knowledge on vaccine, educated respondents who completed above secondary education about 83.3% had more knowledge about vaccine.

DISCUSSION:

Only 25.3% and 22.7% of our respondents had some knowledge about cervical cancer and vaccination respectively. Both these figures are very poor. Surveys conducted previously and before the regulatory approval of HPV vaccines also showed a low level of awareness of HPV (30-40%)22-25.The results of the present study are in line with other recent studies, carried out after regulatory approval of HPV vaccination, that showed limited levels of awareness of HPV. In the United Kingdom and Italy (where HPV vaccine is free of charge for girls of 12 years of age), only about 24% and 30% of respondents, respectively, reported awareness of HPV26,27. We also studied the relationship between HPV awareness and several factors. In this study awareness increased with increase age and education (Table III & IV). Women from high income group have more knowledge about 31.5%. According to some authors report increasing age (women 14-24 years) and having had a personal, familiar, or friendly history of previous STI or cervical cancer were associated with an increased awareness of HPV and accurate knowledge of the HPV-cervical cancer link24,25,27. In a study only 19% and 7% of the participants, respectively, knew that HPV is an STI and that it can cause cervical cancer.28Another study, carried out in north-eastern Brazil, assessing young women (16-23 years) showed similar results to the that study: less than 10% of participants acknowledged that HPV might lead to cervical cancer; however, a higher proportion of those women (67%) knew that HPV is sexually transmitted.29This difference might be explained by the fact that these women had higher educational levels than women in that study (61% and 50% respectively had high school education or above).

Regarding acceptability of the vaccine, despite the inadequate knowledge of HPV and cervical cancer, 83.8% participants reported that they would accept vaccination if the HPV vaccine was available. As other studies have reported, there was a generally favorable attitude toward HPV vaccines; despite the low level of knowledge about the link between HPV and cervical cancer, 91% and 88% of women would agree to receive the vaccine in surveys that found that only 15%30and 38%31, respectively, had heard of HPV.

It was in 2006 that HPV vaccines were licensed in the USA for use in females 9 to 26 years of age with the aim of preventing cervical cancer, precancerous lesion and genital warts by HPV 16 & 18.32 It was indeed an important milestone. The studies demonstrate 100% efficacy in the prevention of persistent specific type HPV infections and CIN 2/3, with follow up data available for up to 4 to 5 years among subjects who were strictly adherent to the study protocol. Gardasil also protect against HPV 6, 11, 16 & 18 related external genital lesion .

Among women aged 15 to 26 years who completed the vaccination regimen, did not violate the protocol and had no virological evidence of infection with respective HPV type at study entry through 1 month after the third dose (vaccine-5301 versus placebo-5258) vaccine efficacy was 100%(97.96% confidence interval[CI], 76% to100%) for preventing HPV 16 OR 18 related CIN 2/3 and adenocarcinoma in situ. Fifteen of the placebo cases had CIN 3.33-36

These vaccines only work to prevent HPV infection, not treat the infection that already there.37,38 That is why to be most effective, vaccines should be given before a person exposed to HPV (through sexual activity).

It is important to realize that no vaccine provides complete protection against all cancer causing types HPV, so routine cervical cancer screening is still necessary. In spite of having preventive measures (screening and vaccination) that can reduce morbidity and mortality from cervical cancer it is difficult to implement, especially in developing countries due to lack of knowledge and partly due to lack of resources. As like success of EPI vaccination program we have to be successful to prevent cervical cancer through HPV vaccination of 9 to 13 aged girls. This study highlights the importance of awareness creation about cervical cancer and its risk factors, screening and importance of vaccination through television, cable line advertisement, poster, billboard and most importantly through health education to prevent cervical cancer.

REFERENCE:

1. Sultana, R. and Sultana, N. Clinical Profile and Treatment Protocol of Invasive Carcinoma of Cervix. Bangladesh Medical Journal (Khulna),2012; 45, 11-14.

2. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre) Human papillomavirus and related diseases report in world. Available athttp://www.hpvcentre.net/statistics/reports/XWX.pdf. Accessed February 24, 2014

3. Ferlay J, Shin HR, Bray F, et al. GLOBOCAN 2008: Cancer incidence and mortality worldwide. IARC Cancer Base. No. 10 Lyon, France: IARC Press; 2010. http://globocan. iarc.fr.

4. Akhter PS, Uddin MM, Sharma SK. Patterns of malignant neoplasm – A three year study, Bangladesh Medical journal 1998;27(20):29-32.

5. levinson, W.Human Papillomavirus. In :revew of medical microbiology and immunology. Levinson, W(eds).10th Ed. The McGraw-Hill Companies,Inc.2008;p:264-5.

6. Winer RL, Hughes JP, Feng Q, et al. Condom use and the risk of genital human papillomavirus infection in young women. New England Journal of Medicine 2006;

354(25):2645–54.

7. Gnanamony, M.P.A. and Abraham,P. An overview of Human Papillomavirus and current vaccine stratigies. Indian .Journal . Medical. Microbiology. 2007;25(1):10-17.

8. Anorlu ,R.I. Cervical cancer: the Sub-Saharan African perspective. Reported. Health. Matters. 2008;16(32):41-49.

9. Nessa A, Hussain MA, Rahman JN, et al. Screening for cervical neoplasia in Bangladesh using visual inspection with acetic acid. Int J GynaecolObstet, 2010; 111, 115-8.

10. Ashrafun Nessa, KhadizaNurunNahar , Shirin Akhter Begum, ShahinAraAnwary, Fawzia Hossain, KhairunNahar. Comparison between Visual Inspection of Cervix and Cytology Based Screening Procedures in Bangladesh, Asian Pac J Cancer Prev, 2013;14 (12), 7607-11

11. Ahmed T, Ashrafunnessa, Rahman J. Development of a Visual Inspection Programme for Cervical Cancer Prevention in Bangladesh. Elsevier Reproductive Health Matters,2008;16, 78-85

12. Basu P, Nessa A, Majid M et al. Evaluation of the National Cervical Cancer Screening Programme of Bangladesh and the formulation of quality assurance guidelines. J Fam Plann Reprod Hlth Care, 2010; 36, 131-4.

13. Sangwa-Lugoma G, Mahmud S, Nasr SH, et al. Visual inspection as a cervical cancer screening method in a primary health care setting in Africa. Int J Cancer, 119, 2006; 1389-95.

14. World Health Organization. Cervical Cancer Screening in Developing Countries: Report of a WHO consultation. France: WHO Publications, 2002; 1-75.

15. Sankaranarayanan R, Budukh AM, Rajkumar R. Effective screening programmes for cervical cancer in low- and middle-income developing countries. Bull World Health Organ. 2001;79:954–62.

16. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). A Summary report on HPV and Cervical cancer statistics in South Africa.2007. [Accessed 28 August 2015

17. Cervical Cancer Health Guide: Can Cervical Cancer Be Prevented. 2008. http:/www.cancer.org/docroot/content/2_4_2X. Accessed 2009/08/05.

18. Adanu, R.M.K. Cervical Cancer Knowledge and Screening in Accra, Ghana. Journal of Women's Health & Gender-based Medicine. 2002; 11(6), pp.487-8.

19. Kjaer, S.K. Risk factors for cervical neoplasma in Denmark. APMIS 1998; Suppl. 80.1-41 Abstract.

20. American Cancer Society Guideline for Human Papillomavirus (HPV) Vaccine Use to Prevent Cervical Cancer and Its PrecursorsCA :Cancer Journal for Clin 2007;57:7-28,

21.Human Papillomavirus (HPV) Vaccines,national cancer center,Morbidity and Mortality Weekly Report 2012; 61(15):258-61.

22.Hanisch R, Gustat J, Hagensee ME, Baena A, Salazar JE, Castro MV, Gaviria AM, Sánchez GI: Knowledge of Pap screening and human papillomavirus among women attending clinics in Medellín, Colombia. Int J Gynecol Cancer. 2008, 18: 1020-6. 10.1111/j.1525-1438.2007.01131.x.

23. Waller J, McCaffery K, Forrest S, Szarewski A, Cadman L, Wardle J: Awareness of human papillomavirus among women attending a well woman clinic. Sex Transm Infect. 2003, 79: 320-2. 10.1136/sti.79.4.320.

24. Nøhr B, Munk C, Tryggvadottir L, Sparén P, Tran TN, Nygård M, Skare GB, Dasbach E, Liaw KL, Kjaer SK: Awareness of human papillomavirus in a cohort of nearly 70,000 women from four Nordic countries. ActaObstetGynecol Scand. 2008, 87: 1048-54.

25. Tiro JA, Meissner HI, Kobrin S, Chollette V: What do women in the U.S. know about human papillomavirus and cervical cancer?. Cancer Epidemiol Biomarkers Prev. 2007, 16: 288-94. 10.1158/1055-9965.EPI-06-0756.

26. Marlow LA, Waller J, Wardle J: Public awareness that HPV is a risk factor for cervical cancer. Br J Cancer. 2007, 97: 691-4. 10.1038/sj.bjc.6603927.

27. Di Giuseppe G, Abbate R, Liguori G, Albano L, Angelillo IF: Human papillomavirus and vaccination: knowledge, attitudes, and behavioural intention in adolescents and young women in Italy. Br J Cancer. 2008, 99: 225-9. 10.1038/sj.bjc.6604454.

28. Cristina H Rama, Awareness and knowledge of HPV, cervical cancer, and vaccines in young women after first delivery in São Paulo, Brazil - a cross-sectional study, BMC Women's Health2010; 10.1186/1472-6874-10-35

29. Moreira ED, Oliveira BG, Ferraz FM, Costa S, Costa Filho JO, Karic G: Knowledge and attitudes about human papillomavirus, Pap smears, and cervical cancer among young women in Brazil: implications for health education and prevention. Int J Gynecol Cancer. 2006, 16: 599-603. 10.1111/j.1525-1438.2006.00377.

30. Sauvageau C, Duval B, Gilca V, Lavoie F, Ouakki M: Human papilloma virus vaccine and cervical cancer screening acceptability among adults in Quebec, Canada. BMC Public Health. 2007, 7: 304-10.1186/1471-2458-7-304

31. Kwan TT, Chan KK, Yip AM, Tam KF, Cheung AN, Lo SS, Lee PW, Ngan HY: Acceptability of human

papillomavirus vaccination among Chinese women: concerns and implications. BJOG. 2009, 116: 501-10. 10.1111/j.1471-0528.2008.01988.

