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## Iron Supplementation in Microcytic Hypochromic Anaemia

Microcytic hypochromic blood picture is one of the commonest hematological abnormalities in our country. A vast majority of such cases, microcytosis occurs due to deficiency of iron. By morphological study of red cells or by red cells indices differentiation between iron deficiency and beta thalassaemia trait becomes very difficult as two entities most often present with very similar blood picture. A conservative world health report said that there are 3.0 percent carriers of beta thalassaemia trait in Bangladesh.<sup>1</sup> These individuals are most often in positive iron balance and iron supplementation to this group is harmful and contraindicated. Excess of this iron can be deposited in endocrine glands, heart muscle and various tissues in the bodies causing organ dysfunction.<sup>2,3</sup>

So it is very much important to distinguish these two entities. This can be done by doing Hb-Electrophoresis supported by iron profile study. In some cases of beta thalassaemia trait there may be co-existing iron deficiency. This group of patient can only be treated with iron for a short period of time to improve the anaemia. This can be done by monitoring the serum ferritin level and other iron profiles. So it is recommended that before administration of iron in microcytic hypochromic anaemia it must be mandatory to confirm beta thalassaemia trait as they can protect positive iron balance.

**Prof. Md. Shamsur Rahman**

Professor of Biochemistry  
Dhaka National Medical College

1. Khan WA. Thalassaemia situation in Bangladesh. DS(Child)HJ 1999; 15: 42-44.
2. LiAM, Cheng MY. Anaemia and thalassaemia in healthy adolescent from southern families. J Paediatr child health 1990; 26: 339-342.
3. Fargion S, Taddei MT, Cappellini MD, Piperno A, Fiorelli G. The iron status in Italian subjects with thalassaemia trait. Acta haematol 1992;68: 109-114

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### **Instruction for Authors:**

Dhaka National Medical College Journal offers manuscript of original articles, review articles and case report based on clinical and laboratory related research in medical and allied science of various disciplines. The aim of this publication is to create a awareness for medical profession to share experiences which will help others to render better patient services. Manuscripts are received provided they are not under simultaneous consideration by any other publication. Submission of a manuscript for publication implies the transfer of the copyright from the author to the publisher upon acceptance. Accepted manuscripts become the permanent property of the Dhaka National Medical College Journal and cannot be reproduced by any means in whole or in part without the written consent of the publisher. It is the author's responsibility to obtain permission to reproduce illustrations, table, etc from other publication.

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Books

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Chapter in a book

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Available from : <http://www.nursingworld.org/AJN/2002/june/Wawatch.htm>

Article.

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Original Article

## Assessment of TSH, FT<sub>4</sub> and TPO-Ab Status During 1st Trimester of Pregnant Women in Dhaka City

Shyamal Chandra Banik<sup>1</sup>, Tahmina Yeasmin<sup>2</sup>, Farjana Ahmed<sup>3</sup>, Ferdous Towhid<sup>4</sup>, Arifuzzaman Chowdhury<sup>5</sup>, Mohib Ullah<sup>6</sup>

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### Abstract

**Background:** Thyroid dysfunction may occur in pregnancy.

**Objective:** To measure serum TSH, FT<sub>4</sub> & TPO-Ab levels during 1st trimester of normal pregnant women.

**Method:** This cross sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from July 2016 to June 2017. The ethical permission was taken from Institutional Ethics Committee (IEC) of SSMC. Total 60 female subjects, age ranged from 20 to 35 years were included in this study, among them 30 were apparently healthy pregnant women of 1st trimester (study group) and 30 were apparently healthy non-pregnant nulliparous women (control group). Serum TSH, FT<sub>4</sub> and TPO-Ab levels were measured. The statistical analysis was done by Unpaired t-test.

**Results:** In this study, mean serum TSH level was significantly ( $p < 0.01$ ) lower and serum FT<sub>4</sub> level was significantly ( $p < 0.01$ ) higher in 1st trimester than that of non-pregnant group. However, among the 1st trimester of pregnant women 13.33% were TPO-Ab positive and 10% were subclinical hypothyroid (SCH).

**Conclusion:** The present study reveals that subclinical hypothyroidism occurs in 1st trimester of pregnant women. So, thyroid screening should be done routinely during this period.

**Key words:** TSH, FT<sub>4</sub>, TPO-Ab, 1st trimester, pregnancy.

### Introduction

Pregnancy is the physiological process in which fertilization of ovum produce a new sequence of events & the fertilized ovum eventually develops into a full term fetus.<sup>1</sup> The average duration of pregnancy is about 40 weeks where 1st trimester is considered as 1st 12weeks.<sup>2</sup> During pregnancy several physiological & biochemical changes occur like hormonal changes, increase nutritional requirements & metabolic demand to adjust the internal environment of mother and also to meet the extra demand of the growing fetus.<sup>3,4</sup> Among the hormones, thyroid hormone change is a predominant one.<sup>5</sup> Thyroid hormone is a calorogenic hormone which increases metabolic activities of almost all cells of the body and also essential for proper development, maturation & myelination of central nervous system during fetal life and first few years of post natal life.<sup>6</sup>

