

# JALALABAD MEDICAL JOURNAL

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## Editorial

### **Empathic Therapy: A Reform Accomplishment in the Field of Psychotherapy**

Empathy means intellectual, emotional awareness and understanding of another's thought, feeling and behavior. It is the ability to recognize and to some extent share the emotion and state of mind of another to understand the meaning and significance of that person's behavior. It is considered now an essential quality of effective psychotherapy. Empathy therapies offer a caring, understanding and empowering attitude toward the individual's emotional struggles, aspirations and personal growth<sup>1</sup>.

We are living in exciting times where people are embracing their individuality and seeking liberty and freedom. As professionals and concerned individual, it is ideal to embrace therapeutic relationship rather than psychiatric diagnosis. The centre for the study of empathic therapy has been developed by a group of professionals. Now it is recognized as an emergency discipline in psychotherapy in different countries especially in USA. The pioneers in this field in USA are Dr. Peter R Breggin and Ginger Ross Breggin. They offered a new school of Psychotherapy to enhance the own style of psychotherapy. They arranged an international conference on 'Empathic Therapy' during the period April 08 to 10, 2011 in New York. A large group of psychiatrist, psychologist, psychotherapist, social workers and educationist participated in this conference.

Many of the Dr. Breggin's accomplishment are documented in detail in the "The Conscience of Psychiatry: The Reform Work of Peter R Breggin, MD (2009)". An international centre has been founded for the study of psychiatry and psychology with a board of director including psychiatrists, other mental health professionals, lawyers, consumers and members of the US Congress. Later on, his wife Ginger Joined him as executive director and arranged orderly transition to new and younger leader and most of the national figures have bought into board of directors and advisory council. They focused on criticizing biopsychiatric theory, practice and emphasized on caring and effective empathic therapeutic, educational and human service approach<sup>2</sup>. They are promoting empowerment, responsibility and engagement rather than psychiatric drugs and shock treatment.

In 1970, they were outraged and conducted international campaign to stop the worldwide resurgence of lobotomy and psychosurgery, which forced to stop all psychosurgery to half in federal and state institution of US, Canada and Europe. In 1979, he published "Electric shock its brain disabling effects" and advocated against shock treatment. 'Psychiatric drugs, hazards to brain' was published by them focusing the dangers of psychiatric drugs to brain and mind, tardive dyskinesia (TD), and effects of long term exposure to neuroleptic drugs in dementia. He was the first psychiatrist to confront the profession and the public about the risks of violence and suicide from newer SSRI (Selective serotonin reuptake inhibitor) antidepressants<sup>2,3</sup>. Various research publication in this field to the FDA (Federal Drug Administration) panel confirmed that antidepressants cause suicidal behavior, over stimulation of CNS (Central Nervous System) that includes akathasia, agitation, insomnia, hostility and mania<sup>4</sup>.

Much of information provided by them alerted the profession to the danger of down-regulation and dangerous withdrawal reaction for new SSRI antidepressants and documented in 'Talking Back to Prozac' and subsequent publications. They are advocating for children to be protected from psychiatric abuse were published in 2008, as 'medication madness and brain disabling treatment in psychiatry'. On the basis his scientific testimony, many of his views and concern were partially confirmed by the NIH (National Institute of Health) consensus development conference on the diagnosis and treatment of ADHD (Attention Deficit Hyperkinetic Disorder) in November, 1998<sup>4</sup>.

**Some guidelines for empathic therapy provided by them are viewed as follow:**

1. This therapy is a sacred and inviolable trust, rely upon the relationship built on trust, honesty and caring and mutual respect. It will create a safe space for self exploration and honest communication by holding themselves to the highest ethical standards including honesty, informed consent, confidentiality, professional boundaries, respect for personal freedom, autonomy and individuality.
2. Therapist encouraged overcoming psychological helplessness and taking responsibility for emotion, thoughts and actions and also offered empathic understanding to identify self defeating patterns learned in childhood and adulthood in order to promote the development of more effective choice making and conduct. They do not treat people against their will and do not reduce others to diagnostic categories which diminish personal identity, over-simplifies life and impedes post traumatic growth.

Empathic therapy does not falsely attribute emotional suffering and personal difficulties to genetics and biochemistry, instead focused on each person's capacity to take responsibility and to determine the course of his or her own life. It also recognized that a drug free mind is best suited for personal growth and to face critical life issues. Children among our most valuable and treasured citizens need to be protected from psychiatric diagnosis, drugs and offer them family life, education, moral and spiritual guidance that will help them to fulfill their potential as children and adults. Basic characteristics of the therapy is to promote basic human values including personal responsibility, freedom, gratitude, love, courage to honestly, self evaluation and appreciation, as well as the ability to empathize others.

Psychiatric diagnoses, drugs, electroshock and other biological intervention are not the absolute answer to human psychological and spiritual suffering. So need of more human and caring approaches will enrich the practices of biological psychiatry.

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## Original Article

# A Descriptive Study of Different Dimensions of Postmortem Heart of Adult Bangladeshi People

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### ABSTRACT

The study was done to standardize the data regarding the different dimensions of adult heart. The descriptive study was carried out on 50 formalin fixed human hearts in the Department of Anatomy, Sylhet M A G Osmani Medical College, Sylhet, during the period July 2007 to June 2008. The gross morphology of all the specimens was studied through careful dissection. The mean length of the heart from base to apex in the present study was  $9.62(\pm 0.96)$  cm in males and  $9.58(\pm 1.12)$  cm in females the mean breadth of the heart was found  $7.94(\pm 0.78)$  cm in males and that in females was  $7.69(\pm 0.81)$  cm the mean antero-posterior diameter of heart was  $6.14(\pm 0.64)$  cm in males and was  $5.92(\pm 0.67)$  cm in females. The observations and results of this study were expected to provide an idea about the different gross parameters of the adult heart in Bangladeshi people.

**Key word:** Ischemic heart disease, cardiac dimension,  
[Jalalabad Med J 2011; 8 (1):3-5]

### INTRODUCTION

Heart disease is the important cause of disability and death. Incidence of heart diseases is increasing day by day. The incidence of coronary heart disease is increasing in the developing countries of South Asia like Bangladesh<sup>1</sup>. Ischemic heart disease (IHD) is responsible for 80-90% of these deaths. Apart from the possible variations in the distribution pattern of the coronary arteries, there may be variations in the size of different coronary arteries and their branches. This is because there may be racial variations in different dimensions of human heart. The frequency of variations differs among variations of human groups<sup>2</sup>. For morphological dimensions of heart, we still have to depend on foreign literatures. There is a very few data on morphological variations of heart of different age groups and sexes. There fore, any attempt at studying

the morphology of heart would be worthwhile in understanding the racial characteristics (if any) of the heart. Such a study is also expected to contribute to the standardization of the morphological measurements of the heart. Having the above background and rationale in mind, the present study was under taken on postmortem hearts.

### MATERIALS AND METHODS

The present study was performed on 50 (fifty) postmortem human hearts of both sexes aging from 18 to 60 years in Sylhet region. The descriptive study was carried out in the Department of Anatomy, Sylhet M A G Osmani Medical College, Sylhet, during the period July 2007 to June 2008. Human hearts were collected from unclaimed dead bodies autopsied on different dates at the autopsy laboratory of Department of Forensic Medicine, Sylhet M A G Osmani Medical College. The hearts along with the pericardium and great blood vessels and adjacent structures were collected from each cadaver. The specimen was washed thoroughly with tap water and gently squeezed

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**Address of correspondence:**

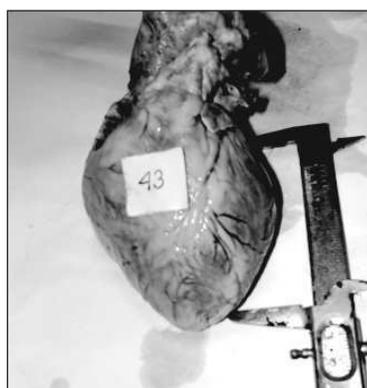
Dr. Jesmin Sultana, Assistant Professor, Department of Anatomy, Jalalabad Ragib-Rabeya Medical College, Sylhet.

to remove the blood clots from the cavity of the heart and from the lumen of the blood vessels as much as possible. The procedure was repeated several times. Then the specimen was kept in 10% formalin solution for fixation and preservation.

The formalin fixed specimens were initially washed with the free-flowing tap water and taken in a metallic tray. All the specimens studied through careful gross dissection to observe the gross morphological features of human hearts. The hearts were divided into (a) Male group consists of only the male hearts (38) (b) Female group consists of only the Female hearts (12).

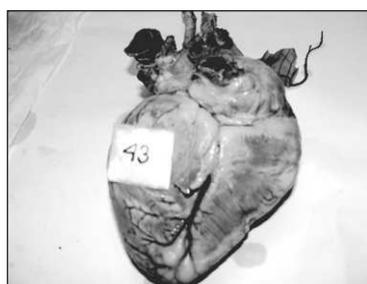
**Procedures and Landmarks of Measurements:**

**Length of the heart:** From the apex of the heart to the left of a point on the left atrium, midway between the two right pulmonary veins<sup>3</sup> was measured with the help of a slide calipers (Figure 1).



**Figure 1:** Photograph showing anterior surface of the heart.

**Breadth of the heart:** The maximum transverse diameter at the broadest part near the crux<sup>4</sup> was measured with the help of a slide calipers (Figure 2).



**Figure 2:** Photograph showing posterior surface and base of the heart

**Antero-posterior diameter of the heart:** The diameter was measured between the crus posteriorly to the infundibulum anteriorly<sup>2</sup> with the help of a slide

caliper.

**RESULTS**

**Length of the Heart:** The mean ( $\pm$ SD) length of the heart in males was 9.62 ( $\pm$ 0.96) cm and that in females was 9.58 ( $\pm$ 1.12) cm. Although the mean length of the male hearts was found to greater than that of the female hearts, statistical analysis showed the difference is non-significant between males and females in the length of the hearts ( $p > 0.05$ ).

**Breadth of the Heart:** The mean ( $\pm$ SD) breadth of the heart in males was 7.94 ( $\pm$ 0.78) cm and that in females was 7.69 ( $\pm$ 0.81) cm. Although the mean breadth of the male hearts was found to greater than that of the female hearts, the difference in breadth between two sexes was not statistically significant ( $p > 0.05$ ).

**Antero-Posterior Measurement of the Heart:** The mean ( $\pm$ SD) antero-posterior diameter of heart in males was 6.14 ( $\pm$ 0.64) cm and that in females was 5.92 ( $\pm$ 0.67) cm. It is evident from the results that the mean antero-posterior diameter of the male hearts was found to greater than that of the female hearts, statistical analysis showed the difference is non-significant ( $p > 0.05$ ) between males and females.

Different cardiac dimensions are shown in Table- I.

**Table I:** Different Gross Dimensions of the Heart in Males (n=38) and Females (n=12)

Dimension	Sex	Measurement ( in cm )	
		Range	Mean $\pm$ SD
Length	Male	7.5 - 12.0	9.62 $\pm$ 0.96
	Female	8.0 - 11.5	9.58 $\pm$ 1.12
Breadth	Male	6.0 - 9.8	7.94 $\pm$ 0.78
	Female	6.0 - 9.0	7.69 $\pm$ 0.81
Antero-Posterior measurement	Male	5.0 - 7.5	6.14 $\pm$ 0.64
	Female	5.0 - 7.0	5.92 $\pm$ 0.67

Male vs Female- Not significant (In unpaired “t” test of significance of difference)

**DISCUSSION**

The present study was performed on fifty (50) human apparently normal hearts of Bangladeshi people in Sylhet region, among them thirty eight (38) were males and twelve (12) were females. The mean length of the adult hearts in the present study was somewhat less than the length of the adult hearts from base to apex observed by (12 cm) Shah<sup>5</sup>. Basir<sup>3</sup>, Rahman<sup>2</sup> and Begum<sup>4</sup> found the mean value to be about 10 cm irrespective of sex, Sarker<sup>6</sup> found it to be 11.48 cm

(Males 11.59 cm, Females 10.94 cm). Thus the values of the present study were somewhat less than those studies. The mean breadth of the heart was somewhat smaller than the value (8-9cm) described by Shah<sup>5</sup>. The values are also less than the values (8-9 cm) found by Basir<sup>3</sup>, Rahman<sup>2</sup>, Sarker<sup>6</sup> and Begum<sup>4</sup>. The mean antero-posterior diameter of heart was  $6.14 \pm 0.64$  cm in males and was  $5.92 \pm 0.67$  cm in females. In the Bangladesh, Rahman<sup>2</sup> observed that the value was  $5.65(\pm 0.42)$  cm and Sarker<sup>6</sup> found the value to be  $5.92(\pm 0.91)$  cm. Begum<sup>4</sup> found it  $6.49(\pm 0.85)$  cm in males and  $6.33(\pm 0.70)$  cm in females. Shah<sup>5</sup> described the antero-posterior diameter as 6 cm. Thus the finding of the present study were almost similar to that described by Shah<sup>5</sup> and in Bangladesh by Begum<sup>4</sup> but somewhat greater than Rahman's<sup>2</sup> and Sarker's<sup>6</sup> findings. To get a local standard of measurement we recommended further more advanced studies on the anatomy of Bangladeshi heart.

#### CONCLUSION

In conclusion, present study determined the gross different diameter of adult heart in Bangladeshi people. The observations and results are expected to provide an idea about the different gross parameters of the heart.

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## Original Article

# Study on Heart Rate Variability in Hyperthyroid Patients by Frequency Domain Method

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### ABSTRACT

*Hyperthyroidism is a common hormonal disorder associated with dysfunction of cardiac autonomic nerve activity (CANa). Heart Rate Variability (HRV) analysis is a promising technique to quantify CANa. To observe the HRV parameters in patients with hyperthyroidism, it is necessary to find out excess thyroid hormonal influence on cardiac autonomic nervous activities. The cross sectional study was carried out on 60 hyperthyroid patients aged 30-50 years in the department of Physiology, BSMMU, Dhaka from 1<sup>st</sup> July 2007 to 30<sup>th</sup> June 2008. Twenty age, sex matched apparently healthy euthyroids were also studied as control (group A). Thirty untreated newly diagnosed patients were grouped in group B<sub>1</sub> and 30 treated hyperthyroid patients with anti-thyroid drugs for at least 2 months in group B<sub>2</sub>. The patients were selected from OPD of Endocrinology, BSMMU, Dhaka. Serum TSH and FT<sub>4</sub> levels were measured by microparticle enzyme immunoassay (MEIA) method (Abbott AxSym system) and frequency domain measures of HRV such as variance (total power), VLF power, LF power, HF power, LF normalized unit (NU) power, HF NU power and LF/HF were assessed from polygraph recording. For statistical analysis Mann-Whitney U test was done. The variance and VLF power of group B<sub>1</sub> were significantly lower than both group A ( $p < 0.001$ ) and group B<sub>2</sub> ( $p < 0.01$ ). The LF power ( $p < 0.01$ ) and HF power ( $p < 0.001$ ) were significantly higher in group A than those of group B<sub>1</sub> and B<sub>2</sub>. The LF NU power, HF NU power and LF/HF ratio of all three groups showed statistically highly significant ( $p < 0.001$ ) differences among them. Decreased vagal modulation on heart rate may occur in hyperthyroidism, and treatment of the patients may return the CANa towards normal.*

**Key words:** CANa, hyperthyroidism, TSH.

[Jalalabad Med J 2011; 8 (1):6-11]

### INTRODUCTION

Hyperthyroidism has tremendous influence on CANa. Changes in serum thyroid hormone levels are usually associated with alteration in sympathovagal balance<sup>1,2</sup>. Clinical features of hyperthyroidism are similar to excess catecholamines but studies demonstrated lower turnover rate of catecholamines<sup>3,4</sup>. Some investigators reported increased sympathetic activity in hyperthyroid

patients with beta-receptor blocking drugs<sup>2,5-8</sup>. But others observed that there may be alteration of catecholamine binding receptors, affinity and mechanism of them in hyperthyroidism<sup>8-12</sup>.