32.Marrazzo JM, Koutsky NB, Kuypers JM, Stine K. Papanicolaou test screening and prevalence of genital human papillomavirus among females who have sex with women. American Journal of Public Health. 2001:91(6):947-52

33. Harper DM, Franco EL, Wheeler CM, et al. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. Lancet 2006; 367:1247–1255.

34. Koutsky LA, Ault KA, Wheeler CM, et al. A controlled trial of a human papillomavirus type 16 vaccine. N Engl J Med 2002; 347:1645–1651.

35. Mao C, Koutsky LA, Ault KA, et al. Efficacy of human papillomavirus-16 vaccine to prevent cervical intraepithelial neoplasia: a randomized controlled trial. ObstetGynecol 2006; 107:18–27.

36. Villa LL, Costa RL, Petta CA, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. Lancet Oncol 2005; 6:271–278.

37. Hildesheim A, Herrero R, Wacholder S, et al. Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: A randomized trial. JAMA 2007; 298(7):743–753.

38. Schiller JT, Castellsague X, Garland SM. A review of clinical trials of human papillomavirus prophylactic vaccines. Vaccine 2012; 30 Suppl 5:F123-138.

Original Article

Correlation of Estrogen with Serum Insulin and Blood Glucose Levels in Post-menopausal Women

*Yeasmin N[1], Akther QS[2], Hasan M[3], Rabbani R[4], Rabbani R[5], Afroz R[6]

Abstract

Hyperglycemia is a major risk factor for cardiovascular diseases in postmenopausal women. Increased incidence of cardiovascular diseases in postmenopausal women may be due to hyperglycemia caused by lower level of estrogen hormone. This cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka, Bangladesh during the period of January to December 2011 to observe the correlation of estrogen with fasting serum insulin (FSI) and fasting blood glucose (FBG) levels in postmenopausal women. A total of 90 women were selected from different areas of Dhaka city, among them, 60 postmenopausal women of age group 50 to 60 years were taken as study group and 30 apparently healthy premenopausal women of age group 20 to 30 years were included as comparison group. The study parameters fasting blood glucose level was estimated by enzymatic method in both groups. Serum insulin level was estimated by Enzyme Linked Immunosorbent Assay (ELISA) and serum estrogen level by RIA method in order to assess the hormonal level of both groups. Data was analyzed by Unpaired Student's 't' test and Pearson's correlation co-efficient (r) test as applicable. Mean serum fasting insulin level and mean blood glucose level was higher in postmenopausal women than premenopausal and result was statistically significant. In postmenopausal women serum estrogen level was lower than premenopausal and serum estrogen level showed negative correlation with serum fasting insulin level. Blood glucose level also showed negative correlation with serum estrogen level. All these correlation were statistically non-significant. It may be concluded that the serum fasting insulin and blood glucose levels are significantly higher in postmenopausal women that may be due to low level of estrogen.

Key word: Fasting serum insulin, Fasting blood glucose, Estrogen, Postmenopausal women.

1.*Dr. Nahid Yeasmin, Assistant professor, Department of Physiology,

Dhaka Medical College, Dhaka. e-mail: masudaatiqua237@gmail.com

2. Dr. Qazi Shamima Akhter, Professor, Head, Department of Physiology, Dhaka Medical College, Dhaka.

3.Dr. Sayeeda Mahmuda, Associate professor, Department of Pathology, National Institute of Ophthalmology and Hospital, Sher-E- Bangla Nagar, Dhaka.

4. Dr. Mahmudul Hasan, Lecturer, Department of Physiology, Dhaka Medical College, Dhaka.

5.Dr. Rukhshana Rabbani, Assistant Professor, Department of Radiotherapy, Dhaka Medical College.and Hospital.

6. Dr. Rumana Afroz, Assistant Professor, Department of Pharmacology, Dhaka Medical College, Dhaka.

*Corresponding Author

INTRODUCTION:

Menopause is defined as the permanent cessation of menstruation resulting from the loss of follicular activity. It is recognized by the presence of amenorrhea for 12 consecutive months without any pathological and physiological factors .A new hormonal pattern is established at menopause, which is characterized by high levels of follicle stimulating hormone (FSH), luteinizing hormone (LH) and low level of estrogen.1 Menopause has a wide starting age range, but usually be expected in the range of 42-58 years..

Following menopause due to lack of estrogen, women have increased risk for insulin resistance or hyperglycemia, central obesity, hyperlipidemia, and hypertension.2 Among these factors the insulin resistance or hyperglycemia is the key factor in the development of type 2 diabetes mellitus, heart diseases and end stages renal diseases.3

Diabetes mellitus (DM) is one of the common non-communicable diseases and it is one of the most challenging health problems in the twenty first century.4 There are two general types of diabetes mellitus, one is type 1 or insulin dependent DM (IDDM) and other is type 2 or non-insulin dependent DM. Among them, type 2 diabetes mellitus is more common and about 90 to 95% of all cases of diabetes mellitus.5

According to American Diabetes Association, diagnostic criteria of diabetes mellitus are fasting blood glucose ≥7.0 mmol/l or 2hours after 75 gm glucose ≥11.1mmol/l or random blood glucose ≥11.1 mmol/l or HbA1c ≥ 6.5%.6

According to International Diabetic Federation (IDF), about 24.4 million diabetic people in USA, 65.1 million in India and 5.1million in Bangladesh. This number is gradually increasing day by day will rise to 592 million by the year 2035 representing about 8.8% of the world population. By the year 2035, the number of diabetic people will be about 29.7 million in USA, 109.2 million in India and 16.8 million in Bangladesh.7

Insulin is a hormone produced by beta cells a specialized kind of cells in the pancreas. Insulin reduces blood glucose by

inducing glucose uptake in insulin sensitive tissue such as skeletal muscle, fat cells and heart. In the skeletal muscle insulin prompts glucose uptake by stimulating translocation of the GLUT4 glucose transporter to the plasma membrane. Insulin also inhibits glucose production in liver, kidney and small intestine.8 Insulin resistance occurs when the insulin sensitive tissue loses response to insulin. The basic effect of insulin resistance on glucose metabolism is to prevent the uptake and utilization of glucose by most cells of the body. As a result, blood glucose concentration increases, cell utilization of glucose falls and utilization of fats and proteins increase. Plasma insulin concentration usually increases as a compensatory response by the pancreatic beta cells for diminished sensitivity of target tissues to the metabolic effects of insulin. As a result raising blood glucose and stimulating a compensatory hyperinsulinemia.9- 11

Diabetes mellitus (DM) is common in postmenopausal women and is a major risk factor for cardiovascular diseases, the leading cause of mortality in women. In the United States, at least 1.8 million women of reproductive age (18-44 years) are estimated to have DM compared with 3.8 million among women aged 45-65. 12

Some epidemiological studies observed that postmenopausal women with diabetes have a coronary heart diseases (CAD) related mortality rate 4to 7 times higher than that of non-diabetic postmenopausal women. Again premenopausal women with diabetes have CAD related mortality 2 to 4 times higher than that of non-diabetic premenopausal women.13

The postmenopausal year is associated with rise of fasting insulin and glucose levels. The marked decline in endogenous estrogen production after menopause, resulting in increased relative androgenicity and change in body composition is suggested to influence pancreatic β-cell function, insulin induced glucose transport and hepatic glucose output.14

Estrogen is a steroid hormone produced primarily in the ovaries and too much lesser extent in other cells like fat tissue. Estrogen production from the ovaries declines around and after menopause.15

Estrogen may have beneficial effect on insulin sensitivity via a number of possible mechanisms direct effects on insulin and glucose homeostasis, involvement in adipose tissue metabolism and body composition and pro-inflammatory markers.16

During menopause decreases the production of estrogen and followed by post-glucose challenge hyperinsulinemia, implying insulin resistance. In postmenopausal women due to lack of estrogen decreased insulin mediated glucose uptake via an impaired insulin stimulated translocation of GLUT4 to the plasma membrane and decreased protein expression of glycogen synthase.17

Some other studies also reported that serum insulin and blood glucose levels are higher in postmenopausal women than that of premenopausal women.1,15,17 Opposite finding was reported by some investigators they did not find any significant difference in serum insulin level between premenopausal and postmenopausal women.18

Increased incidence of coronary artery diseases (CAD) resulting from increased levels of serum insulin and blood glucose, have been reported. But very few publication about the effect of estrogen on serum insulin and blood glucose levels in postmenopausal are available. Therefore, this study has been designed to observe the correlation of estrogen with serum insulin and blood glucose levels in postmenopausal women.

METHOD:

This cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka, during the period of January 2011 to December 2011. A total number of 90 female subjects were selected from different areas of Dhaka city by simple random sampling. Among them, 60 postmenopausal women with age ranging from 50 to 60 years were taken as study group and 30 apparently healthy premenopausal women with age ranging from 20 to 30 years were included as control group for comparison. Subjects having history of heart, liver, kidney diseases and women taking hormone replacement therapy steroid, alcohol user, and smoker were excluded from the study. After selection of the subjects, the objectives, nature, purpose and benefit of the study were explained to the subjects in details. They were encouraged for voluntary participation. They were also allowed to withdraw from the study whenever they feel like. Ethical permission was taken from ethical committee of Dhaka medical College. Written informed consents were taken from the participants. Detailed medical history, menstrual history and family history of the subjects were taken and recorded in a pre-designed data collection form. Then with all aseptic precautions 5ml of venous blood from each subject was collected after an overnight fast (at least 12 hours) from median cubital vein by disposable plastic syringe. Blood was allowed to clot and then centrifuged at a rate of 3000 rpm and supernatant clear serum was separated. Serum was taken in to eppendrof tube and was preserved in refrigerator in Department of Physiology of Dhaka Medical College, Dhaka. Then estimation of serum estrogen level was done by Radioimmunoassay (RIA) method in the Department of Nuclear Medicine, Dhaka Medical College. Estimation of serum insulin level was done by Enzyme Linked Immunosorbent Assay (ELISA) method in the Department of laboratory of National Institute of ENT, Dhaka and fasting blood glucose was estimated by glucose oxidase method in the Department Dhaka Medical College in both groups. Statistical analysis was done by Unpaired Student's't' test. Correlation was analyzed by Pearson's correlation co-efficient (r) test. P value <0.05 was taken as of significance.