First trimester of pregnancy which is up to 12 weeks of

gestation is the most important period, as organogenesis of fetus takes place at this stage.<sup>7</sup> During 1st trimester the fetus solely depends on transplacental passage of maternal thyroid hormone as fetal thyroid gland is not functional until 12 weeks of gestation.<sup>8</sup> So, normal thyroid function of mother during 1st trimester is very important for fetal development.<sup>9</sup> Thyroid disorder is the most common endocrine disorder during pregnancy. So assessment of thyroid function is very important during this period.<sup>10</sup>

Pregnant women have a higher chance to develop TPO-Ab positivity especially in 1st trimester. Usually, TPO-Ab positivity causes increase in TSH & decrease in FT<sub>4</sub> level. This altered thyroid function may cause severe obstetrical complications & also causes severe effects on fetal neuropsychological development.<sup>11,12</sup> Mothers are more vulnerable to develop thyroid disease & subsequently maternal morbidity in later life if they have positive TPO-Ab during early pregnancy.<sup>13</sup> So,

TPO-Ab screening test can be an important tool in early pregnancy, but little work is known on this regard in our country and for that reason this study was undertaken.

**Materials and Methods**

This cross sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from July 2016 to June 2017. The study protocol was approved by the Institutional Ethics Committee of SSMC. A total number of 60 women age ranged from 20 to 35 years were recruited in this study and they were divided into two groups. Study group (group B) was consisted of 30 apparently healthy pregnant women of 1st trimester. They were selected from Out Patient Department (OPD) of Obstetrics & Gynaecology of SSMC and Mitford Hospital by consecutive purposive sampling. For comparison, age matched 30 apparently healthy non-pregnant nulliparous (NPN) women were also included as control group (group A). They were selected by personal contact. All the subjects were belonged to middle socioeconomic status. Subjects having history of any chronic or systemic diseases (hypertension, diabetes mellitus, cardiac disease, renal disease and tuberculosis), known thyroid abnormalities, other endocrine abnormalities, goitre, hyperemesis gravidarum, twin pregnancy, psychiatric illness etc. were excluded from the study.

After selection the aim, benefits, risks and the procedure of the study were explained to each subjects and a written consent was taken. Detailed personal, family, medical and occupational histories were taken and thorough physical examination of all subjects were done and recorded.

With all aseptic precautions, seven (7) ml of venous blood was drawn from antecubital vein. Serum TSH, FT<sub>4</sub> and TPO-Ab levels were measured by chemiluminescent microparticle immunoassay (CMIA) method in the laboratory of Department of Biochemistry, BSMMU, Dhaka. Data were expressed as mean ± SD. Statistical analysis was done by Unpaired t-test by using SPSS version 22. p value ≤0.05 was considered as level of significance.

**Results**

All the groups (subjects) were age matched (Table-I). Table-I shows the mean age of non-pregnant nulliparous women & pregnant women during 1st trimester of gestation.

In this study, the mean (±SD) serum TSH level was significantly lower in group B (p<0.01) in comparison to that of group A (Table-II).

Again, Table-II depicts that the mean (±SD) serum FT<sub>4</sub>

level was higher in group B in comparison to that of group A and the difference was statistically significant(p<0.01).

In this study, the number of TPO-Ab positive pregnant women was found 4 (13.33%) and TPO-Ab negative pregnant women was found 26 (86.67%) during 1st trimester of normal pregnant women (Figure-1).

Again, among the 1st trimester of pregnant women, 10% were subclinical hypothyroid (SCH) and 90% were euthyroid (Figure-2).

**Table-I: Age of the subjects in different groups (N=60)**

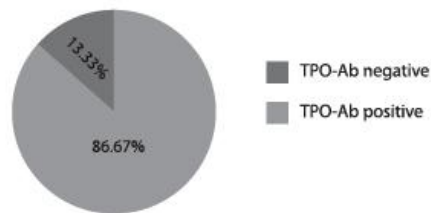
Parameters	Group		
	Group A (n=30)	Group B (n=30)	p-value (A vs B)
Age (years)	24.23 ± 1.83 (21 - 28)	24.70 ± 2.34 (21 - 31)	0.393ns

Data are expressed as mean ± SD. Figure in parentheses indicate ranges. Group A: Control group (Non-pregnant nulliparous), Group B: Study group (1st trimester of gestation), Unpaired t-test was performed to compare between two groups. N= Total number of subjects, ns= Not significant.