In hyperthyroid patients parasympathetic effect on heart rate is reduced<sup>13-17</sup>. Tachycardia of patients results from raised intrinsic heart rate, increased sympathetic activity and reduced parasympathetic tone<sup>13,18-20</sup>.

Power spectral analysis in frequency domain method of HRV demonstrates the impairment in CANa<sup>21</sup>. Heart rate variability is the result of intrinsic cardiac automaticity and cardiac autonomic nervous activity. It is used to detect the individual components of the

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autonomic control of the heart<sup>14,15,19,22</sup>. Several researchers explored the CANA in hyperthyroid patients and observed sympatho-adrenal axis is changed as sympathetic efferent outflow may be exaggerated<sup>8,17,23,24</sup>. Again, other investigators had observed variations of CANA as, lower heart rate in hyperthyroids after treatment<sup>13</sup>.

The variance was higher in hyperthyroid patients and was lower in treated group<sup>8,15,17,25</sup>. Some investigators had observed lower VLF (very low frequency) power in untreated hyperthyroids than that of euthyroids<sup>8,26</sup>. In addition, they also studied VLF power both in untreated and treated hyperthyroids. It has also reported that LF (low frequency) power is lower in untreated hyperthyroids than that of healthy control. Moreover, comparisons of this value between untreated and treated hyperthyroids were reported<sup>15,16</sup>. They have also found lower HF (high frequency) power in untreated patients than those of treated hyperthyroids and euthyroids.

LF normalized unit (NU) power was higher in untreated hyperthyroid patients and also observed lower HF NU power in untreated hyperthyroids than those of other groups. Moreover they have compared these values among these groups<sup>8,15,16</sup>. Again, many researchers have observed significantly higher LF/HF ratio in untreated hyperthyroids than those of euthyroids and also treated patients<sup>8,15,17,26</sup>.

Hyperthyroidism is one of the common endocrine disorders in Bangladesh. Different cardiovascular and metabolic disorders may be associated with hyperthyroidism. Though most of them remain unnoticed, it is possible to prevent the development of such complications. Several studies on cardiac autonomic nerve dysfunction in diabetes mellitus, renal failure, aging, obesity and post-menopausal women were conducted by conventional method but no such data on hyperthyroidism by analysis of HRV is yet available in our country<sup>27-31</sup>.

Therefore, the present study has been designed to assess the autonomic nerve function status in hyperthyroid patients by analysis of HRV in frequency domain method. It is expected that the outcome of this study may be useful in screening of autonomic nerve function disorder in hyperthyroidism to minimize its risk of complications.

## **MATERIALS AND METHODS**

This cross sectional study was carried out to observe the HRV in frequency domain method in 60 hyperthyroid patients with age ranged from 30-50 years in the Department of Physiology, Bangabandhu

Sheikh Mujib Medical University from 1<sup>st</sup> July 2007 to 30<sup>th</sup> June 2008. Hyperthyroid patients were divided into B<sub>1</sub> (untreated patients on their 1<sup>st</sup> day of diagnosis) and B<sub>2</sub> (patients treated for at least 2 months). For comparison, 20 age sex matched apparently healthy euthyroid subjects (group A) were also studied. The study group was selected from the Out Patient Department of Endocrinology, BSMMU, Dhaka. Both the groups were free from heart diseases, hypertension, diabetes mellitus, renal diseases, psychic disorders, hyperthyroidism due to exogenous L-thyroxine, pregnancy and smoking.

After selection, the subject was thoroughly informed about the aims, objectives and detail procedure of the study before examination and collection of blood sample. He/she was encouraged for voluntary participation and was allowed freedom to withdraw from the study whenever he/she liked even after participation. If he/she agreed to enroll to the study, informed written consent was taken. Then subject was prepared for the study by asking to have their meal by 9:00 pm, free from any physical or mental stress, not to take sedatives or any drugs affecting central nervous system, had a good sleep at night before the day of examination. He or she was advised to avoid tea or coffee at breakfast and was asked to attend the Department of Physiology of Bangabandhu Sheikh Mujib Medical University between 9:00 a.m. to 11:00 a.m. on the day of examination. Then the subject was taken to Autonomic Nerve Function Test Laboratory and detail history was taken. Then his/her thorough physical examinations were done and all information were recorded in a prefixed questionnaire. Then he/she was kept under complete bed rest in supine position for 15-20 minutes in a cool and calm environment. During this period subject was advised not to talk, eat or drink and also not to perform physical or any mental activity, even sleep. Then all preparations for recording of the Heart Rate Variability parameters were made by connecting the channels of ECG and Pulse to a polygraph. After recording of HRV parameters, 5 ml of venous blood was drawn from subject. Serum TSH and serum FT<sub>4</sub> levels were measured by microparticle enzyme immunoassay (MEIA) method (Abbott AxSYM system). Heart Rate Variability parameters in frequency domain method like variance (total power), VLF power, LF power, HF power, LF NU (normalize unit) power, HF NU power and LF/HF ratio were collected from Polygraphic recording. Data were expressed in mean and median. For statistical analysis Mann-Whitney U test was used.

## RESULTS

Anthropometric details of groups were matched for age, sex and height. The median body weight and BMI were significantly ( $p<0.001$ ) lower in group B<sub>1</sub> compared to group A and B<sub>2</sub>. But no significant differences in these values were observed between group A and group B<sub>2</sub>.

**Table I:** Serum TSH and FT<sub>4</sub> level in different groups (n=80)

Groups	TSH (mIU/L)	FT <sub>4</sub> (pmol/L)
A (n=20)	3.11 <sup>a</sup> 2.79 <sup>b</sup>	10.25 <sup>a</sup> 10.81 <sup>b</sup>
B <sub>1</sub> (n=30)	0.01 <sup>a***</sup> 0.023 <sup>b***</sup>	51.03 <sup>a***</sup> 51.35 <sup>b***</sup>
B <sub>2</sub> (n=30)	0.01 <sup>a***</sup> 0.022 <sup>b***</sup>	25.06 <sup>a***</sup> 30.39 <sup>b***</sup>

Data were expressed as <sup>a</sup>median and <sup>b</sup>mean. For statistical analysis, \*\*\*=  $p<0.001$ , ns=  $p>0.05$ .

**Table II:** Heart rate variability parameters by Frequency domain method (short term) in different groups (n=80)

Groups	VLF power (ms <sup>2</sup> )	LF power (ms <sup>2</sup> )	HF power (ms <sup>2</sup> )
A (n=20)	498.70 <sup>a</sup> 1269.40 <sup>b</sup>	151.52 <sup>a</sup> 347.38 <sup>b</sup>	65.35 <sup>a</sup> 207.68 <sup>b</sup>
B <sub>1</sub> (n=30)	161.73 <sup>a***</sup> 200.12 <sup>b***</sup>	24.94 <sup>a**</sup> 49.10 <sup>b**</sup>	6.15 <sup>a***</sup> 10.38 <sup>b***</sup>
B <sub>2</sub> (n=30)	410.88 <sup>a</sup> [ns] 1157.47 <sup>b</sup> [ns]	18.55 <sup>a**</sup> 46.50 <sup>b**</sup>	7.93 <sup>a***</sup> 17.66 <sup>b***</sup>

Data were expressed as <sup>a</sup>median and <sup>b</sup>mean. For statistical analysis, \*\*\*=  $p<0.001$ , \*\*=  $p<0.01$ , ns=  $p>0.05$ .

**Table III:** Heart rate variability parameters by Frequency domain method (short term) in different groups (n=80)

Groups	LF (NU)	HF (NU)	LF/HF
A (n=20)	63.1 <sup>a</sup> 63.4 <sup>b</sup>	37 <sup>a</sup> 36.58 <sup>b</sup>	1.71 <sup>a</sup> 1.79 <sup>b</sup>
B <sub>1</sub> (n=30)	81.35 <sup>a***</sup> 81.2 <sup>b***</sup>	18.75 <sup>a***</sup> 18.78 <sup>b***</sup>	4.33 <sup>a***</sup> 4.52 <sup>b***</sup>
B <sub>2</sub> (n=30)	74.55 <sup>a***</sup> 74.65 <sup>b***</sup>	25 <sup>a***</sup> 25.04 <sup>b***</sup>	3.01 <sup>a***</sup> 3.09 <sup>b***</sup>

Data were expressed as <sup>a</sup>median and <sup>b</sup>mean. For statistical analysis, \*\*\*=  $p<0.001$ , \*\*=  $p<0.01$ , ns=  $p>0.05$ .

The mean serum TSH and FT<sub>4</sub> levels were shown in Table I. This median value of TSH was significantly ( $p<0.001$ ) lower and FT<sub>4</sub> was higher in group B<sub>1</sub> and B<sub>2</sub> than group A. Although FT<sub>4</sub> was significantly lower in group B<sub>2</sub> than B<sub>1</sub> but there is no difference in TSH levels between B<sub>1</sub> and B<sub>2</sub>.

The median value of Variance (total power) of HRV parameters of group B<sub>1</sub> was significantly lower than both group A ( $p<0.001$ ) and group B<sub>2</sub> ( $p<0.01$ ). But non significant difference was observed between group A and B<sub>2</sub>.

The median value of group B<sub>1</sub> was significantly lower than both group A ( $p<0.001$ ) and group B<sub>2</sub> ( $p<0.01$ ), but statistically non significant difference was observed between group A and B<sub>2</sub>. Moreover, the LF and HF power of both group B<sub>1</sub> ( $p<0.01$ ,  $p<0.001$ ) and B<sub>2</sub> ( $p<0.01$ ,  $p<0.001$ ) were significantly lower than group A. whereas, statistically non significant difference was found between group B<sub>1</sub> and B<sub>2</sub>. The mean and median value of VLF power, LF power and HF power were shown in Table II.

The mean and median values of LF NU power, HF NU power and LF/HF ratio were shown in Table III. All these parameters of frequency domain method showed statistically highly significant differences among them.

## DISCUSSION

The present study observed some frequency domain measure of heart rate variability (HRV) like variance, VLF power, LF power, HF power, LF NU power, HF NU power and LF/HF ratio in patients with hyperthyroidism to assess CANA. Serum TSH and FT<sub>4</sub> levels were also measured to determine their thyroid hormonal status. All these parameters were compared with healthy age and sex matched adults. The autonomic nerve function status assessed by HRV parameters in healthy control group were almost similar to the findings reported by the various investigators from different countries<sup>8,15-17,25,26</sup>.

In this study, the subjects were matched for age and sex. The weight and BMI was found significantly lower in untreated hyperthyroids in comparison to both healthy control and treated hyperthyroids. But the body weight was significantly higher in treated hyperthyroids in comparison to untreated group and non significant difference of body weight was observed between healthy euthyroids and treated hyperthyroids. Similarly, there was non-significant statistical difference of BMI was observed between healthy control and treated hyperthyroid patients. Serum TSH level was significantly lower and FT<sub>4</sub> higher in both untreated and treated hyperthyroid patients compared

to healthy control.

Variance was significantly lower in untreated hyperthyroid patients compared to both healthy control and treated group. However, statistically non significant difference observed in healthy euthyroids and treated patients. Similar findings regarding variance were also observed by others<sup>8,15,17,25</sup>. Lower VLF power was observed in untreated hyperthyroid patients compared to those of both healthy control and treated hyperthyroids. These findings were consistent with others<sup>8,26</sup>.

In this study, LF power and HF power in both untreated and treated hyperthyroids were significantly lower than that of healthy group, as it was determined in subjects from a short term ECG recording. However, there was statistically non significant difference of these values observed between two groups of hyperthyroids. Similar findings were reported by others<sup>8,15-17,26</sup>.

In our study, LF NU power were significantly higher in both untreated and treated group and HF NU power in these two groups were significantly lower than those of healthy euthyroids. Moreover there were significant differences of these two parameters between untreated and treated hyperthyroids. Similar type of findings of LF NU and HF NU power were also observed by others<sup>8,15,16,25</sup>. LF/HF ratio was determined in subjects from short term ECG recording showed significant higher values both in untreated and treated hyperthyroids than that of healthy control. However, untreated hyperthyroid patients showed significantly higher value of LF/HF ratio compared to that of treated hyperthyroids. This is similar to the findings reported by other groups of investigators<sup>8,15-17,26,32</sup>.

In this study, gradual returning of the values of HRV parameters in treated group towards normal were observed following treatment and this is consistent with others<sup>8,15,17,25</sup>.

All these findings indicate reduced vagal modulation in hyperthyroidism. It has been suggested that reduced cardiac vagal effects in hyperthyroidism may be attributed to interference of peripheral neuroeffector mechanism and central inhibition of cardiac baroreflex reducing vagal discharge<sup>33</sup>. Along with the CNS manifestations, excess thyroid hormones usually affect every single cell of human body and results in exaggerated manifestations as hyperadrenergic state. Thyroid hormones also cause increased sinoatrial nodal activity, potentiate the metabolic activity, oxygen consumption in peripheral tissue and beta receptors activities<sup>34,35</sup>.

Different researchers have measured variance and suggested that alteration of LF power, LF NU power,

HF power and HF NU power occurs in cardiac autonomic dysfunction<sup>8,15,17</sup>. Higher values of LF power and LF NU power are suggestive of sympathetic hyperactivity, whereas lower values of HF power and HF NU power indicate decrease parasympathetic contribution. It has also been suggested that increased LF/HF ratio indicate imbalanced sympathovagal status<sup>8</sup>.

In the present study, all the hyperthyroid patients are most likely to be suffered from cardiac autonomic dysfunction as there are alterations of LF power, LF NU power, HF power and HF NU power. This is further supported by more marked changes of all these values in untreated hyperthyroids than that of treated hyperthyroids. However, improvement of cardiac autonomic functional state in treated hyperthyroids suggested that treatment improve this dysfunctional state, though it is not yet returned to normal condition.

In the present study, the sympathovagal balance is shifted towards sympathetic dominance in hyperthyroid patients. This is evidenced by raised LF/HF ratio, as decrease both of HF power and LF power in these groups of subjects. This is further supported by the positive correlation of LF/HF ratio with serum FT<sub>4</sub> level. All these findings are more pronounced in untreated hyperthyroids than that of treated hyperthyroids. So, it may be understood that treatment improves the conditions.

However, the exact mechanisms involved for the impairment of cardiac autonomic nervous activity in hyperthyroids can not be elucidated from this type of study. Assessment of serum or urinary catecholamines levels may be helpful to establish the involvement of neuroeffector mechanisms both centrally and peripherally in the hyperthyroid patients of the present series.