Table I: Age, fasting serum insulin (FSI) and fasting blood glucose (FBG) level in premenopausal and postmenopausal women

Groups	n	Age (years)l	FSI(μIU/ml)	FBG(mg/dl)
A	30	28.77±6.66	10.05±3.07.	87.90±27.45
B	60	53.90±5.75	19.10±8.41	118.14±50.17

Statistical analysis

Groups	Age (p value)	FSI (p value)	FBG (p value)
A vs. B	0.0001***	0.0001***	0.003**

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.

Group A : Premenopausal women n = Number of subject

Group B : Postmenopausal women ns = Not significant

*** = Significant at P<0.001

In this study, the mean (± SD) of age was 28.77 ± 6.66 years in group A and 53.90± 5.75 years in group B. The age in group B was higher than that of group A and the result was statistically significant (p<0.0001).

Figure-1: Mean fasting serum insulin level in premenopausal and postmenopausal women

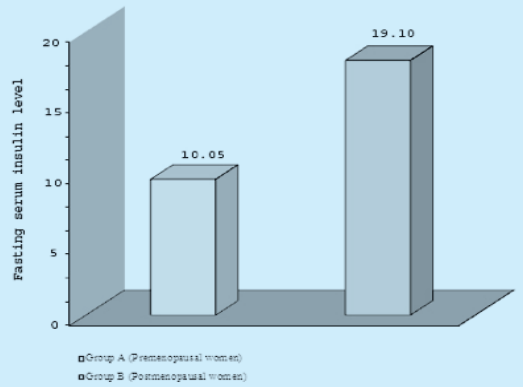


Figure- 1 shows the mean (±SD) of serum insulin level 10.05±3.07μIU in group A and 19.10±8.41μIU in group B. The serum insulin level was higher in postmenopausal women (group B) than those of premenopausal women (group A) and the result was statistically significant (p<0.001).

Figure- 2: Mean serum fasting blood glucose level in premenopausal and postmenopausal women.

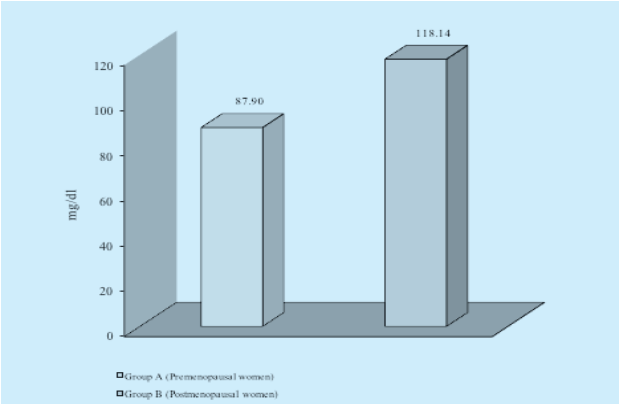


Figure- 2 shows the mean (±SD) of blood glucose level 87.90±27.45 mg/dl in premenopausal women (group A) and 118.14±50.17 mg/dl in postmenopausal women (group B). The result was significantly (p<0.01) higher in postmenopausal women (group B) than those of premenopausal women (group A). (Figure- 2)

Table II: Serum estrogen level in premenopausal and postmenopausal women

Groups	n	Estrogen (pg/ml)
A	30	81.69±36.61
B	60	25.60±17.35

Groups	Serum estrogen (p value)
A vs B	0.003**

Results are expressed as mean±SD

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.

Group A : Premenopausal women n= Number of subjects
Group B :Postmenopausal women **= Significant at P<0.01
***=Significant at P<0.0

The mean (± SD) of estrogen level was 81.69±36.61 pg/ml in group A and 25.60±17.35 pg/ml in group B. The estrogen level was lower in group B than that of group A and the result was statistically significant (p<0.001) (Table-II).

Table-III: Correlation of serum estrogen level with biochemical parameters in postmenopausal women

Parameters	Group B (n=60)	
	R	p
FSI	0.062	0.0638ns
FBG	--0.063	0.632ns

Table-III shows the pearson's correlation coefficient (r) test to compare relationship between parameters. The test of significance was calculated and p value <0.05 was accepted as level of significance

Group B : Postmenopausal women
n =Number of subjects
ns = Not significant

The serum estrogen level negative correlation (r = - 0.062) with serum insulin level in postmenopausal women and result was statistically non-significant. In postmenopausal women the blood glucose level showed negative correlation (r = -0.063) with serum estrogen level and result was statistically non-significant.

Figure- 3: Correlation of serum estrogen and fasting serum insulin level in postmenopausal women

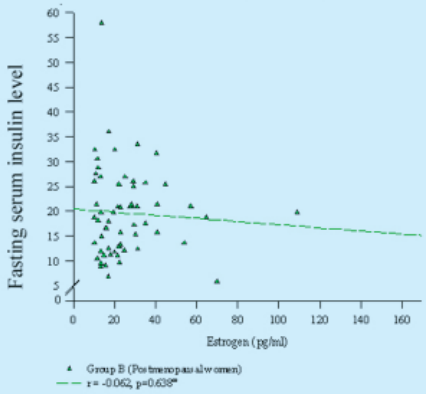


Figure- 3 shows the serum estrogen level negative correlation (r = - 0.062) with serum insulin level in postmenopausal women and result was statistically non-significant. In postmenopausal women the blood glucose level showed negative correlation (r = -0.063) with serum estrogen level and result was statistically non-significant.

Figure- 4: Correlation of serum estrogen and fasting blood glucose in postmenopausal woman

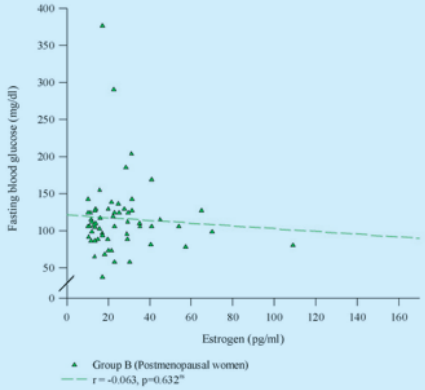


Figure- 4 shows the serum estrogen level negative correlation (r = - 0.062) with serum insulin level in postmenopausal women and result was statistically non-significant. In postmenopausal women the blood glucose level showed negative correlation (r = -0.063) with serum estrogen level and result was statistically non-significant.

DISCUSSION:

In the present study the levels of fasting serum insulin and blood glucose in healthy premenopausal women were almost within normal range and also similar to reported by the several investigators from abroad.1-4

The mean serum insulin level in postmenopausal women was higher than that of premenopausal women and result was statistically significant. Similar types of findings were reported by different researchers of different countries.8,13,15 On the contrary, similar observations were made by other researchers but they did not find any significant difference in fasting serum insulin level. This result may be due to small sample size in their study.18 Again, in our study, fasting serum insulin level showed negative correlation with serum estrogen level in postmenopausal women. Similar type of result was found by other workers.13

The level of fasting blood glucose in postmenopausal was higher than those of premenopausal women and result was statistically significant. Similar types of findings were reported by different researchers of different countries13,15 Again, in our study, blood glucose level showed negative correlation with serum estrogen level in postmenopausal women and result was statistically non-significant. .

Many explanations are suggested by different investigators regarding development of insulin resistant in postmenopausal women. It has been suggested that estrogen has regulatory influence on the function of pancreatic β-cells. Estrogen regulates insulin action directly via action on insulin sensitive tissues or indirectly by regulating factors

like oxidative stress, which plays important role in development on insulin resistance. In skeletal muscle estrogen is thought to have positive effect on insulin signaling and GLUT4 expression. Estrogen enhances insulin-induced glucose transport by activating phosphatidyl inositol-3 kinase signaling, leading to translocation of GLUT4 to the plasma membrane. This process increase insulin mediated glucose uptake into cells.16,17

Again, increased accumulation of central abdominal fat in women at the time of menopause is associated with a decline in the production of a protein called adiponectin. Adiponectin, which is produce by fat cell is important for glucose and fatty acid metabolism. It makes muscle and liver cells more sensitive to the action of insulin. Moreover it stimulates glucose utilization in muscle, thus decreases blood glucose level. So decreased level of adiponectin in postmenopausal women are associated with increased blood glucose level.18,19

It is well known that estrogen has anti-inflammatory properties. In postmenopausal women due to lacking of estrogen there are increased cytokine levels, including TNF, IL-1 and IL-6. These inflammatory markers are associated with insulin resistance either directly by affecting the insulin signaling pathway or indirectly by stimulation of inflammatory pathway.20-22

In the present study, both fasting serum insulin and blood glucose levels are higher in postmenopausal women than premenopausal women. This is most likely due to lower level of estrogen, as the measured value of estrogen was lower in postmenopausal women than premenopausal women. Furthermore, in the present study, fasting serum insulin and blood glucose levels, showed negative correlation with serum estrogen level in postmenopausal women. These correlations further support these findings. But exact mechanism is not elucidated by this type of study due to time and financial constraints.

From this study, it can be concluded that higher values of fasting serum insulin and blood glucose may present in postmenopausal women may be due to their lower level of estrogen hormone.

REFERENCE:

1. ZA,Begum,S,Ferdousi,S, Begum, Ali,T, & Begum,A. FVC,FEV,and FEV/FVC in postmenopausl women and their relationship with serum progesterone and estrogen level..J Bangladesh Soc Physiol.2009; 4(1): 7-13.

2. Hidalgo LA, Chedraul PA, Morocho N,Alvarado M, Chavez D and Hue A. The metabolic syndrome among postmenopausal women in Ecuador. Gynecol Endocrinol .2006; 22(8): 447-54.

3. Heidery R, Masoumeh s, Mohammad T, Kateyour R, Noushin Nizal S. Metabolic syndrome in menopausal transition: Isfahan healthy heart program, a population based study. Diabeto Metab syndr.2010;2:59-67.

4. Sadu MM, Protasiewicz DC, Firanescu AG. Data regarding the prevalence and incidence of diabetes mellitus and prediabetes. Rom J Diabetes Nutr Metab Dis.2016;23(1):95-103.

5. Hall, JE. Guyton & Hall Text Book of Medical Physiology. 12th ed. India :Elsevier limited;2011; p. 618.

6. American Diabetes Association.Classification and diagnosis of Diabetes.Diabetes Care.2015; 38(1): S8-16.

7. Guariguata .L, Whiting. DR, Hambleton I. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Prect. 2013; 103(2014): 137-49.