**Table-II: Serum thyroid stimulating hormone (TSH) and free thyroxine (FT<sub>4</sub>) levels of the subjects in different groups (N=60)**

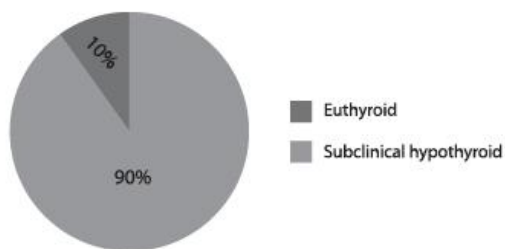
Parameters	Group		
	Group A (n=30)	Group B (n=30)	p-value (A vs B)
TSH (mIU/L)	2.33 ± 0.56 (0.56 - 3.35)	1.42 ± 1.47 (0.52 - 6.02)	0.003**
FT <sub>4</sub> (pmol/L)	14.44 ± 2.07 (9.85 - 17.75)	16.14 ± 1.45 (12.96 - 19.75)	0.001**4

Data are expressed as mean ± SD. For statistical analysis, Unpaired t-test was performed to compare between two groups. Figure in parentheses indicate ranges. Group A: Control group (Non-pregnant nulliparous), Group B: Study group (1st trimester of gestation). \*\*= Significant at p<0.01, N= Total number of subjects.



**Figure-1: Distribution of pregnant women by the level of TPO-Ab during 1st trimester (n=30)**





**Figure-II: Distribution of thyroid dysfunction in pregnant women during 1st trimester (n=30)**

### Discussion

In this study, the mean serum TSH level was significantly lower in 1st trimester in comparison to that of non pregnant women. These findings are in almost consistent with that of some other researchers of different countries.<sup>14</sup> On the contrary, mean serum TSH level was higher in 1st trimester as compared to that of non pregnant women.<sup>15</sup> This discrepancy might be due to variation of methodology implied, maternal age, number of non pregnant women, etc.

In this study, the mean ( $\pm$ SD) serum FT<sub>4</sub> level was significantly ( $p < 0.01$ ) higher in 1st trimester in comparison to that of non pregnant women. Almost similar finding was also reported by different researchers.<sup>16</sup> On the contrary, the mean serum FT<sub>4</sub> level was lower during 1st trimester in comparison to that of non pregnant women.<sup>17</sup>

In the present study, TPO-Ab positivity was found 13.33% during 1st trimester. On the other hand, the prevalence rate of TPO-Ab positivity during 1st trimester was something similar in other country by various researchers such as 11.81% in Malaysia.<sup>18</sup>

In the present study, among the 1st trimester of pregnant women, the subclinical hypothyroidism was found 10%. On the other hand the rate of subclinical hypothyroidism was different in other country such as 12% in India.<sup>19</sup>

The several investigators of different countries proposed various suggestions on these aspects. It has been suggested that, higher concentration of serum human chorionic gonadotropin (hCG) during 1st trimester has thyrotropic activity & thereby directly stimulates maternal thyrocytes and ultimately causes higher FT<sub>4</sub> level and lower TSH level on that period.<sup>20</sup> On the other hand, the presence of TPO-Ab positivity can cause a decrease in FT<sub>4</sub> & increase in TSH and thereby causes hypothyroidism.<sup>21</sup>

### Conclusion

From this study it can be concluded that, thyroid hyper functional state usually observed during 1st trimester of normal pregnancy which is essential for fetal development. This hyper functional state of thyroid gland can decrease in TPO-Ab positive pregnant women which may cause severe pregnancy complications. So, routine screening of these parameters is very much important during 1st trimester of gestation.

### Acknowledgement

We acknowledge the tremendous support from Biochemistry departments of BSMMU for conducting thyroid function testing. We are also thankful to the study subjects for their active & enthusiastic participation & all the faculty members of the Department of Physiology, SSMC for their immense support.

### References

- Bernstein HB, Vanburen G. Normal pregnancy. In: Decherney AH, Nathan L, Laufer N, Roman AS. Lange Current Diagnosis & Treatment Obstetrics & Gynecology. 11th ed. McGraw Hill companies; 2013.p.141-53.
- Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC, Hauth JC, Wenstrom KD. Williams Obstetrics. 21st ed. USA: Mcgraw-Hill Company; 2001.
- Keele CA, Neil E, Joels N. Samson Wright's Applied Physiology. 13th ed. New Delhi: Oxford University Press; 1982.
- Burrow GN, Fisher DA, Larsen PR. Maternal and fetal thyroid function. The New England Journal of Medicine 1994; 331(16): 1072-8.
- Barrett KE, Barman SM, Baitano S, Brooks HL. Review of Medical Physiology. 23rd ed. India: McGraw-Hill companies; 2012.
- Hall JE. Textbook of Medical Physiology. 12th ed. Elsevier India Private Limited; 2016.
- Sadler TW. Langman Medical Embryology. 9th ed. Philadelphia, USA: Lipincott Willis and Wilkin; 2003.
- Casey BM, Leveno KJ. Thyroid disease in pregnancy. CME 2006; 108(5): 1283-92.
- Springer D, Zima T, Limanova Z. Reference intervals in evaluation of maternal thyroid function during the first trimester of pregnancy. European Journal of Endocrinology 2009; 160(5): 791-7.