## CONCLUSION

From the above discussion, it may conclude that dysfunction of cardiac autonomic nervous activities occurs in hyperthyroid patients and adequate treatment may return it towards normal.

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## Original Article

### Prevalence of Obesity among the Medical Students in Sylhet

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#### ABSTRACT

*A cross-sectional study was conducted in the department of Biochemistry, Sylhet M A G Osmani Medical College, Sylhet during the period of July 2008 to June 2009. Randomly selected, 850 medical students were included for the study of prevalence of obesity. Generalized obesity was measured by BMI and central abdominal obesity was measured by WC and WHR. The cutoff value of WC for men was >90cm and for women was >80cm. The cut-off value of WHR for men was >0.9 and for women was >0.8. Generalized obesity was estimated using BMI 25kg/m<sup>2</sup> or greater. The prevalence of generalized obesity among the medical students was 20.82%. In male and female medical students, prevalence of generalized obesity were 20.09 and 21.58% respectively. Prevalence of central abdominal obesity among the students (according to WC) was 23.18 % (In male and female students' 12.93% and 33.81% respectively). Prevalence of central abdominal obesity (according to WHR) among the students was 35.88% (In male and female students 28.40% and 43.65% respectively).*

**Key word:** Central obesity, generalized obesity, BMI.

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#### INTRODUCTION

Obesity may be defined as an increased amount body fat. Body mass index (BMI) or waist circumference (WC), or both may be used for assessment of obesity. The most frequently used definition of obesity is based on BMI<sup>1</sup>. Obesity is often observed clustered in families. If both parents are obese, there is a 70-80% chance of the children being obese. In contrast only 9% of children are fat when both parents are lean. Energy

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dense foods play a role in increased prevalence of obesity. Further, sedentary life styles encouraged by TV watching, automobiles, computer usage and energy sparing devices decrease physical activity and enhance the tendency to gain weight<sup>2</sup>. Obesity is an undesirable outcome of changing lifestyle and behaviors. It is a reversible predisposing factor for the development of several debilitating diseases<sup>3</sup>. In obese individuals two distinct phenotypes are apparent: 1) Generalized obesity, 2) Central obesity. Central obesity is more important indicator for the development of coronary artery disease<sup>4</sup>. Increased modernization, westernized diet and lifestyle are associated with an increased prevalence of overweight in many developing

countries<sup>5</sup>. These developing countries are increasingly vulnerable to the worldwide epidemic of obesity. It affects all segments of the population including men, women and children. Compared with population in industrialized countries, those in the developing world appear to be at greater risk of the diseases associated with overweight<sup>6</sup>. Consequences of obesity are hypertension, diabetes mellitus, atherosclerosis, cerebrovascular disease, coronary heart disease, colorectal cancer, gout, osteoarthritis, cholelithiasis and sleep apnea<sup>7</sup>. Abdominal obesity is one of the key indicators of central fat adiposity in adults. It has been strongly linked with the risk of various chronic illnesses such as cardiovascular disease, diabetes mellitus and breast cancer. The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), American Heart Association (2002) and International Diabetes Federation (IDF, 2006) have recommended abdominal obesity as one of the criteria for diagnosis of metabolic syndrome in adults<sup>8</sup>. The International Association for the Study of Obesity and the International Obesity Task Force have suggested lower BMI cutoff values for the definitions of overweight (23-24.9 kg/m<sup>2</sup>) and obesity (25.0 kg/m<sup>2</sup> or greater) in Asian populations<sup>6</sup>. According to international Diabetes Federation (IDF 2006) cut-offs for South Asians are >90 cm for men and >80 cm for women. Waist-hip Ratio (WHR) for men 0.9 and for women 0.8 is considered to represent the central obesity<sup>9</sup>. Abdominal adiposity assessed by using WC is considered to be more appropriate to predict metabolic disorders than generalized adiposity<sup>10</sup>. This study aimed to find out the prevalence of obesity among the medical students in Sylhet.

## MATERIALS AND METHODS

This Cross-sectional study was carried out in the Department of Biochemistry Sylhet MAG Osmani medical College from July 2008 to June 2009. Eight hundreds and fifty (850) medical students were selected from four medical colleges in Sylhet. For prevalence of obesity, two hundred and fifty (250) medical students, (50 from each class), were taken from each of three medical colleges (Sylhet MAG Osmani Medical College, Jalalabad Ragib-Rabeya Medical College and North-East Medical College). One hundred (100) medical students were selected from Women Medical College, Sylhet (25 from each class). Study students were selected randomly. Data were collected through preformed data collection sheet questionnaire.

## Anthropometric Measurements

Body weight (in Kg) was measured in light clothing and without shoes. The weight was recorded to the nearest kg. Height was measured without shoes with the subjects standing fully erect on a flat surface. Height was taken to the nearest centimeter. Body mass index was calculated by the formula.

BMI = weight in Kg / (Height x Height) in the meter.

## BMI classification for adult Asians<sup>11</sup>

Degree of obesity	BMI (Kg/m <sup>2</sup> )
Normal weight	18.5—22.9
Underweight	<18.5
Overweight	23—24.9
Obese-I	25—29.9
Obese-II	>30

WC (in centimeter) was measured at midway between the costal margin and iliac crest (measured at the end of normal expiration). Hip circumference (in centimeter) was taken as the largest circumference at the posterior extension of the buttocks (Transtrochantaric). WHR is the WC divided by the hip circumference. WC and WHR were measured as an index of central obesity.

## Statistical analysis

Period Prevalence was calculated as per following formula

Period Prevalence =

$$\frac{\text{Number of all current cases (Old and new) of a specified disease existing at a given period of time}}{\text{Estimated population at the same period of time}} \times 100$$

## RESULTS

Total 850 medical students of 18-24 years of age were included in this study. There were 417 female and 433 male students.

Prevalence of generalized obesity among all study subjects were 20.82%. Among male students prevalence of generalized obesity was 20.09%. Among female students prevalence of generalized obesity was 21.58%. Table II showed the prevalence of generalized obesity (as per BMI).

The prevalence of central obesity among all students were 23.18%, in male 12.93% and in female 33.81%. Table III showed the prevalence of central abdominal obesity among the students using WC.

**Table I:** Distribution of study subjects on the basis of BMI (n=850)

BMI (Kg/m <sup>2</sup> )	Study subjects (%)	Male (%)	Female (%)
18.5-22.9 (Normal weight)	54.98	56.16	53.44
<18.5 (Underweight)	7.5	6.9	8.20
23-24.9 (Overweight)	16.70	16.85	16.78
25-29.9 (Obese – I)	16.02	16.59	15.38
>30 (Obese – II)	4.80	3.50	6.20
(I +II) (Obese)	20.82	20.09	21.58

**Table II:** Prevalence of generalized obesity (BMI 25 kg/m<sup>2</sup> or more)

Study subjects	Obese	Prevalence	95% Confidence Interval (CI)
Male n=433	87	20.09%	16.23 – 23.77%
Female n=417	90	21.58%	17.87 – 25.74%
Total n=850	177	20.82%	18.08 – 23.52%

**Table III:** Central abdominal obesity according to WC (male>90 cm, female >80 cm)

Study subjects	Obese	Prevalence	95% Confidence Interval (CI)
Male n=433	56	12.93%	9.8 – 16.32%
Female n=417	141	33.81%	27.55 – 36.5%
Total n=850	197	23.18%	20.90 – 26.62%

The prevalence of central abdominal obesity among all students were 35.88%, in male 28.40% and in female 43.65%. Table IV showed the prevalence of central abdominal obesity among the students using WHR.

**Table IV:** Central abdominal obesity according to waist hip ratio (male>0.9, female >0.8)

Study subjects	Obese	Prevalence	95% Confidence Interval (CI)
Male n=433	123	28.40%	23.84 – 32.3%
Female n=417	182	43.65%	38.4 – 48.38%
Total n=850	305	35.88%	32.67 – 34.09%

## DISCUSSION

Obesity is a progressive problem, both in the developed and developing countries. In South Asia, social and environmental changes are occurring

rapidly. These are increasing urbanization, changing life styles and reduced physical activity, with consequent increased propensity for obesity. In this study, females were found more obese. The majority of obese students had a family history of obesity. Most of them also had history of sedentary life style. Prevalence of Generalized obesity (using BMI) was 20.82 % (male 20.09%, female 21.58%). Prevalence of central obesity (using WC) was 23.18% (male 12.93%, female 33.81%). Prevalence of central obesity (using WHR) was 35.88% (male 28.40%, female 43.65%). Most of relevant studies were consistent with our results with few exceptions. There were some studies, where there was more male predominance in prevalence of obesity. A study on 989 Greek medical students showed that 40% of men and 23% of women were obese (BMI >25 kg/m<sup>2</sup>). Central obesity (WC> 90 cm, WHR >0.9 for male, and WC>80 cm, WHR >0.8, for female) was found 33.4% in male, 21.7% in female students respectively<sup>9</sup>. In a study on students of Lebanese University in Beirut<sup>12</sup> reported that, prevalence of overweight and obesity (overweight with BMI 25-29.9, and obese with BMI >30) was more common among male students than females (overweight and obese 37.7% and 12.5%, versus 13.6% and 3.2% respectively in male and females). It was claimed that female students were more conscious about their weight and figure. High prevalence of grade 1 (BMI>25) and grade 2 (BMI>30) obesity were also reported in Kuwait University students. Among 842 medical students, the prevalence of Grade 1 and Grade 2 obesity were 32% and 8.9 respectively<sup>13</sup>. In United Arab Emirates, a cross-sectional survey conducted among 300 male medical students, prevalence rate of obesity was 35.7% with BMI cut off value for obesity 25 or more<sup>14</sup>. According to WHO in 2008, prevalence of obesity in Bangladesh were 9% among males, 10.2% among females and 9.4% in both sexes (BMI >25 kg/m<sup>2</sup>)<sup>11</sup>. In our study the prevalence of obesity was considerably higher in medical students. The young adults with obesity are potential candidates of increased risk of cardiovascular diseases in their future life.

## CONCLUSION

We may aware our young generation about unhealthy life style and dietary habits. Dietary and life style modifications can be adopted to reduce obesity. Students should be aware of harmful consequence of obesity in their future lives. Further study with larger sample size and students taken from different ages, in addition to medical colleges are recommended.

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Original Article

## Role of Fine Needle Aspiration Cytology in the Diagnosis of Breast Lumps- Analysis of 70 Cases

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### ABSTRACT

*The palpable breast lump is a common diagnostic problem to the general practitioners and the surgeons. This comparative and cross sectional study was designed with the aim to evaluate the diagnostic accuracy of fine needle aspiration cytology (FNAC) of breast lumps in comparison with histopathological findings. A total of 70 cases who had a palpable breast lump, were subjected to fine needle aspiration cytology and subsequent histopathology were included. The findings of FNAC showed effective role in the diagnosis of breast lumps. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of this study were 92.30%, 98.24%, 92.30%, 98.24% and 97.14% respectively. This study was mostly consistent with others study in the literature. FNAC is a valuable investigation in patient with palpable breast lumps.*

**Key words:** Carcinoma of breast, FNAC.

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### INTRODUCTION

The palpable breast lump is a common diagnostic problem to the general practitioners and the surgeons. Although fortunately most are benign, cancer of the breast is the second most common cause of death in women. Breast lump should be diagnosed accurately as soon as possible because malignancy needs urgent treatment. FNAC is the most important method for the diagnosis of breast lesions<sup>1</sup>. FNAC enjoys several advantages over biopsy of masses<sup>2</sup>. The main indication of fine needle aspiration cytology is to confirm cancer preoperatively. A second consideration is to avoid unnecessary surgery. In some situations, diagnosis of inoperable lesions by FNAC can prevent unnecessary surgery<sup>3</sup>. Various studies were done to

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determine the accuracy of FNAC of palpable breast lumps and these ranges from 70.37% to 95.5%<sup>4, 5</sup>. The procedure is readily accepted by the patient and the whole procedure including fixation and staining is so quick that report can be issued in a few minutes<sup>5</sup>.

Aspiration cytology is extremely beneficial in reaffirming the clinical impression of benign diseases. Furthermore, it allows more rapid diagnosis of malignant condition in clinically suspicious masses. For clinically malignant disease, aspiration of breast masses and cytologic diagnosis enable the physician to assess the disease more effectively and can plan treatment such as mastectomy<sup>6</sup>.

This study was designed with the aim to evaluate the diagnostic accuracy of Fine Needle Aspiration Cytology of breast lumps in comparison with histopathological findings.

### MATERIAL AND METHODS

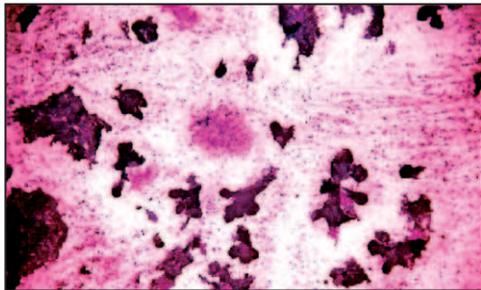
A total of 70 patients were selected from the indoor and outpatient department (OPD) of Surgery, Sylhet MAG

Osmani Medical College Hospital, Sylhet and also from different private clinics in Sylhet city during the period of July 2006 to June 2007. This comparative and cross-sectional study was carried out in the Department of Pathology, Sylhet MAG Osmani Medical College. The clinical history and findings of physical examinations were recorded. FNAC was done with aseptic precaution following standard procedure. The aspirated materials were smeared on glass slides and promptly dropped in to 95% ethyl alcohol for fixation. These smears were then stained according to Papanicolaou's method for microscopic examination. The biopsy was performed in all cases and the specimens were examined histopathologically.

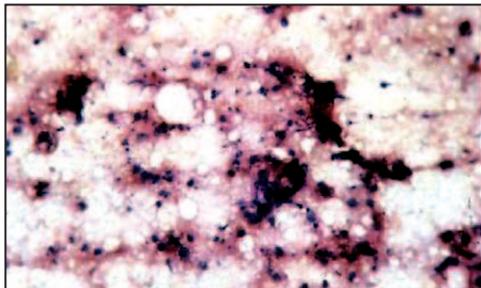
**RESULTS**

The age range of patients was from 11 to 60 years with an average 45 years. Out of the 70 patients, maximum number 23 (32.86%) belonged to the age group of 11-20 years and the next number was 20 (28.57%) belonged to the age group of 21-30 years.