8. Mercurio V, Carlomango G, Fazio V & Fazio S. Insulin resistance is it time for primary prevention? World J Cardiol.2012; 4(1):1-7.

9. Pessin. JH & Sal.Signatiel AR. Signaling pathways in insulin action: molecular targets of insulin resistance. J Clin Ivest.2000; 106(2):64-69.

10. Brand JS,Vaan der Schouw YTand Onland Moret NC.Age at menopause, reproductive life span and type 2 diabetes risk: Result from the EPIC-Inter Act study. Diabetes Care.2013; 36(1):1012-19.

11. Kim C. Does menopause increase diabetes risk? Strategies for diabetes prevention in midlife women. Women Health.2012; 8:155-67.

12. Sathya Bhana CV, Balaji S, Seethalakshni A. Analysis of the degree of insulin resistance in postmenopausal women by using skin temperature measurements and fasting insulin and fasting glucose levels: A case control study.Journal of clinical and diagnostic research.2012;16(10): 1644-47.

13. Duke Appiah,Stephen J andCarlton A. Hornung. Bilateral Oophorectomy and the risk of incident diabetes in postmenopausal women.Diabetes Care.2014;37(1):725-33.

14. Kumagai S,Holmang A, Bjorntorp.The effects of estrogen and progesterone on insulin sensitivity in female .Acta Physol Scand. 1993;149: 91-97.

15. Surapon Tangvarasiittichi. Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus.World journal of Diabetes 2015; 6(3):456-80.

16. Cambell SE,Febbraio MA. Effect of the ovarian hormones on GLUT4 expression and contraction-stimulalated glucose uptake. AMJ Physiol Endocrinol Metab.2002; 282:E1139-E1146.

17. Ying Zhang,Barbara V. Howard, Linda D Crawn, Jeunliang Yeh and Carl F Schaefer. The effect of estrogen use on levels of glucose and insulin and risk of type 2 diabetes in American Indian postmenopausal women.Diabetes

Care.2002; 25(3):500-4.

18. Baily CJ, Ahmed Sorour H. Role of ovarian hormones in the long term control of glucose homeostasis and effect of insulin secretion. Diabetologia.1980; 19:475-78.

19. Mankowska, Lena,N and Grazyna, S.Adiponectin and metabolic syndrome in women at menopause. Diabetic News.2011.

20.Koyong Park,Myron Gross,Duk-Hee Lee,Paul Holvoet, John H Himes, James M Shikany.Oxidative stress and Insulin Resistance. Diabetic Care.2009; 32(1):1302-307.

21. Cari de Luca & Jerrold M, Olefsky. Inflammation and insulin resistance.NIH public Access.2008; 582(1):97-105.

22. Ana L,Guadarrana Lopex,Roxana Valdes Ranos and Beatrize Martinez Carrillo. Type 2 diadetes,PUFAS and vitamin D: Their relation to inflammation.Journal of Immunology Research.2014;(2014):8-13

Case Report

Leflunamide Induced Pneumonitis in Rheumatoid Arthritis - A Case Report and Review of Literature

*Mojumdar SK[1], Islam MN[2] , Ahmedullah AK[3], Shahin MA [4], Hassan MM[5]

Abstract

A 51 year old woman while treated on methotrexate (MTX) and leflunomide (LEF) for rheumatoid arthritis (RA), developed exertional breathlessness and undue tiredness followed by fever and cough, at her 11 years of suffering. Her respiratory symptoms developed around 12 weeks after leflunomide intake. She improved with steroid treatment. The Leflunomide (LEF) induced interstitial pneumonitis is an uncommon condition in absence of prior lung disease but potentially fatal. We report a case of Leflunomide (LEF) induced interstitial pneumonitis.

Key words: Rheumatoid arthritis, drug induced pneumonitis, methotraxate, leflunomide

INTRODUCTION:

Methotrexate (MTX) is the most commonly used disease modifying anti-rheumatic drug (DMARD) in RA.1 At low dose (<30mg), MTX has immunosuppressive and anti-inflammatory properties. 2 Other than therapeutic effect and well tolerability, one of the most serious infrequent side effects of this agent is MTX induced pneumonitis.3 Leflunomide (LEF) is another DMARD that have immunomodulatory effect had clinical outcome similar to MTX. It is also prescribed to manage RA since 1998.4 It has good safety profile but it can cause some side effects and pneumonitis is one of the reported one.5 We discuss here a patient who developed leflunomide induced pneumonitis. Who was on MTX for nine years.

1. *Dr. Sumon Kanti Mojumdar , Phase B rheumatology student, Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh. Email: dskm.noa@gmail.com

2. Dr. Md. Nazrul Islam Professor of rheumatology, Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.

3. Dr. Abul Khair Ahmedullah Assistant professor, Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.

4. Dr. Md. Abu Shahin Associate professor, Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka-1000, Bangladesh.

5. Dr.Md. Masudul Hassan Department of Rheumatology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, Bangladesh

*Corresponding Author

CASE REPORT:

A 51-year-old woman has been suffering from RA since 2005. She was in remission for nine years with MTX at a dose of only 10 mg/week. At 10th year she experienced a mild flare of RA and went into remission after escalation of MTX at 12.5 mg weekly but failed to maintained remission and MTX doses was raised in subsequent flare gradually up to 25 mg but complete remission could not be achieved. To achieve target 20 mg leflunomide was added to MTX. After 3 months of MTX and leflunomide combination she again achieved remission (CDAI-2) and was relatively well until early May, 2016. But she suddenly developed fever, dry cough, progressive exertional shortness of breath and marked tiredness. Her physical findings were unremarkable. Few days later she got herself admitted in hospital for progressive deteriorations. Her respiratory rate was 30 breaths /minute, temperature was normal, pulse was 88 beats /minutes, BP was 120/80 mm Hg and oxygen saturation was 90%. She was evaluated with the clinical consideration of Pneumonia, acute asthma, pneumonitis, DPLD and/or pulmonary hypertension. Asthma, pneumonia, pulmonary hypertension were excluded after both clinical and laboratory evaluation.

Following investigations were done (table 1).

Table 1: Baseline investigations

Hb	11.4 gm/dl
Total WBC	6890/mm3
Eosinophilia	13%
ESR	96 mm in 1st hour
CRP	7.13 mg/dl
X-ray chest P/A view	Bilateral interstitial and alveolar opacities in mid and basal region

Hb = Haemoglobin, WBC= white blood cell count,
ESR= Erythrocyte sedimentation rate,
CRP= C - reactive protein, P/A= posterior/ anterior

Her hematological, renal and liver funcrion tests were normal with normal blood and urine culture. ECG, Echo-cardiography, spirometry and DLCO were normal. X-ray

chest P/A view showed bilateral interstitial and alveolar opacities in mid and basal region. HRCT of chest showed diffuse hyper attenuated areas with interstitial fine septal thickening intermixed with ground glass opacities in all segments of both lung fields predominantly in basal segments. (Figure-1A)

With that drug induced pneumonitis (most probably leflunomide) was suspected and both MTX and LEF were stopped. Prednisolone 40mg/day was started with other supportive treatments. Her fever started settling down and she symptomatically started to improve with lesser cough and breathlessness.

Figure- 1: HRCT of chest before (A) and after treatment (B) with steroid.

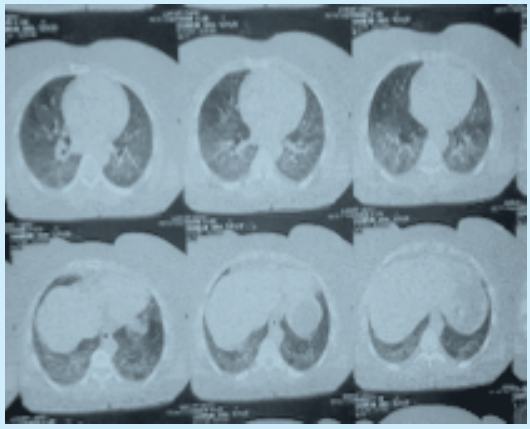


Figure -1(A)

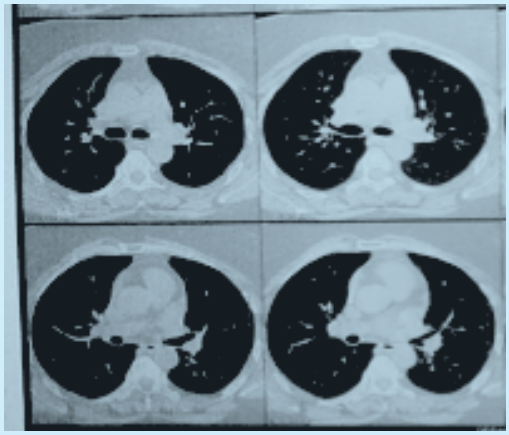


Figure-1(B)

During first follow up after one month, she had no breathlessness or cough but complained of generalized weakness. Physical examination was unremarkable. Serum electrolytes, RBS and Serum creatinine were normal.

After two months of treatment there only was generalized weakness. Physical examination was unremarkable. Investigation reports revealed normalization of eosinophilia (01%) and ESR (26 mm in 1st hour). Repeat HRCT showed few calcified foci with marked improvement of previous shadow. (Figure-1B)

DISCUSSION:

The active metabolite of Leflunomide is A77 1726 which inhibits dehydroorotate dehydrogenase.6 In previous trials, LEF was proved to be as effective as MTX in improving joint symptoms and to halt the radiological progression of RA patients. 7 The relation between onset of pneumonitis and the initiation of LEF makes the strong possibility for the diagnosis of leflunomide induced pneumonitis (LEIP). Most LEIP patients had previous exposure with MTX and it is not surprising because LEF is used as second line therapy after MTX; but LEIP was also reported in MTX naïve patients.8 Both MTX and LEF can induce pneumonitis either as monotherapy or in combination. In most of the cases the LEIP and MTX-P are indistinguishable. Currently, there is no available established clinical criteria that can distinguish LEIP from MTX-P but there are some differences in presentation between MTX-P and LEIP. LEIP symptoms usually appear acutely (median duration is 3 days and the range is 1–10 days), but in MTX-P symptoms appear sub-acutely (median duration is 14 days and the range is 1–56 days) .9 MTX-P occurs within first twelve months of therapy but LEIP commonly occur within the first five months of starting treatment.10 In our patient , though she was on methotrexate but pneumonitis developed 3 months after starting leflunamide which suggest , according to this literature review, pneumonitis was due to leflunamide.