- J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 06-09
10. Fantz CR, Dagogo-Jack S, Ladenson JH, Gronowski AM. Thyroid function during pregnancy. *Clinical Chemistry* 1999; 45(12): 2250-8.
  11. Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A. Thyroid antibody positivity in the first trimester of pregnancy is associated with negative pregnancy outcomes. *Journal of Clinical Endocrinology Metabolism* 2011; 96(6): 920-4.
  12. Pop VJ, Kuijpers JL, Baar ALV, Verkerk G, Vijlder JJD, Vulsma T, et al. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. *Journal of clinical Endocrinology* 1999; 50: 149-55.
  13. Mannisto T, Vaarasmaki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, et al. Thyroid dysfunction and autoantibodies during pregnancy as predictive factors of pregnancy complications and maternal morbidity in later life. *Journal of Clinical Endocrinology and Metabolism* 2010; 95(3): 1084-94.
  14. Memon AS, Shaikh AW, Dodani AL. Effects of pregnancy on thyroid hormone levels. *PJMHS* 2011; 5(3): 524-8.
  15. Mujawar SA, Patil VW, Daver RG. Human chorionic gonadotropin and thyroid hormones status during normotensive pregnancy. *Journal, Indian Academy of Clinical Medicine* 2011; 13(1): 33-6.
  16. Elhaj ET, Adam I, Ahmed MA, Lutfi MF. Trimester-specific thyroid hormone reference ranges in Sudanese women. *BMC Physiology* 2016; 16(5): 1-8.
  17. Sekhri T, Juhi JA, Wilfred R, Kanwar RS, Sethi J, Bhadra K, et al. Trimester specific reference intervals for thyroid hormone in normal Indian pregnant women. *Indian Journal of Endocrinology Metabolism* 2016; 20(1): 101-7.
  18. Thevarajah M, Yean CY, Chin LS, Sabir N, Sicken J. Prevalence of abnormal maternal TPO-Ab and TSH levels in pregnant women in the Malaysian population. *Asian Biomedicine* 2008; 2(5): 403-7.
  19. Nusrat N, Prabha P, Banoo H, Nabi N. Prevalence of thyroid hormone disorder in pregnant females at a tertiary care hospital in the rural area of Mandhana-Kanpur. *Rama Univ. J. Med. Sci.* 2015; 1(4): 8-17.
  20. Hershman JM. The role of Human Chorionic Gonadotropin as a thyroid stimulator in normal pregnancy. *Journal of Clinical Endocrinology and metabolism* 2008; 93(9): 3305-6.
  21. Terraz JPB, Alvarez SI, Flores JLB, Lahuerta RA, Sauca AA, Lopez ER, et al. Thyroid hormones according to gestational age in pregnant Spanish Women. *BMC Research Notes* 2009; 237(2): 1-9.

Original Article

## Incidence of Plasma Leakage in Dengue Hemorrhagic Fever

Humayra Sultana<sup>1</sup>, Sultanuddin<sup>2</sup>, Rashidul Karim<sup>3</sup>, Md. Shafiqur Rahman<sup>4</sup>, Sayeda Farzana Rahat<sup>5</sup>, Mohammed Mahfuzur Rahman<sup>6</sup>, Md. Shakibur Rahman<sup>7</sup>, Rummana Sharmin<sup>8</sup>

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### Abstract

**Background:** Dengue is still existing as an important threat to child health. This virus induces wide spectrum of clinical conditions including dengue hemorrhagic fever (DHF), characterized by plasma leakage and bleeding, which is often life endangering. Dengue is showing a recent upsurge in Bangladesh when Covid 19 is threatening huge number of human lives.

**Objective:** Plasma leakage is the key feature of serious DHF. Early clinical suspicion, establishment of diagnosis of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) and proper therapeutic intervention are crucial for saving lives. This study is undertaken to see the severity nature of Dengue infection in our territory.

**Methods & Materials:** Eighty one admitted children in the Paediatric ward of DNMI H, had been suffering from various dengue infection were included in study. Diagnosis was made by history taking, clinical features and supporting investigative findings like Leukopaenia, Thrombocytopenia and haematocrit (raised or not), NS1 antigen positivity, Dengue antibodies (IgM & IgG) and Radiological & sonographic evaluation of the Chest and Abdomen.

**Result:** 43 children (53%) were male and 38 (43%) female. The age range was from 06 months to 13 years. Fifty eight (71.60%) were urban and the remaining 23 (28.40%) were from rural areas. Chief complaints were fever with unusual weakness. Temperature recorded were 100F to 103F except in 02 cases in whom fever remitted before admission. Other important symptoms were Headache and rarely Haemorrhagic manifestations. Thrombocytopenia found in all cases and Leukopaenia in 56 (69.14%) children. Haematocrit were raised (>10%) in 9 patients only.

Features of plasma leakage (Pleural effusion /Ascites / Bleeding sign) found in 09 children those have raised haematocrit. Among all children 78 recovered, 03 cases (01 with uncontrolled gastrointestinal hemorrhage and 02 with breathing difficulty demanding ICU support) were referred to better center.