Out of 70 cases, cytologic diagnosis were as follows- 2 (2.86%) acute mastitis, 1(1.43%) granulomatous mastitis, 1 (1.43%) chronic non-specific mastitis, 1 (1.43%) suspicious of malignancy, 40 (57.14%) fibroadenoma (Figure 1), 11 (15.71%) fibrocystic changes, 1(1.43%) phyllodes, 12 (17.14%) ductal carcinoma (Figure 2) and in one (1.43%) case smear was inadequate. [Table-I]



**Figure 1:** Smear preparation of fibroadenoma (Pap's stain: x10).



**Figure 2:** Smear preparation of ductal carcinoma (Pap's stain: x 40).

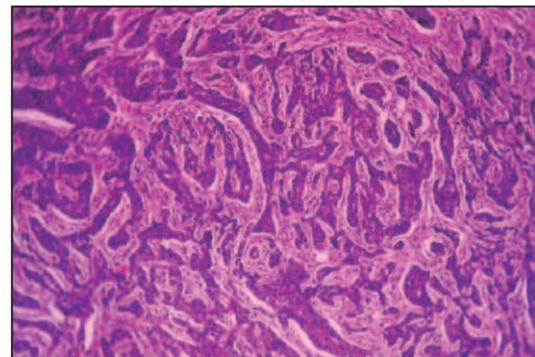
**Table-I:** FNAC diagnosis of breast lump (n=70)

FNAC diagnosis	No of cases	Percentage
Acute mastitis	02	2.86
Granulomatous mastitis	01	1.43
Chronic nonspecific mastitis	01	1.43
Suspicious of malignancy	01	1.43
Fibroadenoma	40	57.14
Fibrocystic change	11	15.71
Phyllodes	01	1.43
Ductal carcinoma	12	17.14
Inadequate smear	01	1.43
<b>Total</b>	<b>70</b>	<b>100</b>

Histopathologic diagnosis of 70 cases were 41 (58.57%) fibroadenoma (Figure 3), 12 (17.14%) fibrocystic change, 11 (15.71%) invasive ductal carcinoma (Figure 4), 2 (2.86%) as acute mastitis, 1 (1.43%) chronic non-specific mastitis, 1 (1.43%) granulomatous mastitis, 1 (1.43%) intraductal carcinoma and 1 (1.43%) low grade phyllodes. [Table-II]



**Figure 3:** Histologic section of fibroadenoma (H&E stain: x10).



**Figure 4:** Histologic section of invasive ductal carcinoma (H&E stain: x10).

**Table-II:** Histological diagnosis of breast lumps (n=70)

Histological diagnosis	No	Percentage
Fibroadenoma	41	58.57
Fibrocystic change	12	17.14
Invasive ductal carcinoma	11	15.71
Acute mastitis	2	2.86
Chronic nonspecific mastitis	1	1.43
Granulomatous mastitis	1	1.43
Intraductal carcinoma	1	1.43
Low grade phyllodes	1	1.43
<b>Total</b>	<b>70</b>	<b>100</b>

**Table-III:** Correlation between Cytopathological and Histopathological diagnosis (n=70)

Cytopathological diagnosis	Histopathological diagnosis								
	No	Fibroa deno ma	Fibrocyc stic change	Invasive ductal carcinoma	Acute mastitis	Chronic nonspecific mastitis	Granulo matous mastitis	Intra ductal carci noma	Low grade phyllo des
Acute mastitis	02	00	00	00	02	00	00	00	00
Granulomatous mastitis	01	00	00	00	00	00	01	00	00
Chronic nonspecific mastitis	01	00	00	00	00	01	00	00	00
Fibroadenoma	40	40	00	00	00	00	00	00	00
Suspicious of malignancy	01	00	01	00	00	00	00	00	00
Fibrocystic change	11	00	11	00	00	00	00	00	00
Phyllodes	01	00	00	00	00	00	00	00	01
Ductal carcinoma	12	00	00	11	00	00	00	01	00
Inadequate smear	01	01	00	00	00	00	00	00	00
<b>Total</b>	<b>70</b>	<b>41</b>	<b>12</b>	<b>11</b>	<b>2</b>	<b>1</b>	<b>1</b>	<b>1</b>	<b>1</b>

**Table-IV:** Validity tests of cytopathological diagnosis of breast lesions

Sensitivity	Specificity value	Positive predictive value	Negative predictive	Accuracy
92.30%	98.24%	92.30%	98.24%	97.14%

In this study, 12 (17.14%) cases were true positive, 1 (1.43%) case was false negative, 55 (78.57%) cases were true negative and 1 (1.43%) was false positive (suspicious for malignancy). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of this study were 92.30%, 98.24%, 92.30%, 98.24% and 97.14% respectively.

## DISCUSSION

In the evaluation of breast masses, the three commonly used methods of obtaining material for microscopic examinations are fine needle aspiration, tru-cut needle biopsy and excisional biopsy. Fine needle aspiration of

the masses of breast to obtain material for cytological analysis has become an accepted procedure. No serious complication has ever been reported.

In this study, FNAC was done in 70 cases. Satisfactory smears were obtained in 69 cases (98.58%) and smear was inadequate in 1 (1.43 %) case. A review of literature revealed that inadequate smears were obtained in many of the studies. Khan<sup>7</sup> reported 1 (2.56%) inadequate smear. Reviewing the literature it is found that inadequate smear were regularly obtained in almost all series and varies from 08.5% to 18.9%<sup>4,8</sup>. This study was not consistent with other studies. It may be due to small sample size.

Out of 70 cases, 68 cytopathologically diagnosed breast diseases were proved histopathologically. Others two cases were inadequate smear and suspicious of malignancy. One (1.43%) inadequate smear was confirmed histopathologically as fibroadenoma (false negative) and 1(1.43%) cytopathologically suspicious of malignancy was confirmed histopathologically as fibrocystic change (false positive). False negative and false positive results were possibly due to sampling error, haemorrhagic aspirates, fibrotic aspirates and aspiration from the necrotic area. Table-III showed the correlation between cytopathological and histopathological diagnosis.

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of this study were 92.30%, 98.24%, 92.30%, 98.24% and 97.14%. Abu-Salem<sup>9</sup> found 92% sensitivity, 97% specificity and Khan<sup>7</sup> found 92.31% sensitivity, 97.50% specificity in the diagnosis of breast lesions by FNAC. Hussain<sup>10</sup> reported 90.90% sensitivity and 100% specificity. Scopa et al<sup>11</sup> reported 90% sensitivity and as high as 100% specificity of FNAC in the diagnosis of breast lumps. The sensitivity ranges from 90.90 - 99.00% and specificity from 97% to 100%, as obtained by different authors.

The diagnostic accuracy seems to be high, nonetheless, some wide variation (70.37 to 95.5%) have been reported. Frable et al<sup>4</sup> reported as low as 70.37% accuracy, Khan<sup>7</sup> reported 94.94% accuracy and Furnival & others<sup>1</sup> reported 95.5% accuracy.

All findings of the present study were not consistent with the findings of other studies. This study was done with a small sample size and the study period was also short. But some findings of this study were more or less similar with other studies.

#### CONCLUSION

Fine needle aspiration cytology is an important pre-operative diagnostic tool for breast lumps. In this study, more than 98% of breast carcinoma was diagnosed cytologically before operation, so it is helpful for pre-operative treatment planning. The above findings of different authors and present study support that FNAC of breast lump is highly helpful, reliable and cost effective procedure both in out-patients clinics and

hospital patients in the diagnosis and management of breast diseases.

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Original Article

## Preoperative Diagnosis of Ovarian Lesions by Risk of Malignancy Index (RMI)

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### ABSTRACT

*The purpose of this study was to evaluate the diagnostic value of Risk of Malignancy Index (RMI). A total of 75 cases from July 2008 to June 2009 who had ovarian tumor and tumor like lesions on the basis of clinical findings were included. Serum CA 125 assay, ultrasonographic examination of whole abdomen, RMI scoring and histopathological examination of ovary were performed in all cases. RMI scoring system showed effective role in the diagnosis of ovarian lesions. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of RMI were 85.70%, 88.88%, 75.00% 94.11% and 88.00% respectively. This study was mostly consistent with others published literature. RMI provides a novel method for assessing the risk of malignant disease in the patients with ovarian lesions.*

**Key words:** CA125, ovarian cancer; RMI.

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### INTRODUCTION

Ovarian neoplasm is one of the complex areas of gynecology because of its greater ranges and varieties than any neoplasm of other organ in the body. Ovarian carcinoma accounts for the greatest number of deaths from malignancies of female genital tract and is the 5<sup>th</sup> leading cause of cancer fatalities in women<sup>1</sup>. The prognosis for survival from ovarian cancer is largely dependent upon the extent of disease at diagnosis. In the past few years, significant progress has been made in identifying novel method for early detection of

ovarian cancer. Among the various markers, CA125 along with ultrasound has been proposed to be more capable of making differential diagnosis of benign & malignant ovarian masses<sup>2</sup>. The development of a mathematical formula uses a logistic model, incorporating menopausal status, the serum level of CA125 and ultrasound finding in score system, has been described in the literature in the form of different malignancy index. The formula is Risk of Malignancy Index (RMI)=U x M x CA125. This index is the product of the ultrasound findings score (U), the menopausal status score (M) and the absolute value of CA125 serum levels. Jacob et al originally developed the RMI to increase the preoperative prediction of ovarian malignancy<sup>3</sup>. The study was done to evaluate the diagnostic value of RMI.

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**MATERIALS AND METHODS**

A total 75 cases presenting with ovarian lesions reported in the inpatient and outpatient department of Obstetrics and Gynecology of Sylhet M A G Osmani Medical College Hospital and Jalalabad Ragib-Rabeya Medical College Hospital from July 2008 to June 2009 were consecutively selected in this study. Ultrasonogram of whole abdomen, serum CA125 assay and histopathological examination of ovarian mass were performed in all cases.

On Ultrasonogram examination, findings of ovary particularly multilocularity, solidity, bilaterality, ascites and presence of metastases of patients were noted. The calculation was based on a simple equation where total ultrasound score of 0 gave U=0, score 1 U=1 and score 2-5 U=3.

Postmenopausal status is defined as more than one year of amenorrhea or age older than 50 years in women who had a hysterectomy. Women who did not meet these criteria were classified as premenopausal<sup>4</sup>. Premenopausal status gave M=1, postmenopausal state M=3.

The serum CA125 was determined by MEIA (Micro-particle Enzyme Immunoassay) technique for quantitative measurement (IMX, Abbott Laboratories, USA)<sup>3</sup>. The optimal cutoff value of serum CA125 was 35U/ml<sup>5, 6, 7, 8</sup>.  $RMI = \frac{S \cdot CA125 \cdot M \cdot U}{100}$  (Where, S. CA125=the absolute value of Serum CA125; U=ultrasound score; M=menopausal score). All the scoring system was taken from Jacob et al<sup>3</sup>.

**RESULTS**

The age of patients ranged from 15 to 75 years. Considering the decade as a group, patients were divided into seven groups. The maximum number 21 cases (28.0%) belonged to the age group 21 to 30 years.

Among the hisopathologically diagnosed cases of 75 ovarian lesions, 54 (72.0%) cases were benign tumors and 21 (28.0%) were malignant tumors. Serum CA125 was <35U/ml in 48 (62.70%) cases and >35U/ml in 27 (37.30%) cases. Serum CA125 in evaluation of ovarian lesions had sensitivity 80.95%, specificity 81.48%, positive predictive value 62.96% and negative

predictive value 91.66%. The results are summarized in Table I.

Of the 75 cases of ovarian lesions, 51 (68.0%) were premenopausal and 24 (32.0%) were post menopausal female age. Of these 51 premenopausal cases, 41 (75.9%) were benign and 10 (47.6%) were malignant tumor. Of the total 24 postmenopausal cases 13 (24.1%) had benign and 11 (52.4%) had malignant tumors.

Of the total 75 cases of ovarian lesions, in 54 benign cases USG score were 1 in 32 (59.3%) cases and 3 in 22 (40.7%) cases. Of the total 21 malignant cases, in 5 (23.8%) cases USG score were 1 and 16 (76.2%) cases USG score were 3. USG in evaluation of ovarian lesions had sensitivity 76.19%, specificity 59.25%, positive predictive value 42.10% and negative predictive value 86.48%. The result are summarized in Table I

Of the total 75 cases of ovarian lesions, RMI was <200 in 51(68.0%) cases and RMI was >200 in 24 (32.0%) cases. Out of the 54 benign cases, in 48 (88.9%) cases RMI were <200 and 6 (11.3%) cases RMI were >200. Out of the 21 malignant cases, in 18 (85.7%) cases RMI were >200 and 3 (14.3%) in cases RMI were <200. RMI in evaluation of ovarian lesions had sensitivity 85.70%, specificity 88.88%, positive predictive value 75.00% and negative predictive value 94.11%. The results are summarized in Table I.

**DISCUSSION**

There are several methods in obtaining a preoperative diagnosis for the evaluation of ovarian lesions. Any method used to obtain a preoperative diagnosis must be entirely reliable and also provide a diagnosis in a large enough proportion of patients to achieve its objective. A risk of malignancy index (RMI), a systemic basis of three combined tests, is a reliable diagnostic scoring system to discriminate malignant from benign lesions. For early detection of ovarian cancer; the most thoroughly assessed ovarian cancer marker is still CA125 but it has some limitation in early detection of ovarian cancer due to nonspecificity and limited clinical use for detecting some ovarian benign

**Table I:** Comparative evaluation of RMI, CA125 and USG score of ovarian lesions

Name of tests	Sensitivity %	Specificity %	PPV %	NPV %
RMI (cut off level 200)	85.70	88.88	75.00	94.11
CA125 (cut off level 35U/ml)	80.95	81.48	62.96	91.66
USG score (cut off level 3)	76.19	59.25	42.10	86.48

**Table II:** Comparative evaluation of RMI with other investigators who worked on ovarian lesions

Study	Sensitivity%	Specificity%	PPV%	NPV%
Jacob et al., (1990) <sup>3</sup>	85	97	NA	NA
Tingulstad et al., (1996) <sup>4</sup>	80	92	89	88
Morgante et al., (1999) <sup>15</sup>	58	95	78	87
Manjunath et al.,(2000) <sup>9</sup>	73	91	93	67
Torres et al., (2003) <sup>11</sup>	73	86	NA	NA
Andersen et al., (2003) <sup>14</sup>	70.6	87.7	66.1	89.8
Shuiqung et al.,(2003) <sup>13</sup>	87.3	84.4	82.1	NA
Obeidat et al., (2004) <sup>10</sup>	90	89	96	78
Pariyar J (2008) <sup>12</sup>	85	94	NA	NA
Asif et al., (2004) <sup>2</sup>	87	88	NA	NA
Present study (2009)	85.70	88.88	75.00	94.11

PPV= Positive predictive value; NPV= Negative predictive value; NA= Not available

neoplasms or mucinous carcinomas. On Ultrasonogram examination, findings of ovary particularly multilocularity, solidity, bilaterality, and ascites, presence of metastases of patients were noted. Different workers used different scoring systems of USG findings. Some used scoring system as 0, 1 and 2<sup>4</sup>, some used scoring system as 0,1,2,4 and 5<sup>11</sup>, some used scoring system as 0, 1 and 3<sup>3,9,10</sup> on the basis of ultrasound findings. In this study scoring system was taken from Jacob<sup>3</sup> due to some limitation of non-availability of new ultrasonogram technique. Using the ultrasound score alone produce slightly more false positives. RMI overcomes the false positive problem found in using single factor alone, and increases the sensitivity and specificity in the pre-operative diagnosis of ovarian malignant neoplasm.

In reviewing the observations of my known studies by different authors it had been seen that sensitivity of RMI ranged from 58% to 90% and specificity ranged from 88% to 96%. The result of RMI may be variable due to sample size, variation of histologic subtype and technique of USG, Scoring system is different from others and CA 125 does not raised in all histologic types of malignancy. But the present study correlates well with other published studies (Table II)<sup>2,3,4,9,10,11,12,13,14,15</sup>.