Many patients were on methotrexate prior to leflunomide, and methotrexate can be presumed as the cause of DPLD. While a patient is on methotrexate, development of pneumonitis soon after adding leflunomide suggests that leflunomide is responsible for pneumonitis and this are similar reports .11

LEIP incidence varies from 0.08% to 0.49% with a mortality of 0.7% .12 LEIP can occur while treated with leflunomide alone or combined with MTX.13 Some author claimed that previous treatment with MTX augment the development of LEIP.14¬¬ Ground glass appearance, bilateral interstitial nodular pattern, alveolar consolidation and honeycomb appearances are common findings in HRCT in LEIP.13 Which is consistent with our patient. Higher dose (100mg), age, body weight <40 kg male sex, presence of previous lung injury, genetic predosposition, treatment history with MTX are the risk factors for LEIP.16

In this case, there was diffuse alveolar consolidation, ground glass densities, and septal thickenings, consistent with the

findings reported in the literature. Especially discontinuation of LEF and MTX, faster clinical and radiological regression after steroid justified the diagnosis of LEIP in this case and plasma exchange could be an alternative method to clear the active metabolites.15

CONCLUSIONS:

During the treatment period with leflunomide, we suggest for giving importance to the nonspecific pulmonary symptoms even in absence of physical signs as high index of suspicion and a prompt treatment with steroid might bring successful outcome in LEIP.

REFERENCES:

1. Chan V, Tett SE. Changes in use of disease-modifying antirheumatic drugs in Australia over the period 1992-2004. PharmacoepidemiolDrug Saf 2006; 15: 462-8.

2. Emery P, Breedveld FC, Lemmel EM, et al. A comparison of the efficacy and safety of leflunomide and methotrexate for the treatmentof rheumatoid arthritis. Rheumatology (Oxford) 2000; 39: 655-65.

3. Kinder AJ, Hassell AB, Brand J, Brownfield A, Grove M, Shadforth MF. The treatment of inflammatory arthritis with methotrexate in clinical practice: treatment duration and incidence of adverse drug reactions. Rheumatology 2005; 44: 61.

4. Cohen S, Cannon GW, Schiff M et al. Two-year, blinded, randomized, controlled trial of treatment of active rheumatoid arthritis with leflunomide compared with methotrexate. Utilization of Leflunomide in the Treatment of Rheumatoid Arthritis Trial Investigator Group. Arthritis Rheum 2001; 44:1984–92.

5. Sakai F, Noma S, Kurihara Y, Yamada H, Azuma A, Kudoh S, et al. Leflunomide-related lung injury in patients with rheumatoidarthritis. Mod Rheumatol 2005; 15:173–9.

6. Chong AS, Huang W, Liu W et al. In vivo activity of leflunomide: pharmacokinetic analyses and mechanism of immunosuppression. Transplantation 1999; 68:100–9.

7. Cohen S, Cannon GW, Schiff M et al. Two-year, blinded, randomized, controlled trialof treatment of active rheumatoid arthritis with leflunomide compared with methotrexate.Utilization of Leflunomide in the Treatment of Rheumatoid Arthritis TrialInvestigator Group. Arthritis Rheum 2001; 44:1984–92.

8. Otsuka T, Koyama T, Ohtani R et al. Leflunomide-induced lung injury that developedafter its withdrawal, coinciding with peripheral blood lymphocyte count decrease.Mod Rheumatol 2008; 18:96–9.

9. Chikura B, Sathi N, Lane S, Dawson JK. Variation of immunological response in methotrexate-induced pneumonitis. Rheumatology 2008; 47:1647–50.

10. Savage RL, Highton J, Boyd IW, Chapman P. Pneumonitis associated with leflunomide:a profile of New Zealand and Australian reports. Intern Med J 2006; 36:162–9.

11. Savage RL, Highton J, Boyd IW, Chapman P. Pneumonitis associatedwith leflunomide: A profile of new zealand and australian reports.Intern Med J 2006;36:162-169.

12. Kelly C. Leflunomide and the lung. Rheumatology (Oxford) 2009; 48:1017-8.

13. Carloni A, Piciucchi S, Giannakakis K, Nori G, Zobel BB, Poletti V. Diffuse alveolar hemorrhage after leflunomide therapy in a patient with rheumatoidarthritis. J Thorac Imaging 2008; 23: 57-9.

14. Chikura B, Lane S, Dawson JK. Clinical expression of leflunomide-induced pneumonitis. Rheumatology (Oxford) 2009; 48: 1065-8.

15. Inokuma S, Sato T, Sagawa A, Matsuda T, Takemura T, Ohtsuka T,Saeki Y,TakeuchiT, SawadaT. Proposals for leflunomide use to avoidlung injury in patients with rheumatoid arthritis. Mod Rheumatol 2008;18:442-446.

16. Güzel, A., Köksal, N., Gök, A., & Elmalı, M. Leflunomide-Induced Interstitial Lung Disease: A Case Report. Eurasian J Pulmonol 2015; 17: 67-9.

Case Report

Acute Lymphoblastic Leukemia Presenting as Acute Low Back Pain in a Young Man- A Case Report

*Islam KA[1], Hassan MN[2], Mafruha S[3], Ahmed M[4], Islam KMK[5], Kabir AL[6], Yunus ABM[7]

Abstract

Here we describe a case of a 20-year-old, otherwise healthy man, who consulted a physician due to acute low back pain presenting for a couple of days. Pain appeared suddenly, without any preceding trauma. Physical examination was unremarkable. Initial laboratory tests showed elevated inflammatory marker and thrombocytopenia. Patient was treated conservatively but due to increasing pain MRI of spine with contrast was advised which showed feature suggestive of infiltrative disease. Eventually patient was diagnosed as a case of acute lymphoblastic leukaemia on further peripheral blood film and bone marrow study.

Key words: acute lymphoblastic leukaemia, low back pain, leukaemic infiltration.

INTRODUCTION:

Acute lymphoblastic leukaemia (ALL) is a malignant tumor of haemopoietic progenitor cell of lymphoid lineage of mostly unknown etiology. Though it is most common malignancy in children but rare leukaemia in adults (0.7-1.8/100000 annually)1. It is commonly presented with the features of bone marrow failure like weakness due to anaemia, bleeding manifestations due to thrombocytopenia and recurrent infections due to neutropenia. CNS, testes and gut involvement or bone pain due to marrow expansion are some other uncommon features. ALL is usually diagnosed by peripheral blood film and bone marrow examination. Low back pain is a rare symptom for ALL, but the initial hint of MRI report present with unusual lumbo-sacral spine was leaded us to present this case.

1.*Dr. Khaza Amirul Islam,MD phase-B resident, Department of Haematology, Bangabandhu Sheikh Mujib Medical University , Dhaka, Email: khazaamirulislamrubel@gmail.com

2. Dr. Nazmul Hassan, Assistant Professor, Department of Internal Medicine Bangabandhu Sheikh Mujib Medical University, Dhaka.

3. Dr. Sharmin Mafruha, MD phase-B resident ,Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

4. Dr. Munim Ahmed, Medical Officer, Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

5. Dr. Kazi Mohammad Kamrul Islam, Research Assistant, Department of Haematology Bangabandhu Sheikh Mujib Medical University, Dhaka.

6. Dr. Amin Lutful Kabir, Associate Professor,Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

7. Prof. Dr. A.B.M. Yunus , Professor, Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

*Coresponding Author

CASE PRESENTATION:

A twenty years old man presented to a physician with acute low back pain for a couple of days. Symptoms appeared suddenly and were not associated with preceding trauma. Pain was intensified especially during night and waking him from sleep. Pain was exacerbated by movement, there was no radiation, no morning stiffness and not associated with lower limb weakness. On query, he did not give any history of heavy weight lifting, fever, weakness or bleeding from any site of body.

On examination temperature was 36.5 ˚c, heart rate- 78/min, blood pressure- 120/70 mm 0f Hg, respiratory rate 16 breath/min but no anaemia, jaundice, lymphadenopathy or bony tenderness. Examination of spine reveals movement of lumber spine restricted in all direction with mild local tenderness. There was no local deformity. Examination of SI joint was normal. CBC showed Haemoglobin- 11.4 gm/dl, Platelet- 80 ×109/L, WBC- 8×109/L including Neutrophil- 49 %, Lymphocyte- 38 %, Monocyte- 9 %, Eosinophil 2%, Basophil-2% and ESR- 32mm in first hour. On peripheral blood film examination revealed no atypical cell. Inflammatory marker CRP was 138 mg/L. Chest X-ray P/A view, X-ray SI joint AP and oblique view revealed normal finding. Patient was started on NSAID (Naproxen 250 mg bid) and muscle relaxant (Baclofen 10mg bid), without clinical improvement rather the patient deteriorated.

As pain was deteriorating, patient was advised to do an MRI of lumbo-sacral spine with contrast which revealed diffuse marrow reconversion changes with few irregular enhancing altered signal intensities – suggestive of infiltrative disease.(Figure- 1) Then peripheral blood film was examined and bone marrow biopsy was done. Peripheral blood film showed RBC- anisocytosis with anisochromia, WBC- Neutropenia with some atypical looking mononuclear cell, Platelet- Reduced. Comment- Thrombocytopenia with atypical looking cell.(Figure- 2) In bone marrow biopsy image was hyper cellular, both myeloid and erythroid series were depressed and lymphocyte were increased in number having shift to the left. About 50% cells were atypical

looking mononuclear cells having increase nucleo-cytoplasmic ratio, dense chromatin and most of the cells are vacuolated giving an impression of acute lymphoblastic leukaemia (ALL).(Figure- 3) On flow cytometry- cells were CD 79a +, CD 19+, HLADR +.So patient diagnosed as a case of B cell linage acute lymphoblastic leukaemia. Unfavorable prognostic fusion gene BCR-ABL was negative but full panel of cytogenetic study could not be done due to financial constrain.