**Conclusion:** Ultrasonographic signs and changes in hematocrits are useful tools for detecting plasma leakage in dengue infection. Pleural effusions and ascites are common features. With careful therapeutic intervention patients improve rapidly but should be monitored closely as leakage may continue for couple of days.

**Key words:** Plasma leakage, Dengue hemorrhagic fever, Pleural effusion in dengue.

### Introduction

Dengue is remaining an important health issue worldwide. Dengue viruses, a group of four serologically distinct viruses belonging to genus *Flavivirus*, are the cause of this serious viral diseases. This viral infections induces wide spectrum of clinical conditions including dengue hemorrhagic fever (DHF), a haemorrhagic disease characterized by plasma leakage and bleeding. The common feature of DHF is a transient period of plasma leakage and a hemorrhagic episode. This occurs

mostly during a secondary dengue infection. WHO reported significant increase in dengue cases, from approximately 900 cases per year in 1950's & 1960's decade to about 500,000 cases every year in 1990's decade.<sup>1</sup> It is endemic in Southeast Asia and South America, causes significant morbidity, mortality, and economic burden. In Indian subcontinent and Oceania, dengue is emerging as most important viral infectious diseases.<sup>2,3</sup>

*Aedes aegypti* is the principal mosquito vector in virus

transmission.<sup>4</sup> The genome of dengue virus encodes 10 different gene products: C (capsid), prM (matrix), E (envelope) and nonstructural proteins including NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5.<sup>5</sup> NS1 is the only nonstructural protein with a soluble form that can be detected in circulation.<sup>6</sup>

Most primary infections in children are usually clinically unnoticeable but some patients may manifest undifferentiated fever. Primary infections in older children and adults are likely to produce characteristic dengue fever (DF), a febrile illness along with non-specific symptoms like headache, retro-orbital pain, myalgia and occasionally hemorrhagic manifestations.<sup>7</sup> A small portion of patients develop dengue hemorrhagic fever (DHF), the most serious form of disease. The hallmark of DHF is the plasma leakage which may lead to the loss of intravascular fluid volume and circulatory insufficiency. Bleeding is another feature of severe disease. Bleeding may occur in both DF and DHF, but more severe bleeding, specially bleeding from the gastrointestinal tract, is found more frequently in DHF. Raised level of liver enzymes and thrombocytopenia are found in both DF and DHF patients but are more severe in DHF. Evidence of plasma leakage are the presence of pleural and/or ascitic fluid or hemoconcentration.<sup>7</sup> DHF patients who have narrow pulse pressure (less than 20 mmHg) or show signs of shock are classified as dengue shock syndrome (DSS). Other severe clinical manifestations including hepatic failure and encephalopathy have been reported in dengue cases.<sup>8-10</sup>

Dengue is showing a recent upsurge in Bangladesh when Covid 19 is threatening huge number of human lives in mid-2021. This study is undertaken to see the severity nature of Dengue infection in our territory.

**Methods & Materials**

Eight one admitted children in the Paediatric ward of DNMI H from April to September, 2019, suffering from various dengue infection were included in this study after obtaining informed consent from parents. Diagnosis was made on basis of history, clinical features and supporting investigations like CBC to see Leukopaenia & Thrombocytopenia (Platelet count < 100,000 cell/cu mm) and haematocrit (raised or not ), NS1 antigen positivity , Dengue antibodies (IgM & IgG), Radiological & Sonographic evaluation of the Chest and Abdomen. Patients suffering from other diseases like enteric fever along with dengue diseases were not included.



Apethetic child DHF



Picture showing rash in the leg skin

**Result**

Total number of cases included in this study were 81, among them 43 (53%) were male and 38 (43%) female. The age range was from 06 months to 13 years. Fifty eight (71.60%) were urban and the remaining 23 (28.40%) were from rural areas. Out of them 79 (97.43%) were immunized as per our country schedule .Only two child, aging 06 months and 09 months had not been completed their schedule at that time.

**Table-I: (n = 81)**

Age & sex distribution according to age group.

Age	Male	Female	Total
< 01 year	01	02	03 (3.70%)
< 05 years	12	09	21 (25.93%)
< 10 years	22	17	39 (48.19%)
< 15 years	08	10	18 (22.22%)

The main complaints were fever with unusual weakness. Duration of fever ranges from 02 days to 07 days. Temperature recorded at the time of admission were 100F to 103F except in two cases in whom fever remitted before admission. Other associated symptoms were headache, myalgia and / or arthralgia, rash and rarely haemorrhagic manifestations.

**Table-II: (n= 81)**

Presenting symptoms

Fever	79 (97.53%)
Headache	23 (28.40%)
Myalgia & Arthralgia	19 (23.46%)
Rash	13 (16.04%)
Haemorrhagic manifestations	04 (4.94%)

The investigations done after admission were CBC, Haematocrit, NS1 antigen test, Chest X-ray, USG of the chest & abdomen and also Dengue antibodies (IgG & IgM ) in demanding cases.