The present study of RMI showed that sensitivity and specificity were better than single test of CA125, ultrasonogram and menopausal status. On evaluation of result of known studies including this one it is noted that RMI is superior to individual level of CA125 and ultrasonogram score for sensitivity that is RMI can

more accurately identify the malignant tumor of ovarian lesions than others. The risk of malignancy index is a simple scoring system which can be applied directly into clinical practice without establishing expensive, laborious and complicated methods.

## CONCLUSION

It may be concluded that, this easy, highly beneficial method would be used as guide to a surgeon about surgical treatment of ovarian lesions to be undertaken.

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Original Article

## Socio-demographic Profile of the Patients with Psychiatric Disorders Admitted in A Tertiary Hospital

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### ABSTRACT

*This cross sectional and descriptive study was done to estimate the pattern of the socio-demographic distribution of psychiatric disorders among patients admitted in the Psychiatry department of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet. A total of two thousand two hundred three patients with different psychiatric disorders were studied during the period 1<sup>st</sup> April 2004 to December 2008. The mean age of these patients was 26.54 ( $\pm$  18.7) years with male female ratio was 1:4. About 82.98% patients were Muslim, 60.83% were married and 54.88% were educated up to primary level, 37.99% were illiterate and 57.88% of rural residence. 70% patients were referred by medical personnel. Only 10% and 18% patients had positive family history and past history of psychiatric disorders respectively. Associated physical diseases found in 10% of patients. In this study, an attempt was made to find out the pattern of psychiatric disorders in relation to socio demographic and socio economic background among the people of north-east region of the country.*

**Key words:** Psychiatric disorder, socio-demographic profile, conversion disorder.

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### INTRODUCTION

Psychiatric morbidity is major public health problem in the world across the developed and the developing countries<sup>1</sup>. According to the WHO, at least 40 million peoples in the world suffer from severe mental disorders such as Schizophrenia & dementia<sup>1</sup>. Studies in developed countries such as USA, Australia & England have shown 15-25% prevalence of Psychiatric illness in different populations<sup>1</sup>. The data is similar or even worse in developing countries including Bangladesh, where prevalence ranges from 17% to 66%<sup>1</sup>. Recently conducted national survey on mental

health in Bangladesh showed that 16.05% of adult populations are suffering from some sorts of mental disorders<sup>1</sup>. The available mental health services in the country are inadequate in comparison to the need of the people. In this study, an attempt was made to find out the pattern of psychiatric disorders in relation to socio demographic and socio economic background among the people of north-east region of the country.

### MATERIALS AND METHODS

This cross-sectional descriptive study was conducted in the department of psychiatry in Jalalabad Ragib-Rabeya Medical College & Hospital during the period of 1<sup>st</sup> April 2004 to 31<sup>st</sup> December 2008. A total of 2203 patients with different psychiatric disorders were included in this study. Sample was collected by using a questionnaire containing socio-demographic or other

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relevant information such as age, sex, religion, marital status, habitat, education, occupation family size which was developed in the department. Psychiatric disorders were diagnosed according to Diagnostic and Statistical Manual of Mental Diseases-IV TR (DSM-IV TR). Physical examination and supportive investigations were done in appropriate cases. Simple statistical analysis such as standard deviation, mean & percentage, were done for data analysis.

Three family sizes are classified as, (1) Small (having less than 5 members), (2) medium (having 6-10 members) and (3) large (having more than 10 members) were discriminated.

### RESULTS

The information collected on socio-demographic variables in 2203 subjects is given in tables. The highest percentage of psychiatric patients were in 21-30 years age (38.99%) group in both sexes. The mean age of these patients were 26.54 ( $\pm 18.7$ ) years (Table-I). Most of the patients were female (79.98%) with male to female ratio was 1:4 (Table –II).

Table- III showed the distribution of the patients by socio-demographic status. 57.88% patients had rural background and to urban counterpart. Highest number

of cases were Muslim (82.98%). Table-III showed 60.83% patients were married but unmarried divorced and widow patients contributed 34.04% and 5.13% respectively. 37.99% patients were illiterate in comparison to 54.88% patients educated up to primary level. About 7.13% patients read up to secondary level of education. The housewife group as occupation contributed largest group (36.54%) followed by students group (24.35%) in the series. 25.78% patients were referred by treated psychiatric patients and/or their relatives. But referral from general practitioners & specialists was 40.10%. Only 9.95% patients were self motivated 16.47% patients had family history of psychiatric disorders mostly in 1<sup>st</sup> degree relatives (11.23%). 16.9% patients had past history of psychiatric disorders and in 9.84% associated physical disease were found. Most of the patients were female (79.98%), two-third was from lower socio economic class 57.88% and 82.98% were Muslim. A little more than half of the patient had primary education. Half of the participants hailed from rural area (57.88%). The age of the respondents ranged from 11 years to 65 years. 54.88% patients had at least school level. Most of the female respondents were housewives. Three-quarter were recently married.

**Table-I:** Age distribution of patients (n=2203)

Age group (years)	Number of patients			Percentage (%)
	Male	Female	Total	
11-20	146	599	745	33.82
21-30	170	689	859	38.99
31-40	77	266	343	15.57
41-50	24	134	158	7.17
51-60	19	55	74	3.36
61-70	6	18	24	1.09

Mean age : 26.54 ( $\pm 18.7$ ) years

**Table-II:** Sex distribution of patients (n=2203)

Sex of the respondent	No. of patients	Percentage (%)
Male	442	20.06
Female	1761	79.94

**Table- III:** Distribution of the patients by socio-demographic status (N=2203)

Socio-demographic characteristics		No. of patients	Percentage
A. Habitat:	Urban	928	42.12%
	Rural	1275	57.88%
B. Religion	Muslim	1828	82.98%
	Non-muslim	375	17.02%
C. Marital status:	Married	1340	60.83%
	Unmarried	750	34.04%
	Divorced/Widowed	113	5.13%
D. Education	Illiterate	837	37.99%
	Primary	1209	54.88%
	Secondary	157	7.13%
E. Occupation	Housewife	805	36.54%
	Service	178	8.08%
	Student	536	24.33%
	Unemployed	490	22.24%
	Others	194	8.81%
F. Referral System	General physician	1275	57.88%
	Specialist	837	37.99%
	Self	91	4.13%
G. Family Size	Small	361	16.39%
	Medium	840	38.13%
	Large	1002	45.48%

**Table IV:** Distribution of the patients according to diagnosis (n=2203)

SI. no	Diseases	No. of Patients	Percentage (%)
1.	Conversion disorder	1275	57.88
2.	Anxiety disorder (Generalized, phobic, acute stress disorder, Obsessive compulsive disorder & others)	203	9.21
3.	Other somatoform disorder (Somatization disorder and Dissociative disorder)	190	8.62
4.	Depressive disorder	221	10.03
5.	Schizophrenia	105	4.77
6.	Bipolar affective disorder	95	4.31
7.	Substance related disorder	45	2.04
8.	Organic mental disorder (Dementia and Delirium)	3	0.14
9.	Others (Psychotic disorders not otherwise specified, Mental retardation, Attention deficit hyperkinetic disorders and Delusional disorder).	66	3.0

Table-IV showed distribution of psychiatric disorder by diagnostic categories with anxiety and somatoform disorder (75.71%) was highest in percentage followed by major depressive disorder (10.03%) schizophrenia (4.77%) and affective disorders (4.31%) respectively.

Substance related disorders were found only in 2.04% of patients. The predominant psychiatric disorders was conversion disorder (57.88%) followed by depressive disorder (10.03%), and psychosis (12.08%).

## DISCUSSION

This study has been describing the socio-demographic and morbidity characteristics of patients with psychiatric disorders in Jalalabad Ragib-Rabeya Medical College Hospital, which is rendering psychiatric services mainly to the people of greater Sylhet. Majority of the patients were younger and about 90% of all below the age of 40 and was consistent with the findings of Ahsan<sup>2</sup> and Chowdhury<sup>3</sup>. Female patients in this study were more than male and number of female patients decline significantly after age of 40. This was not consistent with the findings of Ahsan's study<sup>2</sup>. This higher frequency of female (n=1761, 79.94%) in this sample may be because of the somatic presentation were more common in female in our society which is more conservative and where direct expression of any intense emotion is prohibited. In our sample, somatoform disorder including conversion disorder was the major group of sufferer (75.71%) and majority were female (79.94%). There was a higher percent of somatoform disorders specially conversion disorder in this sample of patients with somatic presentations usually preferred to admit themselves in a general hospital rather than a psychiatric hospital or clinics. The reason may be due to excessive stressful life situation and conservativeness of the families in this region. Moreover a large groups spouse of the patient were staying aboard for years together creating excessive filling of insecurity in the wives. As well as they were the victims of maladjustment in the family. Conservativeness of family, lack of emotional sharing, economic dependency of the patients to others and different types of family anxiety were the important contributory factors in this psychopathology. This sample was highly selective and not reflecting the actual population representation, so no definite conclusion could be done. The present findings that 37.99% patients were illiterate which was not similar that of the figure of 18.8% reported by national mental health survey in Bangladesh 2006<sup>1</sup>. Poor socio-economic condition, lack of awareness, cultural prejudice regarding mental disease were important factors for the under representation of the figure. This was supported by the findings of other study<sup>4</sup>.

About a half of these patients (54.88%) in this series were educated either primarily or secondary standard indicating that education has a positive impact on psychiatric consultation possibly due to more awareness and orientation to scientific methods of psychiatric treatment. This is not consistent with

national survey. In the national survey in Bangladesh, a little more than one-third (36.2%) of patients had primary education and it was a represented the population of the country<sup>1</sup>. This difference found in our study due to small sample size, highly selective only for hospitalized patients and region specific in the small region of the country. So it would not reflect the total population representation.

Female patients were mostly housewives, whereas unemployed and student formed the main bulk of male patients. These findings raised the possibility that these groups were more vulnerable to psychiatric problem possibly due to increased psychosocial stress in their life. There were some studies suggesting a casual relationship between unemployment and psychiatric problem<sup>5</sup>, and adverse effects of unemployment on mental health<sup>6</sup>. In our social context, number of women employment outside home was insignificant. They were maintaining all types of family works and care of the child and other family members and economically dependent to others. As a result most of them confronted adverse life situations and unable to express their normal emotion, desire and drive spontaneously. That is why they become vulnerable to emotional & somatoform disorders. Bebbington et al<sup>7</sup> predicted that employment was protective for both sexes. Here student population (62.01%) in both sexes is over represented showing inconsistency with that of Islam et al (5.82%)<sup>8</sup> and Ahsan<sup>2</sup> (23.2%). The adverse and critical environment in academic institutions, academic work load are the important potential factors for increased anxiety disorder in this group.

This is study reflected the increasing trend of reference by medical professionals. This is possibly due to gradual development of psychiatric orientation. Training of mental health in thana health complex doctors, health assistant and different motivational programme may have the role for such improvement in comprehensive referral system<sup>4,8,9,10</sup>. An intriguing finding of considerable importance was that a good number of patient attended by self reference. The observation about past history of psychiatric illness in these patients suggested the relapsing tendency of some of the psychiatric problem as well as development of new psychiatric problem in a already cured patient. Reaction to environment, psychosocial stress and individual vulnerability factors were thought to be involved in the pathogenesis. Family history of psychiatric disorders in first degree relatives of these patients accounted an increased familial risk for such psychopathology and this was supported by different

research workers<sup>11</sup>.

The positive association of physical with psychiatric disorders found here was also supported by Eastwood et al<sup>12</sup> in a survey of randomly chosen sample of general population. In another study in a general psychiatric in patient unit, 33.5% patients were found to have concurrent physical disease of these 9% required transfer to medical side.

In present study, Neurotic group of illness (85.74%) contributed largest share which was comparable to that of Islam et al & Ahsan<sup>2</sup> where schizophrenia were relatively higher in proportion, In the other hand, schizophrenia was found significantly higher in percentage (77%) at Pabna Mental Hospital out patients than other's general hospital studies. This could be explained by the fact that majority of chronic schizophrenic patients in addition to acute ones were usually brought to mental hospital for long stay treatment. In fact, affective and neurotic disorder groups were higher in proportion in almost all the studies in general hospital than the mental hospital which suggested advantages of psychiatric units in general hospital for treatment of these types of patients. This concept was initially advocated by Mosher<sup>13</sup> in 1909.

## CONCLUSION

Mental disorders are important public health problem in the country. Findings of national health survey showed the gravity of mental disorders in Bangladesh. Our small data was from a selected population showing some inconsistencies with national survey results. All this pictures demands to organize national health programme to improve service and facilities for a large group mentally ill patients. Nationwide mental health programme and the pervasive role of the ever expanding media may be the reasons for the social achievement. In the same time, educational and training programme is highly essential to develop awareness in society. Improvement of service facilities and quality in general hospital, primary healthcare and also in tertiary level of hospital are also needed to meet up the demand of the large number of psychiatric patients in the community.

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## Review Article

# Recent Advancement in the Management of Postmenopausal Osteoporosis

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### PURPOSE OF REVIEW

*Osteoporosis is a major public health threat and economic burden in developed countries as well as developing countries. Globally, more than 200 million women have osteoporosis. Osteoporotic hip fractures occurring in the world each year will rise from 1.66 million to 6.26 million by the year 2050, thereby implying an urgent need for preventive strategies. Sufficient intake of calcium and vitamin D is recommended as baseline therapy for osteoporosis prevention and treatment. Available pharmacological agents for the management of postmenopausal osteoporosis may not be appropriate for all women. Oral bisphosphonates are generally considered first-line therapy for patients with osteoporosis, but their use may be limited by gastrointestinal side effects. Other agents include hormone therapy, the selective estrogen receptor modulator (SERM) raloxifene, salmon calcitonin, teriparatide (human recombinant parathyroid hormone) and strontium ranelate. Besides these pharmacological agents, dietary intervention and life style modification are also important. The purpose of this review is to put forward recent advancement about the management of postmenopausal osteoporosis approaches to health care practitioners, thereby it reduce morbidity & mortality.*

**Keywords:** bone mineral density, bisphosphonates, osteoporotic fracture.

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### INTRODUCTION

Postmenopausal osteoporosis is a silent progressive disease of bone characterized by decrease in bone mass and a deterioration of tissue of the bone which leads to increased fragility and susceptibility to fracture. The composition of bone tissue is normal but the quantity is reduced, therefore, decreased bone mineral density. Osteoporotic bone fracture are most commonly occurs in spine, hip and wrist<sup>1,2</sup>. Fractures related to osteoporosis are a major public health problem in all developed countries and are estimated to affect up to 30% in women and 12% in men at some times in their

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life<sup>3</sup>.

The aim of treating osteoporosis is to prevent further skeletal deterioration, and to increase bone mass and improve bony micro-architecture to reduce the risk of vertebral and other bone fractures. One of the major causes of skeletal fractures is bone loss that occurs after menopause either natural or surgical within 15 to 20 years from the cessation of the ovarian function<sup>4</sup>.

Primary prevention of osteoporosis initiated in the immediate post menopause is not yet considered a public health priority by most. Many physicians are faced with situations in which women seek treatment at later stages of the disease, when the diagnosis is obvious<sup>5</sup>. None of the available medications (such as estrogen, estrogen-progestin, calcitonin and early generation bisphosphonates) has unequivocally demonstrated their ability to fully prevent the

occurrence of new vertebral or peripheral fractures once the disease is established. This review will focus along with the conventional drugs, on the newer drugs that provide a better preventive and therapeutic approach to the postmenopausal osteoporosis.