Adult BFM protocol was planned for treatment, meanwhile patient became icteric. On examination patient had firm, smooth hepatomegaly. Workup for jaundice reveled S. bilirubin (total) 5.31 mg/dl, S. bilirubin (direct) 4.91 mg/dl, SGPT- 62.18 U/L, SGOT- 215.75 U/L, Alkaline Phosphatase- 468.48 U/L, prothrombin time- 12 s. All the viral markers were negative. Ultrasonography of Hepatobiliary system revealed hepatomegaly with prominent periportal echo. Due to financial constrain complete evaluation of jaundice such as liver biopsy, MRCP, CT scan of abdomen could not be done. As per available supporting evidence we consider leukaemic infiltration of liver or obstruction of biliary channel at porta hepatis by enlarged lymph node as the cause of jaundice. So we start BFM protocol in compromised dose. Though there was initial rise of hepatic enzymes, but ultimately liver function improved.

After giving compromised dose of induction chemotherapy due to impaired hepatic function patient is now in partial bone marrow remission status(Figure-4) but liver function improves (Table-I).

Table- I. Evolution of liver function tests.

	8-4-17	20-4-17	30-4-17	6-5-17	15-5-17	31-5-17	22-6-17
S. Bilirubin (mg/dl)	4.91	22.65	7.97	4.15	3.01	1.33	0.74
SGPT(U/L)	62.18	244.29	88.31	114.11	97.73	77.89	51.81
SGOT(U/L)	215.75	161.2	53.70	62.34			34.79
Alk. Phosphatase(U/L)	468.24	326.5	498.68	578.50	434.83	373.04	162.04

DISCUSSION:

Typical clinical picture of hematological malignancy is in the form of pale skin and mucous membrane, weakness, fever, bruising, bleeding, bone pain, abdominal pain or lymphadenopathy may mimic other disease2. On the other hand low back pain is a common symptom in adult usually mechanical but may also be a presentation of ALL.

Atypical presentation as well as normal blood picture in early routine test may lead to delay in diagnosis2. Leukemia should always be considered in patients with unexplained pain in the back or of the epiphysis of the long bones, or joint pain out of proportion to the severity of existing arthritis when there is no history of trauma .3,4 Such patient often pose a significant diagnostic dilemma for physician. Frequently they received NSAIDs with lack of clinical improvement and subsequent symptoms including weakness, loss of appetite and bruising led to blood test, which often reveals profound anemia and severe thrombocytopenia. This led to undue delay in diagnosis. Here in this case, patient present with only low back pain and initial PBF was normal but MRI of lumbo-sacral spine with contrast gives the clue of marrow infiltrative disease and ultimately BMS reveals the diagnosis.

For the treatment of ALL cytotoxic chemotherapy are used which have significant hepatotoxic properties. So, normal liver function is a prerequisite for treatment. Though a postmortem study showed liver infiltration in >95% of ALL but it is usually mild and clinically silent at the time of diagnosis5, 6. Jaundice may occur after starting chemotherapy due to hepatotoxicity, but before starting of chemotherapy jaundice may develop if there is preexisting chronic liver disease, viral hepatitis, massive leukaemic infiltration or obstruction of biliary channel due to enlarge lymph node at porta hepatis7. In case of later two liver function should improve after chemotherapy due treatment response which we observe in this case.

LIST OF FIGURES:

Figure-1: MRI of lumbosacral spine showing irregular marrow enhancement.

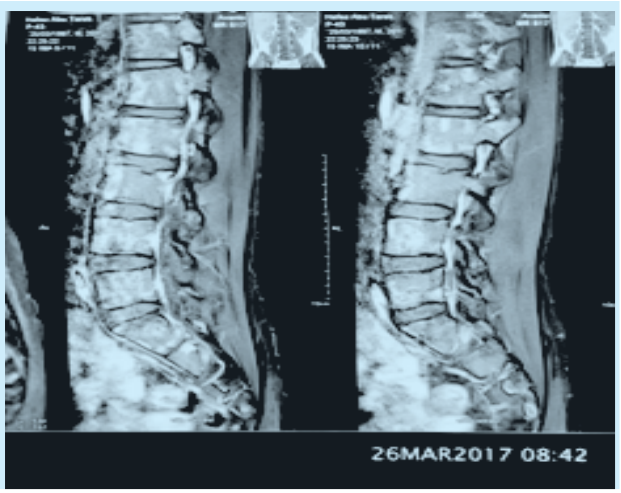


Figure -2: peripheral blood film showing atypical looking atypical looking mononuclear cells.

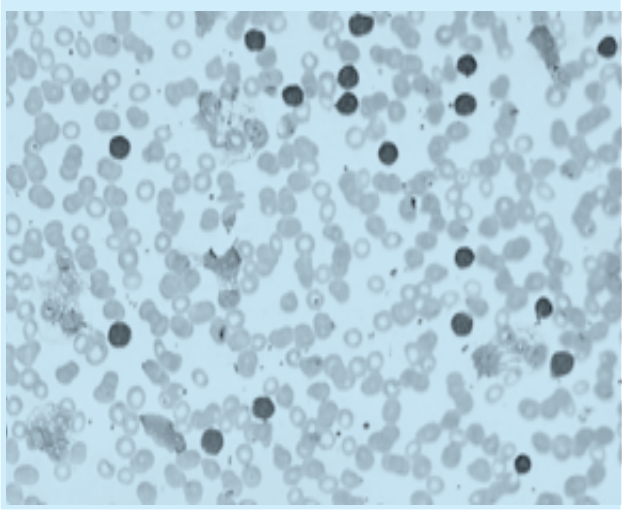


Figure -3: Bone marrow biopsy showing >50% cells are lymphoblast (before treatment)

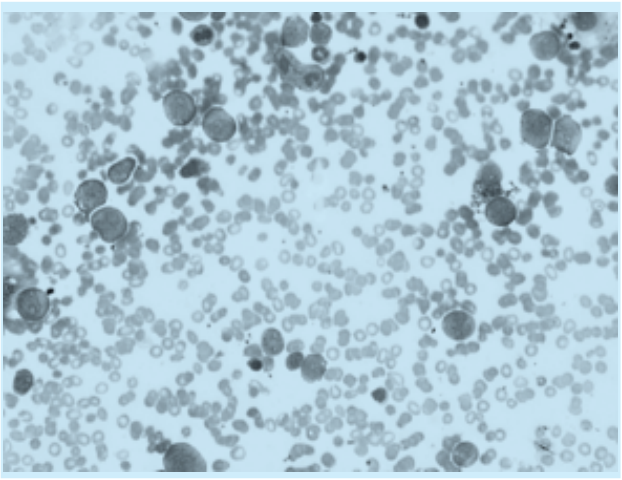
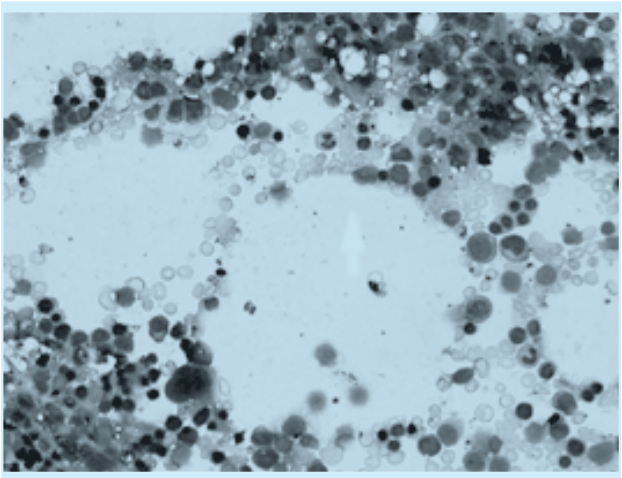


Figure- 4: Bone marrow in partial remission after induction therapy.



REFERENCES

1. Provan D, Baglin T, Dokal I, Vos Jd. Oxford handbook of clinical haematology, 4th ed. Oxford: Oxford university press;2015. p. 138.

2. Szudy A, Litak J, Zawitkowska J, Kowalczyk J. Back pain as a first symptom of hematologic malignancy in a 9-year-old girl. Pediatr Pol 2012;

87(1): 95–8

3. Schaller J, Wedgwood RJ. Juvenile rheumatoid arthritis: a review. Pediatrics 1972; 50: 940–53.

4. Tuten HR, Gabos PG, Kumar SJ et al. The limping child: a manifestation of acute leukemia. J. Pediatr. Orthop. 1998; 18: 625–9.

5. M. Bruguera and R. Miquel, "The effect of hematological and lymphatic diseases on the liver," in Textbook of Hepatology, J. Rod´es, J. P. Benhaumou, A. T. Blei, J. Reichen, and M. Rizzetto, Eds., p. 1662, Blackwell,Oxford, UK, 3rd edition, 2007.

6. D. L. Thiele, "Hepatic manifestations of systemic disease and other disorders of the liver," in Sleisenger & Fordtran's Gastrointestinal and Liver Disease, M. Feldman, L. S. Friedman, and M H. Sleisenger, Eds., p. 1603, Elsevier Science, Philadelphia, Pa, USA, 7th edition, 2002.

7. CESUR S, Topcuoglu P, Asik O, Birengel S, Ozcan M. Acute Hepatic Failure in a Case of Acute Lymphoblastic Leukemia. Turk J Med Sci. 34 (2004): 275-9.

Review Article

The Basics of Ultrasonography

Rashid SQ[1]

Abstract

Ultrasound is sound whose frequency is above the human hearing range. It is nowadays widely used for the evaluation of a patient's internal organs. Ultrasound waves are transmitted into the human body by an instrument called the transducer. Inside the body the sound waves are reflected and scattered differently by the different tissues and organs. The reflected sound waves are used by the computer to form an image of the internal structures and tissues. Use of ultrasound is safe with negligible bio-effects.

INTRODUCTION

Ultrasonography is one of the new tools that we have acquired for diagnostic purpose. It is the brainchild of Dr. Ian Donald who was a gynecologist by profession. His invention has brought newer dimensions to the diagnostic field of not only obstetrics and gynecology but also to the other fields of medicine like internal medicine, surgery, ophthalmology, orthopedics, cardiology etc. and more and more fields are coming into its folds for not only diagnosing diseases but also for therapeutic purpose.

It is a very popular modality with both the physicians as well as the patients. Reason being it is cheap, easily available, non-invasive, and with no radiation hazard. Also because some of the images that it displays on the screen are quite easily understood by the patients even. So that when a pregnant lady views her baby still inside her womb for the first time her joy and her husband's too is quite obvious. The thrill of seeing their baby moving, its heart beating, gives them so much of happiness. A top film star's husband after seeing their baby inside his wife's womb was so excited that he wanted to buy one such machine and keep it at his house!