**Table-III: (n=81)**

Blood picture at presentation

Thrombocytopenia	<100000 cells per mm <sup>3</sup> in 47 cases	< 50000 cells per mm <sup>3</sup> 34 cases
Leukopaenia	Present in 56 patients	Absent in 25 patients
Haematocrit	Raised (>10%) in 9 patients	Not raised in 72 patients

Features of Plasma leakage found in 09 children. Both the ascitic patients had associated pleural effusion also. Two patients with bleeding manifestation had concomitant pleural effusion.

**Table-IV: (n=9)**

Features of Plasma leakage

Nature of leakage	Number of patients
Pleural effusion	09
Ascites	02
Bleeding sign	02

NS1 antigen test were done in all the cases . Out of them 74 cases were positive, 04 weakly positive and the rest 03 children were negative. Immunoglobulin (IgM) were advised in some cases particularly those were NS1 negative and weakly positive. Features of Plasma leakage found in 09 children. Both the ascitic patients had associated pleural effusion also.

Among these children 78 recovered ,03 cases ( 01 with uncontrolled gastrointestinal hemorrhage and 02 with breathing difficulty demanding ICU support ) were referred to better center.

**Discussion**

Dengue fever is caused by the dengue virus. Symptoms usually starts 03 to 07 days after getting infected. Generally recovery occur in the following 02 to 07 days. In a small fraction of cases, the disease continue for longer period and may turn into a more severe form, Dengue hemorrhagic fever, manifested by haemorrhage, thrombocytopenia and /or plasma leakage, and in some case into a more dangerous form i.e. Dengue shock syndrome, where blood pressure decrease sharply.<sup>11</sup> Aedes aegypti virus has five serotypes.<sup>12,13</sup> Infection with one type generally offers lifelong immunity to that particular type, but a short-term immunity to the others. Subsequent infection with a different type increases the risk of severe complications.<sup>14</sup>

Plasma leakage means the protein rich, fluid component of the blood starts leaking from blood vessels into the surrounding tissue. Pleural effusion and/or ascites usually become clinically evident. This is a serious complication that distinguishes dengue

haemorrhagic fever from common dengue fever. Plasma leakage may begin to appear when fever begins to disappear.<sup>15</sup>

In our study out of 81 children 09 cases develop signs of plasma leakage, pleural effusion in all the 09 cases and ascites in 02 patients. Both the ascitic patients had simultaneous pleural effusion also. Time of our first clinical suspicion were variable, from 3rd to 5th days after the onset of fever. Vascular leakage usually becomes evident 3–6 days after the onset of illness, and known as the critical phase<sup>16</sup> Dengue fever may progress through three distinct clinical phases, the febrile phase, the critical phase and the recovery phase.<sup>17</sup> After being infected there may be an initial incubation period of 3-7 days, followed by sudden onset of high fever, related to high viraemia, which is termed as febrile phase.<sup>17</sup> Some patients may proceed to critical phase manifested by features of plasma leakage, lasting for 24–48 hours while others progress to recovery phase directly.<sup>18</sup> WHO suggested three dengue clinical phases based on the days of onset of illness, febrile phase/viremic phase (day(s) (1-3), critical phase (days 4-6) and recovery phase (days>7). But this does not happen always, prolonged febrile phase may be followed by the recovery phase, sometimes the febrile and critical phases may overlap each other. Plasma leakage is the hallmark of critical phase, if there is no evidence plasma leakage, the case is considered as prolonged febrile illness.<sup>19</sup>

Clinical suspicion had arisen when the usual symptoms were more pronounced along with newer complaints like breathing difficulty, right lower chest pain, enlarged tender liver and/or bleeding signs. etc. To confirm following investigations were done e.g. Chest X-ray P/A and Rt. Lateral view, Ultrasonography of the Chest and Abdomen and also Haematocrit to detect haemoconcentration. Sonography appeared to be more sensitive than radiology as chest X-ray could detect only in 03 (33.33 %) cases where as USG could do it in 08 patients ( 88.89%) developed pleural effusion in our study. Pleural effusion is the most common ultrasonographic sign of plasma leakage (62%). Thickening of the gallbladder wall and ascites were detected less frequently (43% and 52% respectively).<sup>20</sup> Researches using Chest X-rays and serial USG of the chest and abdomen to detect plasma leakage have demonstrated that progressive and significant accumulation of fluid only occurred in a subset of dengue cases.<sup>20,21</sup>

Bleeding were present in 02 cases, one epistaxis the other with haematemesis. Both had concomitant

pleural effusion. Haematocrit assessment is another indirect evidence of plasma leakage. Sudden drop in platelet count and rising haematocrit (>10%), are haematological markers for the progression of plasma leakage.<sup>22</sup> Haematocrit was not statistically significant between febrile phase and critical phase but significant in the group of plasma leakers.<sup>23</sup> In our series all the 09 cases platelet count were below 50000 per cubic mm and significantly raised haematocrit values (>10%) were found in eight patients (88.89%) among the plasma leakers. DHF is usually accompanying with a transient upsurge in vascular permeability because of endothelial dysfunction in critical phase. Increase vascular permeability is concomitant with vascular leakage and subsequent accumulation of fluid in pleural and peritoneal cavities, and with reduced blood pressure, pulse pressure and poor organ perfusion.<sup>24</sup>

Among all these eighty one children seventy eight recovered including 06 babies of plasma leaker group by medication only. Three children (01 with uncontrolled gastrointestinal hemorrhage and 02 with breathing difficulty demanding ICU support) were referred to better center.