**EPIDEMIOLOGY**

Currently, it is estimated that over 200 million people worldwide suffer from this disease<sup>6</sup>. Approximately 30% of all postmenopausal women have osteoporosis in United States and Europe. At least 40% of these women<sup>7</sup> and 15-30% of men<sup>8</sup> will sustain one or more fragility fractures in their remaining lifetime. Ageing of populations worldwide will be responsible for a major increase of the incidence of osteoporosis in postmenopausal women<sup>9</sup>. Asia look forward to the most dramatic increase in hip fracture during the coming decades, mainly because of an aging population but also due to a changing life style<sup>10</sup>.

**BONE MINERAL DENSITY (BMD)**

The term low bone mineral density is the only measurable determinant of bone strength. Bone fragility is also the result of micro-architectural changes but these cannot be readily measured or used in practice as yet<sup>11</sup>. Table-I, lists the definitions of normal or low BMD.

**CONCEPTS OF Z-SCORE AND T-SCORE**

The Z-score is a measure of how many standard deviation the patient’s measurement differs by from age matched control, while the T-score is a measure of how many standard deviation the patient’s measurement differs from young healthy control. The comparison with average or mean peak bone mass is called the T-score. A T-score between -1 standard deviation (SD) and -2.5 SD is defined as osteopenia, whereas a T-score of less than -2.5 standard deviation is defined as osteoporosis and if accompanied by fractures, as severe osteoporosis. A Z-score less than -2 SD would indicate an abnormal low bone mineral density. To improve readability the present review will use the term osteoporosis for Z-score less than -2.5 SD and osteopenia for Z-score less than -1 SD<sup>13</sup>.

**PATHOGENESIS**

Osteoporosis is reduced bone mass caused by an imbalance between bone resorption and bone formation. Individual who have normal peak bone mass are protected against osteoporosis, even though they suffer age-related bone loss whereas patients with low peak bone mass are at risk of developing osteoporosis from age-related bone mass. Osteoporosis can also occur in patients with normal peak bone mass if bone resorption substantially exceeds bone formation are at risk of severe osteoporosis<sup>3</sup>.

**Table-I:** Classification of bone mineral density level.

Description	Meaning
Normal BMD	BMD above -1SD from the young normal mean
Low BMD or Osteopenia	BMD between -1SD and -2.5 SD
Osteoporosis	BMD is reduced below -2.5 SD
Severe or established osteoporosis	BMD is reduced below -2.5 SD in the presence of fracture

Adapted from the WHO Technical Report Series. 1994<sup>12</sup>. SD= Standard deviation.

**Table-II:** Risk factors for osteoporosis and osteoporotic fracture.

Genetic	: Race, Low body weight, Family history
Lifestyle	: Diet/Calcium intake, Exercise, Highly trained athletes*
Endocrine	: Pituitary disease*, Early menopause*, Thyrotoxicosis, Hyperparathyroidism
Inflammatory disease	: Ankylosing spondylitis, Rheumatoid arthritis, Inflammatory bowel disease
Gastrointestinal disease	: Malabsorption, Chronic liver disease
Drugs	: Corticosteroids, Anticonvulsants, Sedatives, GnRH agonists*
Substance misuse	: Alcoholism, Smoking
Others	: Anorexia nervosa*, Myeloma, Homocystinuria, Gaucher’s diusease

\*Underproduction of sex hormones plays an important role in osteoporosis associated with these conditions.

**Role of fall in causing fracture**

Fracture occurs in only 3% to 6% of older person, who fall even though at least 30% to 40% of the elderly have osteoporosis. Even in the presence of documented osteoporosis fracture seldom occur in elderly persons who do not fall. In contrast, those who have both low bone density and multiple risk factors for falling are 27 times more likely to experience an osteoporotic fracture<sup>14</sup>.

**CLINICAL PRESENTATION OF OSTEOPOROSIS**

Most frequent symptoms from vertebral body fracture are pain in the back and deformity of spine<sup>15</sup>. Pain usually occurs in dorsal and lumbar region, is typically acute in onset and often radiates around the flank into abdomen<sup>16</sup>.

**Physical Examination<sup>16</sup>:**

As part of the comprehensive physical examination, particular attention should be made about posture (signs related to osteoporotic compression changes), gait (flexibility), muscle tone, coordination, height and body proportion, body mass index, body composition and waist circumference, breast examination, pelvic examination and eye sight and hearing acuity.

**Laboratory findings in osteoporosis**

Biochemical measurements in osteoporosis are usually normal. The concentration of calcium and inorganic phosphorus in the blood are usually normal<sup>17</sup>. However, recent immobility in a young person considerably increases the urine calcium and after the menopause the ratio of calcium and of hydroxyproline to creatinine measured in the urine after an overnight fast, both may be increased which implies increased bone resorption. About 20% of postmenopausal women with osteoporosis, have hypercalciuria. The Alkaline phosphatase level in uncomplicated instances is normal but it may increase after recent fracture. Immunoassays for urinary excretion of type-I collagen derived pyridinoline cross links such as free and total pyridinoline and N-telopeptide cross links are better than assays of hydroxyproline. Such assays and serum assay of bone specific alkaline phosphatase, osteocalcin and C-terminal procollagen peptide are particularly useful in monitoring the effect of therapy<sup>18</sup>.

**Radiological Studies<sup>18</sup>**

Plain films of skeleton do not detect osteoporosis until there is 30% loss of bone mass. They are useful in detecting the major complication of osteoporosis.

Recommended specific indication for densitometry measurement of skeleton are<sup>17</sup>: to confirm a radiological suggestion of osteoporosis, the monitoring and evaluation of therapy, aid with decision about hormone replacement therapy, corticosteroid induced osteoporosis, early menopause, hypogonadism and family history of osteoporosis.

**Different Methods of Measuring Bone Mass or Density**

Conventional skeletal radiography, Radiographic photodensitometry, Radio grammetry, Single Energy Absorptiometry, Dual Energy Absorptiometry, Dual Energy X-ray Absorptiometry (DXA), Ultrasound evaluation of bone etc.

**DIFFERENTIAL DIAGNOSIS OF OSTEOPOROSIS**

There are several disease conditions which can mimic osteoporosis. There are some other disease in which osteoporosis is a mode of presentation<sup>18</sup>. So, in the presence of bone pain with or without fracture or deformity, it is important to establish the presence or absence of known cause of osteoporosis.

Malignancies of various types particularly multiple myeloma, lymphoma, leukemia and metastatic carcinoma may result in diffuse loss of bone, especially the tubercular bone of the vertebral column even in the absence of hypercalcaemia. The absence of anemia, elevated ESR, abnormal electrophoretic patterns of serum proteins and Bence-Jones proteinuria is helpful to exclude multiple myeloma<sup>18</sup>.

Radiological evidence of osteoporosis is common in patients with primary hyperparathyroidism who may not have osteitis fibrosa and elevation of serum alkaline phosphatase. An element of secondary hyperparathyroidism may be present in some patients with type-II osteoporosis and in others with impairment of renal function, inadequate oral calcium intake or decrease of intestinal calcium absorption.

Osteomalacia may mimic osteoporosis or coexist with it; yet specific radiologic sign of osteomalacia are not always present. Although the presence of abnormalities such as low or under detectable circulating levels of 25-hydroxy vitamin-D and PTH with or without hypophosphatemia suggest the possibility of osteomalacia, bone biopsy may be essential for diagnosis. Occasionally, patients with Paget's disease pure lytic radiologic features may be confused with osteoporosis. High alkaline phosphatase levels and increased urinary excretion of pyridinoline cross-links are clues to the presence of Paget's disease<sup>16</sup>.

## MANAGEMENT OF POSTMENOPAUSAL OSTEOPOROSIS

There are two modalities for the management of postmenopausal osteoporosis.

A) General and B) Pharmacological

**General:** Patients with mild to moderate reduction in BMD (T-score values of between -1.0 SD and -2.5 SD) who do not have fractures may be benefited by this modality of treatment. Following points are worthwhile in the non-pharmacologic management of osteoporosis.

**I. Life style modifications:** Habits such as tobacco and caffeine use should be avoided. Alcohol should be consumed in a restricted amount such as less than 20 units/week for men and less than 15 units/week for women. A sedentary life style is also a risk factor, so it should be avoided. Weight bearing exercise is associated with increase in bone density. Dietary calcium intake and fluoride supplementation are additional measures which prevents osteoporosis and its related fracture<sup>17</sup>.

**II. Preventing falls:** Frequent falls plays a significant role in causing fracture in osteoporotic elderly. Therefore, medication that affect perception and balance cause frequent falls in persons and subsequently increases the likelihood of fracture. In particular, long acting sedative hypnotics, tricyclic antidepressants and anticonvulsants are associated with a significant increase in the incidence of fracture and should be avoided. Good lighting and removal of environmental hazards may reduce the risk of falls. Exercise to maintain mobility and quadriceps strength should be undertaken.

**III. Medical Conditions:** Various medical conditions may exacerbate the risk of fracture.

**Pharmacological:** In patients with greater reduction in bone density (T-score values of -2.5 SD and below) with or without fracture, specific drug therapy should be considered. Over the last 5 years, a number of new drugs have appeared and more are expected in the near future. Some agents that specifically treat osteoporosis (Bisphosphonates, Calcitonin); others such as tissue selective estrogens (SERMs) have broader effects. The evidence supporting the effectiveness of each remedy is variable in part because these treatments are new.

**I. Hormone Replacement Therapy (HRT):** For postmenopausal women, estrogen replacement or hormone replacement therapy has been considered the gold standard for the treatment of both menopausal symptoms and osteoporosis<sup>19</sup>. HRT is defined as the "replacement of estrogen only or estrogen and progesterone in combination for menopausal women". Estrogen acts on bone cells which contain both

isoforms of estrogen receptors. Estrogen deficiency is the cause of postmenopausal osteoporosis. When estrogen is deficient, bone turnover increases and bone resorption increases more than bone formation, leading to bone loss. In current users who had taken HRT for 5 years or more, the risk of developing breast cancer increase by 40% , though this arose to as high as 70% among older women<sup>20</sup>.

**II. Bisphosphonates:** Bisphosphonates are stable analogues of pyrophosphate. They are poorly absorbed from the intestine and must not be taken with food. They are deposited in bone at sites of mineralization and in resorption lacunae or eliminated by the kidneys. The exact mode of action is uncertain but their net effect on osteoclasts or their precursors with a resultant increase in cell death and therefore a decrease in bone resorption. Bisphosphonate therapy results in increased bone mineral density and a decreased fracture rate. Several alendronate compounds of this family have been evaluated for the prevention of bone loss (Clodronate, Pamidronate, Tiludronate, Residronate and Ibandronate)<sup>21</sup>.

**Alendronate** is given at a dose of 10 mg per day for the treatment of osteoporosis in postmenopausal women. It increased bone mineral density 8.8% in the lumbar spine and 5.9% in the femoral neck after three years. Alendronate therapy also resulted in a 48% decrease in the proportion of women with new fractures and prevented height loss. In a report from a two years study, 5 mg of alendronate per day had less effect on bone mineral density than estrogen replacement therapy but resulted in fewer adverse events<sup>22</sup>. Among the 2027 women with vertebral fractures in the Fracture Intervention Trial 30 who were treated with 5 mg of alendronate daily for two years, with a subsequent increase to 10 mg per day for the final nine months of the study, the rate of new vertebral fractures decreased by 47% as compared with the rate in the placebo group. There were similar decreases in the frequency of hip and wrist fractures but of other fractures<sup>23</sup>. It has been associated with esophagitis including erosive esophagitis. The symptoms of esophagitis usually begin within one month after therapy is started. To minimize the risk of esophagitis and increase drug absorption, the patient should take alendronate with a glass of water while upright 30 minutes before breakfast<sup>24</sup>.

**Etidronate** was the first bisphosphonates to be approved; initially it was used in Paget's disease and hypercalcemia. This agent has also been used in osteoporosis trials & vertebral fracture of smaller magnitude than those performed for alendronate and

residronate. Etidronate given continuously at high doses can result in impaired mineralization which can be avoided by low dose intermittent therapy. Therefore the drug is usually given at a dose of 400 mg per day for 2 weeks followed by 500 mg of supplemental calcium per day for 11 weeks<sup>16</sup>.

**Ibandronate** is orally administered, daily and intermittent use significantly reduced the risk of radiological confirmed vertebral fractures by 62% and 50% respectively, compared with placebo and showed sustained effect over the trial period<sup>25</sup>. Once weekly ibandronate (20 mg) and daily 2.5 mg administration induced almost identical increases in lumbar spine BMD after 48 weeks and the once weekly regimen was proven to be statistically non inferior to daily administered oral ibandronate. Three monthly 2 mg intravenous ibandronate bolus injections were related 5% increases of lumbar spine BMD after 1 year. Significant benefits were also reported at the femoral neck or at the trochanter<sup>26</sup>.

**II. Selective Estrogen Receptor Modulators (SERM):** Estrogen replacement therapy or hormone replacement is the gold standard for the management of postmenopausal osteoporosis. Long term hormone replacement therapy increases the risk of breast and endometrial cancer<sup>20</sup>. The first clues to the possibility of ideal estrogen were provided by compounds that were associated traditionally with estrogen antagonist activity for breast cancer and thus were categorized as antiestrogen. These agents exemplified by tamoxifene and raloxifene. The effect of raloxifene on bone are well established. Raloxifene at a dose of 60 mg per day is effective in preventing and treating postmenopausal osteoporosis. As with other medications used as anti resorptive therapy, combined treatment with 1000 mg or more of elemental calcium and 400 units of vitamin D daily advisable. It also decreased the incidence of vertebral fractures by 30 to 50 percent, depending on dosage but did not decrease the incidence of hip fracture or other non-vertebral fractures<sup>27</sup>.

**III. Vitamin D and its metabolites and analogues:** In a recent randomized controlled study of elderly French women, supplementation with 800 IU cholecalciferol (Vit-D) and 1.2 gm elemental calcium daily, resulted in a significant reduction (30%) in the rate of hip and other non-vertebral fracture. Calcium alone may be partially effective in preventing bone loss, especially in older women and those with a low calcium intake. In a study of women who were over 60 years old and consumed less than 1000 mg of calcium per day, a calcium supplement of 1200 mg per day prevented bone loss from the forearm over a period of four years.

There was a 59% reduction in the rate of vertebral fracture in the women who had vertebral fractures at base line<sup>28</sup>.

**IV. Calcitonin:** Salmon or human calcitonin is given by subcutaneous or intramuscular injection at doses up to 100 IU daily. Calcitonin therapy results in an increase in bone mineral density and in one un-blinded study it resulted in a decrease in the rate of vertebral fracture. It is less effective at preventing cortical bone loss than cancellous bone loss in postmenopausal woman. It is expensive must be given by injection and can cause nausea, flushing and diarrhea<sup>29</sup>.