Then the sight of a moving worm swimming in the bile inside the gall bladder is amazing even for the doctor performing the scan.

ULTRASONOGRAPHY:

Physics of Ultrasound

The basic principle of all ultrasound imaging is that, the ultrasound waves are send into the body, it is then reflected back from the interfaces of the organs and tissues. The reflected waves are then detected and displayed as an image on the monitor.

To produce, detect and process ultrasound data, numerous variables, many under direct user control, must be managed. To do this the user must understand the methods used to generate ultrasound data and the theory and operation of the instruments that detect, display and store the acoustic information generated in clinical examinations.1

Basic Acoustics

Sound is the result of mechanical energy traveling through matter as a wave, producing alternating compression and rarefaction. In the use of ultrasound to produce image of body tissues and organs brief bursts of energy are transmitted into the body where it propagates through the tissue. In the body, propagation velocity of sound is determined by the physical properties of tissue. The velocity of sound in tissues is increased by increase in stiffness and reduced by increase in density. The propagation velocity of sound is assumed to be 1540m/sec. This value is the average of measurements obtained from normal soft tissues.2 Propagation velocity of sound is 4080m/sec in bone and 330m/sec in air. Propagation velocity is important in clinical ultrasound as it is used to determine the distance of the interface or the tissue from the transducer.

To produce an echo, a reflecting interface must be present. Sound passing through a totally homogenous medium, like water, encounters no interface to reflect sound, and the medium appears anechoic or cystic. When sound passes from one tissue to another, some of the incident sound energy is reflected.1 The way ultrasound is reflected when it strikes an acoustic interface is determined by the size and surface features of the interface. If the interface is large and relatively smooth, it reflects sound much as a mirror reflects light. They are called specular reflectors, eg. Diaphragm, and walls of a full urinary bladder. Most echoes in the body do not arise from specular reflectors but come from smaller interfaces within solid organs. Interfaces that are either smaller than the wavelength or not smooth are nonspecular .(Figure-1) The echoes from these nonspecular interfaces are scattered in all directions. They are also called diffuse reflectors and produce the echoes that form the echo patterns seen in different solid organs and tissues eg. liver parenchyma, red blood cells, and other materials representing the tissue characteristics of an organ.[3]

1. Dr. Sabrina Q Rashid , Assistant Professor, department of radiology, University of Science & Technology Chittagong., Dhaka.

Tel: 9116940 (C), 8825365 (R).

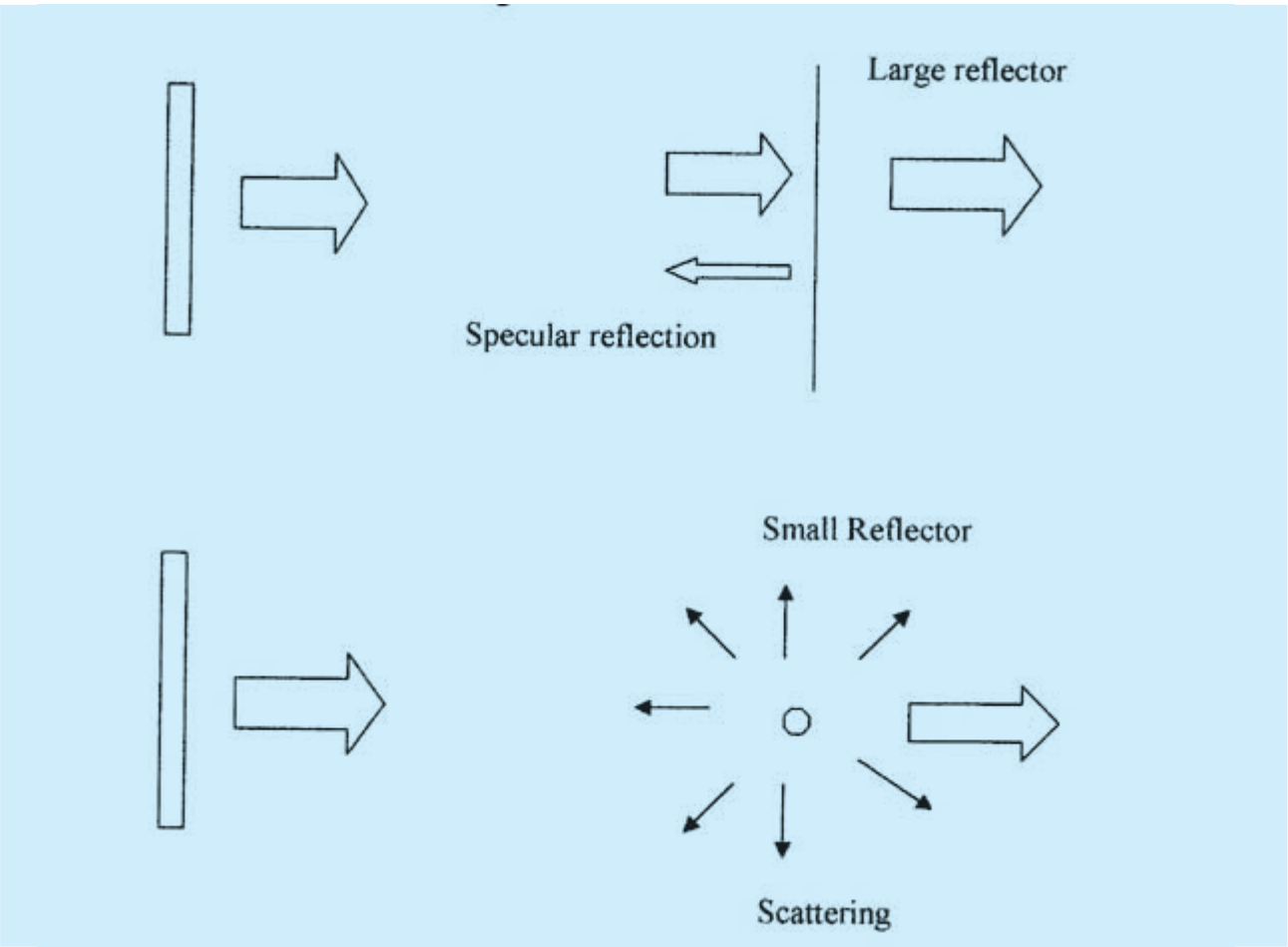


Figure-1: Two distinct patterns of reflection give rise to the echoes that make up an ultrasound image – specular reflection and scattering.

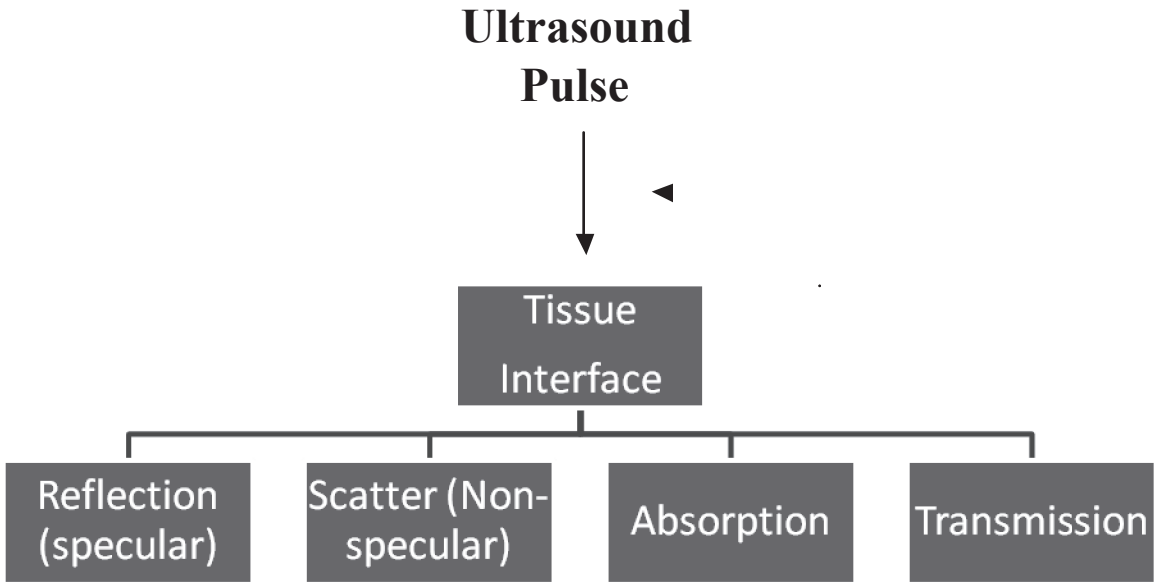


Figure- 2 : Illustration of phenomena which result when an ultrasound pulse encounters a tissue interface.

Resolution is the minimum reflector separation required to produce separate reflections in a pulse-echo system. Attenuation is the decrease in energy as a wave travels through a medium. Attenuation is caused by absorption, reflection, beam divergence and scattering. In bone attenuation is greater but in water it is very low.3 As sound passes through tissue it loses energy and pressure waves decrease in amplitude as they travel further from their source. Attenuation is therefore the result of the combined effects of absorption, scattering, and reflection. (Figure-2) High frequencies are attenuated more rapidly than lower frequencies, and transducer frequency is a major determinant of the useful depth from which information can be obtained with ultrasound.[1]

High frequency transducers are used to generate the ultrasonic energy. The major component of an ultrasound transducer is the piezoelectric element. Piezoelectric materials are capable of converting one form of energy into another. A voltage supplied to a piezoelectric element initiates vibrations. Its another function is to receive echoes that return from the object being studied. It than converts this mechanical energy into an electrical voltage, which forms a visual image of the studied structure. Transducers come in many different frequencies- typically 2.5, 3.5, 5, 7 and 10 MHz. Increasing the frequency improves resolution but decreases penetration. Decreasing the frequency increases the penetration but diminishes resolution.[4]

Transducers have an effect on image. Therefore transducers are chosen according to the structure being examined and the size of patient. Pediatric patients can be examined at 5 to 7.5 MHz. Lower frequencies (eg. 2.5 MHz) permit greater penetration and may be needed to scan larger patients.[4]

Doppler is used to detect blood flow through vessels. The Doppler technique detects not only the presence of blood flow but also the direction of flow by measuring the difference in the frequency of the reflected sound compared with the transmitted sound.[3]

As a general rule, medical diagnostic ultrasound energy will not travel through air. This is why acoustic couplants (water, oil or gel) are needed. Acoustic couplants are used to provide a good sound path between the transducer and the skin.3

Bioeffects

Bioeffects or biological effects are the effects of ultrasound on tissue. The categories of bioeffects are

1. Heat
2. Cavitation
3. Others

Heat is the effect created by the motion of the vibrating molecules. Any heating is negligible when pulse ultrasound is used for diagnostic purposes. Cavitation results in the production of gas bubbles. It can result in damage of cell walls. 'Others' include various minor mechanical effects that are not related to heat or cavitation.3

Instrumentation

Types of ultrasound display

A-mode or amplitude mode is the most basic form of diagnostic ultrasound. Its use is almost obsolete.