All the patients plasma leakage were managed by isotonic intravenous fluids and colloids infusion to replace plasma, but carefully monitored, because unnecessary fluid infusion may precipitate pulmonary edema and respiratory failure. In our series 06 patients out nine improved satisfactorily. Close monitoring should be maintained as leakage may continue for next couple of days.

#### Conclusion

Ultrasonographic signs of plasma leakage and changes in hematocrits are useful tool for detecting plasma leakage in dengue infection. Pleural effusions and ascites give rise to respiratory problems. Severe plasma leakage can lead to hypovolemic shock. Isotonic intravenous fluids and colloids are administered to replace plasma, but the amount must be carefully monitored because too much IV fluid may precipitate pulmonary edema and respiratory failure. Patients can improve rapidly but should be monitored closely as leakage may continue for couple of days.

#### References

1. Organization WH. [accessed 1 December 2008]; Dengue and dengue haemorrhagic fever. <http://www.who.int/mediacentre/factsheets/fs117/en/>
2. Pinheiro FP, Corber SJ. Global situation of dengue and dengue haemorrhagic fever, and its emergence in the Americas. *World Health Stat Q.* 1997;50(3-4):

- J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 10-14 161-9. [PubMed] [Google Scholar]
3. Kouri G, Guzman MG, Valdes L, et al. Reemergence of dengue in Cuba: a 1997 epidemic in Santiago de Cuba. *Emerg Infect Dis.* 1998 Jan-Mar;4(1):89-92. [PMC free article] [PubMed] [Google Scholar]
  4. Gubler D, Kuno G, Markoff L. *Flavivirus, Field's Virology.* 5. Lippincott Williams & Wilkins; 2007. [Google Scholar]
  5. Lindenbach BD, Thiel H-J, Rice CM. *Flaviviridae: The Viruses and Their Replication, Field's Virology.* Lippincott Williams & Wilkins; 2007. [Google Scholar]
  6. Avirutnan P, Punyadee N, Noisakran S, et al. Vascular leakage in severe dengue virus infections: a potential role for the nonstructural viral protein NS1 and complement. *The Journal of infectious diseases.* 2006 Apr 15;193(8):1078-88. [PubMed] [Google Scholar]
  7. Organization WH. *Dengue Hemorrhagic Fever: diagnosis, treatment, prevention and control.* 2. WHO; 1997. [Google Scholar]
  8. Pancharoen C, Rungsarannont A, Thisyakorn U. Hepatic dysfunction in dengue patients with various severity. *J Med Assoc Thai.* 2002 Jun;85(Suppl 1):S298-301. [PubMed] [Google Scholar]
  9. Cam BV, Fonsmark L, Hue NB, et al. Prospective case-control study of encephalopathy in children with dengue hemorrhagic fever. *The American journal of tropical medicine and hygiene.* 2001 Dec;65(6):848-51. [PubMed] [Google Scholar]
  10. Janssen HL, Bienfait HP, Jansen CL, et al. Fatal cerebral oedema associated with primary dengue infection. *J Infect.* 1998 May;36(3):344-6. [PubMed] [Google Scholar]
  11. Kularatne SA (September 2015). "Dengue fever". *BMJ.* 351: h4661. doi:10.1136/bmj.h4661. PMID 26374064. S2CID 1680504.
  12. Normile D (October 2013). "Tropical medicine. Surprising new dengue virus throws a spanner in disease control efforts". *Science.* 342 (6157): 415. doi:10.1126/science.342.6157.415. PMID 24159024.
  13. Mustafa MS, Rasotgi V, Jain S, Gupta V (January 2015). "Discovery of fifth serotype of dengue virus (DENV-5): A new public health dilemma in dengue control". *Medical Journal, Armed Forces India.* 71 (1): 67-70. doi:10.1016/j.mjafi.2014.09.011. PMC 4297835. PMID 25609867.
  14. Dengue and severe dengue Fact sheet N°117". WHO. May 2015. Archived from the original on 2 September 2016. Retrieved 3 February 2016.