**V. Parathyroid hormone:** Daily injections of parathyroid hormone stimulate bone formation. In 34 women with osteoporosis who were already receiving estrogen replacement therapy, administration of parathyroid hormone for three years increased the bone mineral density of lumbar spine 13%, femoral neck 3% and total body 8% with a borderline decrease in vertebral deformities. Drug that stimulate the secretion of endogenous parathyroid hormone or mimic its action might also be effective. Parathyroid hormone had minor side effects the occasional nausea and headache<sup>30</sup>.

**VI. Other potential anabolic agents:** Several small studies of growth hormone alone or in combination with other agents have not shown consistent or substantial positive effects on skeletal mass. In selected patient, testosterone and synthetic anabolic steroid-nandrolone decanoate and androgenic progestin such as norethindrone acetate in women may be combined with a bisphosphonate therapy to obtain synergistic effect on BMD. Testosterone has been shown to enhance the efficacy of estrogen on increasing BMD. Similarly combined administration of norethindrone acetate and ethinyl estradiol dose- dependently increases the BMD in postmenopausal women than with estrogen alone<sup>17</sup>.

**VII. Other therapies:** A number of cytokines and growth factors have potent effects on bone cells. These factors also affect other organs; for example cytokines modulate the immune system. The challenge will be to target such as factors to bone. Others drug that have been developed for the treatment of osteoporosis include vitamin D analogues, strontium salts, Ipriflavone, Tibolon<sup>31</sup>.

## CONCLUSION

New therapeutic approaches have emerged during the past 5 years that significantly improve the daily management of postmenopausal osteoporosis. Controversies exist regarding this safety of HRT for long term use. Alendronate and Residronate have

unequivocally shown their ability to reduce fractures of axial appendicular skeleton. Their weekly formulations reduce the discomfort generated by the requirements for its oral ingestion without compromising the activity of the drug hence improving the potential for patient compliance. Intermittent regimens with the new agents Ibandronate and Zoledronate may substantially modify the prospective of bisphosphonate treatment by offering efficient, more friendly and safer therapeutic regimens. Raloxifene has a rapid and sustained anti-fracture efficacy both in men and women with prevalent vertebral fractures and those with low BMD. In the choice between Bisphosphonates and Raloxifene, the collateral benefits reported with the SERM i.e. the significant reduction in estrogen receptor- positive breast cancer incidence in older osteoporotic women and the decrease in the rate of cardiovascular events, in a high risk population may be important in consideration. A potent anabolic action on bone is mediated by the parathyroid hormone fragment PTH. This compound has demonstrated the ability to reduce the risk of vertebral and non vertebral fractures. In Bangladesh, we have seen a major change in the osteoporosis scene with the advent of reliable ways to measure bone density and the availability of Alendronate, Risedronate, Ibandronate, Zoledronate and Raloxifene. All that is needed for us to increase our awareness of osteoporosis so that we can offer our patients a better postmenopausal life.

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## Case Report

# Condylomata Lata: A Finding of Congenital Syphilis in An 8 Months Baby

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### ABSTRACT

An eight months female baby with her parents, hailing from Habigonj, came to Dermatology and Venereology Out Patient Department, Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet on 20<sup>th</sup> July 2009 with the complaints of multiple masses over the perineum & perianal areas for 3 months. On investigation, Venereal Disease Research Laboratory Test (VDRL) was reactive and Treponema pallidum Hemagglutinin Assay (TPHA) was positive. The parents had no history of blood screening for syphilis during perinatal period. The baby delivered by normal vaginal delivery at home without any complication. Their blood was tested for syphilis. The results of VDRL were reactive and TPHA tests were positive in both parents. According to the history, physical examination & investigations the baby was diagnosed as a case of condylomata lata – a finding of congenital Syphilis.

**Key Words:** *Treponema pallidum*, neurosyphilis.

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### INTRODUCTION

Although syphilis was first recognized as a distinct syndrome in Europe in the 15<sup>th</sup> century, it still poses a serious health problem in many countries in spite of wide spread use of penicillin to treat syphilis since the early 1950<sup>1,2,3</sup>. *Treponema pallidum* is the etiologic agent of the venereal disease syphilis. It is found world wide. The most common route of spread is by direct sexual contact. The disease can also be acquired congenitally or by transfusion with contaminated blood<sup>4</sup>.

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A case of congenital syphilis is confirmly defined as an infant in whom *Treponema pallidum* is identified in lesion, placenta, umbilical cord or autopsy tissue. A case of congenital syphilis is defined presumptively as any infant or child with a reactive treponemal test for syphilis and any one of the followings:

- \* Evidence of congenital syphilis on physical examination or X-ray of long bones.
- \* Presence in the cerebrospinal fluid of lymphocytosis, elevated protein (without any cause).
- \* Reactive cerebrospinal fluid VDRL<sup>5</sup>.

The rate of congenital syphilis have shown a decrease since reaching a maximum incidence of 108/100000. In 1997 the rate dropped to 30/10000<sup>6</sup>.

The physical finding of congenital syphilis at birth are quite variable. The infant may have many or minimal

signs or even no signs until 6-8 weeks of life (delayed type). The most common findings are on the mucous membranes and skin- maculopapular rash, condylomata lata, mucous membrane patches and serous nasal discharge (snuffles). Other common findings are hepato-splenomegaly, anaemia and osteochondritis. These early active lesions subsequently heal and if the disease left untreated it produces the characteristic stigmas of syphilis – interstitial keratitis, Hutchison’s teeth, saddle nose, saber shins, deafness and central nervous system involvement<sup>7</sup>. We are reporting a case of congenital syphilis, describing the clinical implications of the disease and emphasizing that global antenatal screening is still mandatory to prevent this serious yet largely preventable disease in high risk mothers.

### CASE REPORT

Liza, an eight months female baby of Mr. Zakir and Mrs. Ayesha Khatun, hailing from Enatgonj, Nabigonj, Habigonj came to the Out Patients Department of Dermatology and Venereology of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet with the complaints of multiple masses over the perineum and perianal areas for 3 months.

According to the history of parents, baby was born by normal vaginal delivery at home and she was normal at birth. The parents were not screened for syphilis during antenatal period. The baby was the 1<sup>st</sup> child of that couple. The mother had no history of abortion or still birth and had no history of any lesion on her breasts. The baby was breast fed.

Physical examination at presentation including height, weight and head circumference were normal. There was no anaemia or lymphadenopathy. Regarding examination of integumentary system, multiple soft, dull, pink coloured mushroom like plaques, 1-2 cm in diameter with a smooth moist weeping surface were found over the perineum and perianal area (Figure 1). There was no other skin, hair or mucous membrane lesion. There was no hepatosplenomegaly. Other system were alright including eye, dental or skeletal system.

On investigation, VDRL (Venereal Disease Research Laboratory) test was reactive (titer 1:32) and TPHA (Treponema Pallidum Hemagglutination assay) was positive. We tested blood of both parents for syphilis. The results reveals that VDRL were reactive (titer 1:32) and TPHA were positive. The patient’s blood culture and screening for HIV, HBV and HCV were negative. CSF examination revealed normal findings. Skeletal survey revealed no radiological evidence of

syphilis. USG of whole abdomen was done and was normal.

Though CSF finding was normal, Intramuscular injection of benzathin penicillin (50,000 units/kg) was given to patient<sup>8</sup>. Her parents also were treated accordingly. On follow up visit, patients affected part was free of any lesion by 2 months (Figure 2). Her VDRL titer dropped to normal by 3 months.



**Figure 1:** Before treatment- Multiple, soft, dull red colored plaques over the perineum and perianal area.



**Figure 2:** After treatment- Clearance of lesion 2 months with residual post inflammatory hypopigmentation.

### DISCUSSION

Sometimes condylomata can be found as a finding of secondary syphilis, but condylomata lata in congenital syphilis is less common<sup>9</sup>. One case of congenital syphilis in a 4 yrs boy was reported in Kuwait with the finding of anaemia, poor weight gain and hepatosplenomegaly. In contrast several reports have been published about – non venereal syphilis in Middle East<sup>1</sup>.

Three cases of congenital syphilis having hepatosplenomegaly, anaemia and maculopapular erythematous rash all over the body including palm and sole, two cases were reported in Singapore in 1988. But in our case there was no other skin rash and anaemia or hepatosplenomegaly<sup>10</sup>.

Although syphilis occur global antenatal screening is still warranted. The reason is that congenitally acquired syphilis is serious, yet largely preventable. At least half of infected life born infants have no sign of congenital syphilis at birth. Many of them were often not reported even though they usually receive presumptive treatment. There were several reasons for not identifying these infants at birth such as (i) being asymptomatic at birth (ii) confusion about interpretation of test titers, especially when mothers titers were positive and infants were negative (less than 1:4), (iii) difficulty to document the adequacy of treatment of mothers who were positive, (iv) newborns usually discharged within 1 day of birth before obtaining RPR titers<sup>11,12</sup>. It is estimated that of all pregnant women with untreated syphilis, only 20% will have a term normal child. The disease in affected fetus may be complicated by still birth (30%), neonatal death (10%) and mental handicap (40%)<sup>8</sup>. Our patient was not identified at birth as she was born at her home and was normal at birth without knowing that her parents were patients of syphilis.

Congenital syphilis usually results from transplacental transfer of the spirochetes to the developing fetus. Although extremely rare, syphilis can also be acquired by contact with chancres at birth<sup>13</sup>. The majority of infants do not have skin lesions or snuffles (a profuse nasal discharge). In addition, the placenta and amniotic fluid are often not available for testing. In these cases, the diagnosis may be difficult and will depend on a combination of physical, radiographic and serologic examination.

The Clinical spectrum of early congenital syphilis is remarkably variable, ranging from asymptomatic infection to fulminant disease<sup>14</sup>.

Laboratory diagnosis of syphilis can be established by identifying the pathogen. Dark field examination of clinical specimens taken from a moist genital lesion or a regional lymph node may yield *Treponema pallidum* when patients are infected with primary or secondary syphilis. In our patient, Dark field examination was not performed due to unavailability of that microscope. Screening was accomplished by non treponemal test such as the VDRL which was done for our patient or the rapid plasma reagin (RPR) test. When a positive test is obtained with a non treponemal test, a specific test for anti treponemal antibodies should be performed to

confirm that diagnosis. These test are the Microhemagglutination Assay for Antibodies to *Treponema pallidum* (MAH-TP) test, which is equivalent to the TPHA test done for our patient, or the fluorescent treponemal antibody absorption (FTA-ABS) test<sup>14,15</sup>.

The finding in cerebrospinal fluid (CSF) of a positive VDRL or an increase in leucocytes and protein are the hall marks of neurosyphilis in adults, but the interpretation of results on CSF specimens from the newborn is more difficult because these results are neither sensitive nor specific for neurosyphilis<sup>16</sup>.

A retrospective study was designed in 1996 in Washington D.C. to evaluate the usefulness of lumbar puncture (LP) in the initial evaluation of symptoms free infants for congenital syphilis. The study concluded that the rule of routine LP in the initial evaluation of these infants should be reconsidered because of the low yield of reactive CSF VDRL, and the similar CSF leukocyte and protein values in the syphilis group and the control infants<sup>16</sup>. In spite of this, evaluation of CSF should still be performed to permit abnormalities to be monitored and also because positive CSF may provide the only evidence of congenital syphilis in asymptomatic infants born to treated mothers<sup>17</sup>.

Prenatal diagnosis of fetal syphilis is possible by the use of ultrasonography. The sonographic findings may include hydrops fetalis, hepatosplenomegaly, placentomegaly, and dilated small bowel. Amniotic fluid examinations can be done by either rabbit infectivity testing (RIT) to confirm presence of *Treponema pallidum* by the more specific PCR technique<sup>18, 19, 20</sup>.

Although penicillin was first used to treat congenital syphilis in the 1940s, many studies have been designed to determine the optimal treatment for this disease. In 1989, both the American Academy of Paediatrics and the Centers for Disease Control (CDC) recommend treating all infants born to women with untreated syphilis with parenteral penicillin regardless of clinical examination or laboratory finding<sup>21,22</sup>. In 1998, the CDC recommended that treatment is required in the following situation: a confirmed or presumptive diagnosis of congenital syphilis, unknown or undocumented maternal therapy, maternal treatment within four week of delivery, insufficient fall in maternal titer response to therapy or delivery before a four fold fall in titer, maternal treatment with drugs other than penicillin or in situation in which infant follow up may be inadequate<sup>23</sup>.

Regarding treatment of congenital syphilis during neonatal period, treatment of congenital syphilis is aqueous penicillin with 50,000 unit/kg intravenously every 12 hours for the first 7 days of life and every 8

hours for the next 3 days, or procaine penicillin, 50000 unit/kg intramuscularly daily for 10 to 14 days. During post neonatal period treatment of congenital syphilis is injection benzathine penicillin 50,000 units/kg (up to 2.4 million units) intramuscularly if CSF examination is negative. If positive, aqueous penicillin G 50,000 units/kg every 4 to 6 hours intravenously for 10 to 14 days<sup>5</sup>. Our patient was treated with benzathine penicillin, 50000 units/kg as her CSF examination was negative.

## CONCLUSION

Because of the high morbidity associated with congenital syphilis, screening of all pregnant women has been shown to be cost effective even in populations with low prevalence. In high risk populations, serological screening for syphilis at the first prenatal visit, in the third trimester, and at delivery are important and recommended and additional screening of infants born to high risk mothers may be appropriate at first and at 8 weeks of age. Indeed prevention is better than cure.

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## Case Report

# Kallmann's Syndrome (Idiopathic Hypogonadotropic Hypogonadism)

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### ABSTRACT

*Kallmann's Syndrome (Idiopathic Hypogonadotropic Hypogonadism) is a very rare disorder found in clinical practice which describes the association of isolated hypogonadotropic hypogonadism with hyposmia or anosmia. Congenital hypogonadotropic hypogonadism (CHH) results from abnormal gonadotropin secretion and it is characterized by impaired pubertal development. CHH is caused by defective GnRH release, or by a gonadotropic cell dysfunction in the pituitary. A man of 20 years came to the private chamber with symptoms suggestive of Kallmann's Syndrome. After examination and laboratory investigations the diagnosis was confirmed. Rarity of the disease encouraged us to report.*

**Key words:** Hyposmia, anosmia, Kallmann's Syndrome.

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### INTRODUCTION

Kallmann's syndrome (KS) is the condition where there is association of isolated hypogonadotropic hypogonadism (HH) with hyposmia or anosmia. It may be associated with ulcerative colitis with positive family history<sup>1</sup>. In 1944, Kallmann recognized the genetic basis of this condition in three families, and thereafter this association has been known as Kallmann's syndrome<sup>2</sup>. Hypogonadism in one form of KS was later shown to be due to deficient gonadotropin releasing hormone (GnRH) secretion caused by defective migration of GnRH neuron which depends on the guidance of olfactory terminal nerve axons to reach the hypothalamus<sup>3-5</sup>. Kallmann's syndrome can be sporadic or familial and affects more males than females<sup>6</sup>. The male-to-female ratio ranges from 4 to

5:1. Familial cases display different modes of inheritance: X-linked, autosomal dominant and, very rarely, autosomal recessive inheritance<sup>7</sup>. So far, inactivating mutations in two distinct genes have been implicated in this condition, KAL1 and FGFR1<sup>8-11</sup>. KAL1 mutations are responsible for X-linked KS (XKS) and fibroblast growth factor receptor type 1 (FGFR1) mutations underlie one form of autosomal dominant KS (AKS), but mutations in these two genes account for only 20-25% of KS cases<sup>10, 12-14</sup>. KAL1 encodes anosmin1, a secreted glycoprotein expressed in various extracellular matrices, and FGFR1 encodes FGFR1, a member of the receptor tyrosine kinase super family that binds fibroblast growth factor 2 (FGF2) and other FGF ligands. Anosmin1 and FGFR1 are both expressed during organogenesis of the olfactory nerve. GnRH system where they regulate neuronal migration and axon elongation and branching<sup>15-17</sup>. Mutations in these genes lead to defective olfactory tract formation and are likely to account for associated defects in other developing tissues observed in KS patients, such as

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renal agenesis, synkinesia and cleft lip, cleft palate, and dental agenesis<sup>8,13,14,18</sup>. A defective migration of GnRH neurons to their normal destination in the hypothalamic anterior septo-preoptic area has been documented in a 19-week human fetus with a KAL1 deletion, but a similar defect has not been investigated in KS patients with FGFR1 mutation<sup>18</sup>.