In **B-mode or brightness mode** a stronger (high amplitude) echo will display a brighter dot than a weaker (low amplitude) echo. The depth of the reflector is displayed by the location of the dot. 5 An image of the organ or tissue is formed in gray-scale as different dots of different intensities appear on the monitor.

In M-mode or motion mode, a series of B-mode dots is displayed on a moving time base graphing the motion of mobile structures. M-mode is currently used in conjunction with real-time imaging in adult, pediatric and fetal echocardiography.[5]

Types of Transducers

Mechanical Transducers. The transducer crystal is physically moved. Most of these provide a sector image with a fixed focus. It is not now commonly used in modern equipment.

Electronically steered systems. In this type of transducer, multiple piezoelectric elements are used. A separate electrical supply is provided for each element. Focusing is controlled electronically. The images are displayed in a sector, linear or curved-linear format. [5] (Figure-4)

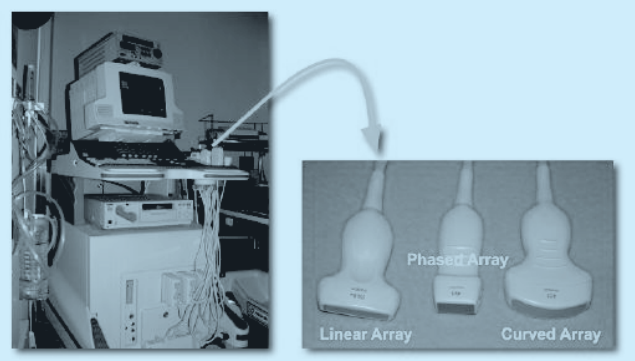


Figure-4 : Photos of a sonography system and typical transducers:

Specialized Ultrasound Systems

Small Parts Scanners use probes capable of high- resolution, for example 7.5 to 10 MHz transducers. They are designed for visualizing the fine details of superficial structures, usually at a depth of less than 4cm from the skin surface (eg. Thyroid, carotid arteries, testes, breast or structures in an infant).

Endo-ultrasound Systems (Trans-vaginal and trans-rectal probes). The transducer is placed on the end of a rod. This is then inserted into the vagina or rectum.

Endo-luminal or trans-luminal transducers. Even smaller transducers on the end of catheters can be introduced into vessels, the billiary duct or the ureters.

Operative Systems. Probes are modified to be used in sterile

fashion in the operating room. Special high-frequency ultrasound probes are used for this purpose.5

Doppler ultrasound instruments are optimized to display flow information. The simplest Doppler devices use continuous wave rather than pulsed wave ultrasound, using two transducers that transmit and receive ultrasound continuously (continuous wave or CW Doppler). [1] The most common form of Doppler ultrasound to be used is color flow Doppler imaging.6 Signal phase provides information about the presence and direction of motion, and changes in echo signal frequency relate to the velocity of the target. Flow within the vessel is observed at all points, and stenotic jets and focal areas of turbulence are displayed.1

CONCLUSIONS

In conclusion, ultrasound is one of the latest technologies given to the doctors and patients by modern science. But in the hands of an ill trained or minimally trained physician it is a bane rather than a boon for both the doctor and the patient. Because the misdiagnosis of important and emergency or life threatening diseases can greatly harm the patient e.g. mis-diagnosing an ectopic pregnancy, a major fetal anomaly or masses in the organs. The bio-effects of ultrasound is essential to understand but it is minimum in the modern machines compared to the hazards of radiation in other diagnostic modalities.

It is a versatile tool in the hands of the physician and can give him/her a wealth of information in the management of the patient in the best possible manner. It can be used without hesitation for the benefit of the patient. Ultrasound is now also used for therapeutic purpose as for crushing gall bladder and renal stones.

Ultrasound is a very practical and personal skill, which take a considerable amount of practice to perfect.

REFERENCES

1. Merritt CRB. Physics of Ultrasound. In: Rumack CM, Wilson SR, Charboneau JW (eds.), Diagnostic Ultrasound, 2th Ed. St. Louis. Mosby, Inc. 1998, p 3-33.

2. Chivers RC, Parry RJ. Ultrasonic velocity and attenuation in mammalian tissues. J Acoust Soc Am 1978; 63:940-53.

3. Pinkney MN. Physics. In: Curry RA, Tempkin BB (eds.), Sonography, 2th Ed. St. Louis. Saunders, Elsevier. 2004, p 17-22.

4. Sanders RC. Basics. In: Sanders RC, Miner NS (eds.), Clinical Sonography, 3rd Ed. Philadelphia. Lippincott. 1998, p 2-7.

5. Saylor MM, Sanders RC. Instrumentation. In: Sanders RC, Miner NS (eds.), Clinical Sonography, 3rd Ed. Philadelphia. Lippincott. 1998, p 8-21.

6. Merritt CRB. Doppler color flow imaging. J Clin Ultrasound 1987;15:591- 7.

Obituary news January-17

BMA would like to express deep condolence on deaths of the following notable physicians in recent past:

SL.No	Name	Age	Name of District	Date of Death
1	Dr. M. Moazzem Hossain	68	Dhaka, Ex- Vice President of BMA	23/9/2016
2	Dr. Abdur Rashid	99	Dhaka	24/9/2016
3	Dr. A.H.M. Manzurul Islam	49	Rangpur	25/9/2016
4	Dr. A.K.M. Mahbubur Rahman	62	Secretary, BMA Election Commission-2016-2017.	30/9/2016
5	Dr. Abdullah Al Mamun (Omit)	27	Sirajgonj	06/10/2016
6	Dr. Md. Babar Ali	52	Naogaon	14/10/2016
7	Prof.(Dr.) M. R. Khan	88	BMA Life Member -1402898 Dhaka City House # 27 (Old-125), Road # 3, Dhanmondi R/A, Dhaka-1205.	05/11/2016
8	Prof.(Dr.) M. A. Quashem	95	House # 27 (Old-125), Road # 3, Dhanmondi R/A, Dhaka-1205. Phone : 01711525423	05/11/2016
9	Dr. Lutfor Rahman	73	Ex-Vice President, Bangladesh Aomelig Jalokati Dist.	07/11/2016
10	Dr. Modan Mohan Roy	85	Senior Doctor of Lalmonirhat District.	15/11/2016
11	Language Fighter Dr. Abdul Mutaleb Khan	86	Sirajgonj	27/11/2016
12	Dr. Razib Kumar Roy	33	Bagerhat	01/12/2016
13	Alhaj Dr. Matlubor Rahma Chowdhury	82	Nilphamari	10/12/1620
14	Freedom Fighter Dr. Azahar Hossain	66	Naogaon	14/01/2017
15	Freedom Fighter Dr. Hanif Uddin	87	NilPhamari	14/01/2017
16	Dr.Golam Mushtakim Mison			22/01/2017

May Allah bless the departed souls. Our heartiest commiseration to the deceased's family, our prayers are with them during this difficult moment of their life.

Oceancal-D

Calcium 500 mg (from coral source) + Vitamin D_3 200 IU Tablet

Oceancal-DX

Calcium 600 mg (from coral source) + Vitamin D_3 400 IU Tablet

Caplet shape Tablet

Ensures easy swallowing

GENERAL Pharmaceuticals Ltd.

Healthy life
Healthy living

* শুধুমাত্র রেজিস্টার্ড চিকিৎসকের ব্যবস্থাপত্র মোতাবেক এন্টিবায়োটিক বিক্রয়, সেবন বা গ্রহণ করতে হবে।
* সংক্রমণের হার কমানোর জন্য হাত ধোয়াসহ সকল সাধারণ স্বাস্থ্যবিধি মেনে চলতে হবে।

GPO registration number, Dhaka-1725 Vol. 46 No. 1 January 2017

Call for paper

To reach the doctors throughout the country and ensure their participation as author, contents and presentation of the Bangladesh Medical Journal have been updated & changed to some extent. In addition to original articles, review articles and case reports; we are going to publish following sections regularly.

Letters to the editor

With a view to increase the bondage with the readers, we encourage to write letters to the editor. Letters may include original research presented in a research letter format or case reports or series. Alternatively, readers may express their ideas, opinions on important national or international issues related to doctors, medical science or medical profession.

On being a doctor

Doctors are encouraged and advised to share their sweet, bitter, sad, memorable & illuminating experiences as a professional doctor in the hospital and private chamber.

Medical news

Important recent updated inventions and ideas that may change the knowledge, attitude & practice of a doctor and courses of the medical sciences, both at home and abroad; may be written to us for publication in Bangladesh Medical Journal.

Medical jokes/poems

Meaningful jokes or poem writing related to medical profession and submitting to us by soft copies are encouraged. There is no deadline of submission.

Please send your writings to the e-mail address of Bangladesh Medical Association Journal : info@bmaj.org

Published by: Dr. Md. Ehteshamul Huq Chowdhury on behalf of the Bangladesh Medical Association, BMA Bhaban, 15/2, Topkhana Road, Dhaka-1000, Bangladesh. Phone: +88-02-9568714, Fax: +88-02-9562527, +88-02-6566060, e-mail: info@bmaj.org, website: www.bmaj.org. Subscription: Local-Tk. 15 for single and Tk. 60 for annual. Overseas-$5 for single and $20 for annual.
Printed by: Neetol, Graphic & Commercial Printer, 10, Purana Paltan Line, Dhaka, Bangladesh.
Tel: +88 01711531685, E-mail: neetol03@yahoo.com