### CASE REPORT

A 20 years old man hailing from Biswanath, Sylhet came to my private chamber on the 23.02.2007 with complaints of loss of sexual urge and small genital organs from the age of sexual development. After asking, he told about some impairment of smell sensation. He had no symptom related to other system. Clinical examination revealed that his blood pressure was 130/75 mm Hg and pulse was 75 b/minute. His height and weight were 163cm and 54kg respectively. He had no pubic and axillary hair. Beard and mustache were also absent (Figure 1).

Examination of genital organs showed small penis, both testes within scrotum but these were very small and soft in consistency. Examination of cardiovascular, respiratory, gastrointestinal, musculoskeletal and hepatobiliary system revealed no abnormality. Neurological examination revealed only some impairment of smell sense. Higher psychic function, motor, sensory reflexes and cerebellar functions were normal.

On questioning, no previous history of any serious disease, use of cytotoxic drugs or radiation exposure was found. His mother also gave no history of any disease or pregnancy related complication during the antenatal, perinatal and postnatal period in case of this son. There was no history of consanguineous marriage and birth defects. He was a man of high income group family. His parents were only hypertensive and brothers and sisters who were five in number having good health.

He was advised to perform ultrasonogram (USG) of scrotum and estimation of serum testosterone level. The USG of scrotum revealed bilateral small testes (Right 1.5x0.8 cm<sup>2</sup>, Left 1.4x 0.8 cm<sup>2</sup>) (Normal Size 4-7 x 2-3 cm<sup>2</sup>). His serum testosterone level was 0.58 nmol/L (Normal 4.56-28.20 nmol/L)

After that, I discussed about the case with senior teachers, they suggested for other hormone study. After investigation, it was found that serum T<sub>3</sub>, T<sub>4</sub>, TSH were within normal level. FSH- 0.85 μ IU/ml (Normal 1.0-12 μIU/ml) and Prolactin 12.7 μg/ml (Normal 2.2-18.5 μg/ml). After clinical evaluation and laboratory investigations the diagnosed was established.

The patient was then referred to BIRDEM, Dhaka for further evaluation and better management. In the Department of Clinical Endocrinology of BIRDEM, hormone analysis reports were repeated and the new reports coincided with previous reports. In addition they also suggested MRI of sella and parasellar region which revealed no abnormality (Figure 2). After evaluation treatment was started there, on 02/09/2008 with Injection Sustanon 250 (Testosterone preparation, Nuvista Pharma Ltd), ½ ampoule deep I/M monthly for 6 months and then from 01/03/09 dose increased to 250mg deep I/M, 3 weeks interval. From 08/09/2009 1 ampoule I/M fortnightly was given for life long.

The patient was clinically evaluated three monthly and found gradual improvement of symptoms. His pubic and axillary hair, beard and mustache were gradually arising (Figure 3). Size of penis was also gradually increasing. Before the starting of treatment testicular volume (TV) was 1ml and pubic hair was absent. On 11/03/2009 TV was 1.75 ml and pubic hair Stage .



**Figure-1:** Kallmann's syndrome- Before treatment (at 16 years of age).



**Figure-2:** Kallmann's syndrome- Sagittal section of MRI scan showing sella and parasellar region.



**Figure-3:** Kallmann's syndrome- After treatment (at 22 years of age).

### DISCUSSION

Episodic secretion of GnRH from the hypothalamus is a key requirement for the initiation and maintenance of a normal reproductive axis in humans. However, the genetic and environmental factors modulating the secretion of this hormone remain poorly understood. Usually patients present due to their acute or troublesome symptoms. All patients with Kallmann's syndrome have either anosmia or severe hyposmia and may exhibit symptoms of associated conditions including those of congenital heart disease (e.g. fatigue, dyspnoea, cyanosis, palpitations, syncope) or neurologic manifestations (e.g. color blindness, hearing deficit, epilepsy, paraplegia), absent or incomplete puberty, decreased libido and erectile dysfunction. These symptoms are almost universal in men with either Kallmann's syndrome or idiopathic hypogonadotropic hypogonadism. Decreased muscle strength and diminished aggressiveness and drive (in men), these symptoms are ameliorated significantly by androgen replacement which also improves libido and erectile function and almost all untreated patients are infertile. In the reporting case there was no troublesome symptoms except failure of development of secondary sex character and some impairment of smell sensation. Developmental anomalies arising from abnormal closure of the anterior neural tube (median cranio-encephalic dysraphias) may be associated with endocrine disturbances following mal-development of the pituitary gland<sup>1</sup>. Patient had no relevant family history or he is not a child of consanguineous parents. It should be mentioned that he had no cardiac, respiratory, GIT and CNS problems. Kallmann's syndrome has been associated with many structural disorders including renal, cardiac and intracranial

abnormalities<sup>2</sup>. Ulcerative colitis is a disorder associated with Kallmann's syndrome in which there is evidence of a hereditary component, 29% of patients in one recent study having a positive family history<sup>2</sup>. Demonstration of the association between ulcerative colitis and hereditary conditions may therefore contribute to an understanding of the aetiology of inflammatory bowel disease. The association of inflammatory bowel disease with chromosome abnormalities, particularly those affecting the X-chromosome, may be of aetiological significance. Unfortunately in the absence of a suitable family history it is not possible to determine whether the present patient conforms to the X-linked variety.

Presentation, clinical examination, hormonal study and imaging of intracranial structures give almost a confirmatory diagnosis. Though, to understand associated illness some other systemic investigation can be suggested. Evaluation and therapy can usually be implemented on an outpatient basis. All postpubertal-age patients with Kallmann's syndrome and idiopathic hypogonadotropic hypogonadism are candidates for gonadal steroid replacement therapy in the absence of specific contraindications. Additional therapies to restore fertility can be implemented on request. Medical therapies are used to treat associated conditions, including osteoporosis, adrenocortical insufficiency, congenital heart disease, and neurologic disorders. Patients with Kallmann's syndrome and congenital heart disease, cleft lip or palate may need corrective surgery.

### CONCLUSION

The case was associated with some impairment of smell sense, micropenis and hypogonadal features. But he had no disorders of renal, cardiac, GIT and intracranial structures. However, rapid diagnosis and proper treatment improved his symptoms dramatically. But the success of the treatment will depend on if the patient be fertile during his conjugal period and can maintain normal sexual life.

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## Miscellaneous

### News

#### **Postgraduate Training Recognized by BCPS**

A high powered inspection team consisted of eight members from Bangladesh College of Physicians and Surgeons (BCPS) Dhaka, headed by Professor Syed Mokarrom Ali, visited the Jalalabad Ragib-Rabeya Medical College and Hospital on 27-12-2010. On the recommendations of the inspection team, the Council of Bangladesh College of Physicians and Surgeons (BCPS) has renewed recognition to the departments of Paediatrics, Ophthalmology, Otolaryngology, Psychiatry, Pathology (Histopathology) and Orthopaedic Surgery for imparting training to the resident doctors provisionally for a period of five years with effect from 21-09-2009. The Council has granted recognition to the department of Paediatric Surgery for imparting training to the resident doctors provisionally for a period of five years with effect from 13-02-2010. The training will be accepted for appearing in the FCPS Part-II examination in these specialties. The postgraduate training imparted from the departments of Surgery, Medicine and Obstetrics & Gynaecology were recognized by Bangladesh College of Physicians and Surgeons (BCPS) earlier in 2003.

#### **Approval of 63 Crore Taka Budget for Jalalabad Ragib-Rabeya Medical College and Hospital**

41<sup>st</sup> meeting of Governing Body for Jalalabad Ragib-Rabeya Medical College and Hospital was held in the college conference room on 27-12-2010. The Governing Body anonymously approved the budget of Taka 62,59,14,837.00 for the year of 2011. The meeting was presided over by Founder of the College and Chairman of Governing Body Danobir Mr. Ragib Ali. The Member Secretary and Principal of JRRMC, Maj Gen (Retd) Prof Md Nazmul Islam; Mr. Abdul Hye Tipu, Senior Vice President of Ragib-Rabeya Foundation; Mrs Khodeja Akhter and other members of the Governing Body were also present in the meeting.

### Seminars

The following seminars held in JRRMCH during the July 2010 to December 2010

1. A seminar on “**Management of Ectopic Pregnancy**” held on 01-07-2010 organized by Department of Obstetrics and Gynaecology, JRRMCH.
2. A seminar on “**Recent Concept on Low Back Pain**” held on 22-07-2010 organized by Department of Physical Medicine, JRRMCH.
3. A seminar on “**Diabetic Ketoacidosis**” held on 12-08-2010 organized by Department of Medicine, JRRMCH.
4. A seminar on “**Anthrax**” held on 07-10-2010 organized by Department of Department of Dermatology and Venereology, JRRMCH.
5. A seminar on “**Rota Virus Diarrhoea**” held on 04-11-2010 organized by Sandhani, JRRMC Unit, Sylhet.
6. A seminar on “**Rheumatoid Arthritis**” held on 25-11-2010 organized by Department of Medicine, JRRMCH.
7. A seminar on “**Suicide and Attempted Suicide**” held on 02-12-2010 organized by Department of Psychiatry, JRRMCH.
8. A seminar on “**Optic Atrophy**” held on 09-12-2010 organized by Department of Ophthalmology, JRRMCH.

### Corrigendum

In the Jalalabad Medical Journal Vol-07, No-02 July 2010, the word “Scandinavian” was mistakenly written as “Scandinivian” in cover page and page 60.



## Instructions for Author(s)

Manuscripts on clinical, review, experimental and historical topics pertinent to medical sciences are accepted for the publication in this journal. The papers are accepted for the publication with an understanding that they are solely submitted for this journal. The statements, comments or opinions expressed in the papers are exclusively of author(s), not of editor(s) or publisher. The manuscripts are to be prepared as described in following instructions. 3 (three) hard copies are to be submitted. Letters about potentially acceptable manuscripts will be sent after review process is complete. No manuscripts will be returned if not accepted for publication. In addition an electronic/digital version of the manuscript composed in MS word 98/2000 should be submitted in a diskette.

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### Abstract and key words

An informative abstract not more than 250 words should briefly describe the objectives, materials and methods, results and conclusion. Number of key words should not be more than ten and none that are in the title.

**Text** should contain Introduction, Materials and Methods, Results and Discussion in sequence.

### Introduction

It should briefly disclose the purpose of study. It will help the readers with the problem finding. It should be clear in nature and purpose.

### Materials and Methods

Clearly it should include materials, experimental procedures, methods etc. Mention the nomenclature, source of material, equipment with manufacturer's details in parentheses. Describe new methods in

sufficient detail indicating their limitation. Established methods should be cited with authentic references. Ethical standards should be followed in reporting experiments done in human subjects. Precisely identify the dosage and route of administration, when drugs or chemicals are used. Measurements and data should be stated in SI unit, or if SI unit does not exist, use an internationally accepted unit. Abbreviations and acronyms should be used for widely used terms and names, which occurs consistently and frequently in the manuscript.

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It should be presented in logical sequence in text, tables or illustrations. Duplications of data in the tables or illustrations should be avoided. Emphasize or summarize only important observations.

### Discussion

Emphasize the new and important aspects of the study and conclusion derived from them. Detail data written in introduction and other portions of text should not be repeated. The implication of results and their limitations including suggestion for future research should be included in the discussion.

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Number the references consecutively in order mentioned in the text. Full list of reference should include all authors. Avoid using abstracts as references. References to paper accepted but not yet published should be designated as 'in press' or 'forthcoming'. Authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited as 'unpublished observations' with written permission from the source. Use the styles of example below, which are based on the formats used by US National Library of Medicine (NLM) in the Index Medicus. The title of journals should be abbreviated according to the style used in Index Medicus.

### Article in journal

- List all six authors when six or less  
Vega KJ, Pina I, Krevsky B. Heart transplantation in associated with an increased risk for pancreatobiliary disease. *Ann Intern Med* 1996; 124 (11): 980-3.  
As an option, if a journal carries continuous pagination

throughout a volume (as many journals do) the month and issue number may be omitted.

b) More than six authors

Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after chernobyl: 5 year follow-up. *Br J Cancer* 1996; 73:1006-12.

c) No author given

Cancer in South Africa (editorial). *S Afr Med J* 1948; 84:15

d) Organization as author

The cardiac society of Australia and New Zealand. Clinical exercise stress testing. Safely and performance guidelines. *Med J Aust* 1990; 146: 267-9.

**Books and monographs**

a) Personal author(s)

Laurence DR, Bennett PN, Brown MJ. *Clinical Pharmacology*. 8th ed. New York: Churchill Livingstone; 1997.

b) Editor(s), compiler(s) as author

Norman IJ, Redfern SJ, editors. *Mental health care for elderly people*. 5th ed. New York: Churchill Livingstone; 1999.

c) Organization as author and publisher

World Health Organization. *Ethical criteria for medical drug promotion*. Geneva: World Health Organization; 1988.

d) Chapter in a book

Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. *Hypertension: pathophysiology, diagnosis and management*. 2nd ed. New York: Raven Press; 1995. p 465-9.

e) Dissertation or thesis

Kaplan SJ. *Post hospital home health care: the elderly access and utilization (dissertation)*. St. Louis (MO): Washington Uni; 1995.

**Other published material**

a) Newspaper article

Lee G. Hospitalization tied to ozone pollution: study estimates 50,000 admissions annually. *The Washington post* 1996; June 21; sect. A: 3 (col. 5).

b) Dictionary and similar references

*Student's medical dictionary*. 26th ed. Baltimore: Williams and Wilkins; 1995. Apraxia; p.119-20.

**Unpublished material**

a. In press

Leshner AI. Molecular mechanisms of cocaine addiction. *N Eng J Med* (in press) 1997.

**Electronic material**

a) Journal articles in electronic format

Morse SS. Factors in the emergence of infectious

diseases. *Emerg Infect Dis* [serial online] 1995 Jan-Mar [cited 1996 June 5]; 1(1): [24 screens]. Available from: URL: <http://www.cdc.gov/ncidod/EID/eid.htm>

b) Monograph in electronic format

CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia group, producers. 2nd ed. Version 2.0. San Diego: CAEA; 1995.

C) Computer files

Haemodynamics III: The ups and downs of haemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational Systems; 1993.

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