- J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 10-14
15. Anon Srikiatkhachorn, M.D, Plasma Leakage in Dengue Hemorrhagic Fever *Thromb Haemost*. 2009 Dec; 102(6): 1042–1049. doi: 10.1160/TH09-03-0208 PMID: PMC5527705, PMID: 19967133
  16. Lee TH, Lee LK, Lye DC, Leo YS. Current management of severe dengue infection. *Expert Rev Anti Infect Ther* 2017; 15: 67– 78.
  17. WHO, editor. *Comprehensive Guidelines for Prevention and Control of Dengue Fever and Dengue Haemorrhagic Fever*. New Delhi, India: SEARO, World Health Organization, 2011.
  18. Malavige GN, Ogg GS. T cell responses in dengue viral infections. *J Clin Virol* 2013; 58: 605– 11.
  19. World Health Organization. *Dengue: guidelines for diagnosis, treatment, prevention and control*. Geneva: World Health Organization; 2009.
  20. Srikiatkhachorn, Anon MD\*; Krautrachue, Anchalee MD†; Ratanaprakarn, Warangkana MD† et al, Natural History of Plasma Leakage in Dengue Hemorrhagic Fever, A Serial Ultrasonographic Study. *The Pediatric Infectious Disease Journal*: April 2007 - Volume 26 - Issue 4 - p 283-290 doi: 10.1097/01.inf.0000258612.26743.10
  21. Balasubramanian S, Janakiraman L, Kumar SS, et al. A reappraisal of the criteria to diagnose plasma leakage in dengue hemorrhagic fever. *Indian pediatrics*. 2006 Apr; 43(4): 334–9. [PubMed] [Google Scholar]
  22. Ralapanawa U, Alawattegama A, Gunrathne M, Tennakoon S, Kularatne S, Jayalath T. Value of peripheral blood count for dengue severity prediction. *BMC Res Notes*. 2018; 11(1): 400.
  23. Jayadas T.T.P Kumanan, T. Arasaratnam, V, et al. The clinical profile, hematological parameters and liver transaminases of dengue NS1 Ag positive patients admitted to Jaffna Teaching Hospital, Sri Lanka.. *BMC Research Notes* volume 12, Article number: 604 (2019)
  24. Yacoub S, Wertheim H, Simmons CP, Screaton G, Wills B. Microvascular and endothelial function for risk prediction in dengue: an observational study. *Lancet* 2015; 385(Suppl 1): S102. Crossref PubMed Web of Science®Google Scholar

Original Article

## Evaluation of Undergraduate Medical Student's Perception on Online Learning During COVID-19 Pandemic

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### Abstract

**Background:** Sudden outbreak of COVID-19 pandemic created panic, anxiety among the population worldwide. The education sector was among many which had taken a strong blow due to pandemic. In the wake of institute shut down, this was a challenging time for professional education which was combated through introduction of e-learning through online classes so as to ensure continuation of teaching-learning process for the medical students.

**Aims and Objectives:** The aim of the study was to rank the effectiveness and satisfaction of online classes compared to classroom conventional teaching among medical students and to evaluate student's overall perception regarding online learning.

**Materials and Methods:** This study has been designed to get opinion from 4th year MBBS medical students of Shaheed Monsur Ali Medical College, Dhaka regarding the perception on online learning during COVID -19 pandemic. In this survey, total 103 medical students of 4th year took part. This online survey was carried out from 2nd August, 2021 to 10th August, 2021, after completion of 12 weeks of online classes. A set of self designed questionnaire based on 5-point Likert scale was given to the students, to rank the effectiveness of online learning and their understanding with the satisfaction level on various parameters. The remaining items in the questionnaire comprised a mixture of question styles. All the students voluntarily participated in the survey.

**Results:** The study result shows that in 2 parameters, students rated the online-classes to be equally effective, the parameters which are contributing to offering convenience and meeting individual learning needs. In other 2 parameters, regarding building skills and knowledge, offering better understanding through recorded classes the students found it to be somewhat more effective. But regarding interaction level, contributing to effective communication and balancing of practical and theoretical knowledge, the students found it to be somewhat less effective. We could come to an interpretation that students were not much satisfied with this way of teaching but definitely it was the need of the hour. Most of the students had positive perception towards online classes.

**Conclusion:** We could conclude from our study that online education can supplement the process of present education system, but it cannot be a substitute for the established system of education.

**Key words:** Online learning, Covid-19 pandemic.

### Introduction

The Corona virus Disease 2019 (COVID-19) outbreak which was originated and restricted only in China until February 2020 had suddenly altered into a global pandemic disease from 11th March, 2020.<sup>1,2</sup> This pandemic has affected not only on physical health but also the lifestyle, business, stock market and even the education system worldwide. A large part of the world experienced a lock down that closed educational institutions affecting more than 70% of the world's student population. The nationwide lockdown

restrictions to control the spread of disease and 'flatten the curve' have impacted all aspects of life;<sup>3,4,5</sup> inevitably, medical education has also been affected, with the halting of lectures, clinical placements and key examinations.<sup>6,7</sup> In many countries, typical face-to-face classes had to be suspended to ensure the safety of students, lecturers, and patients. Such measures have resulted in a sudden shift in teaching methods towards online teaching. Online teaching has played a key role in medical education over recent years,<sup>8,9,10</sup> demonstrated several benefits in enhancing student learning.<sup>11</sup>



Online learning is a virtual learning system which integrates internet connection with teaching and learning process.<sup>12</sup> The interaction of teaching and learning activities can be carried out from the distance with the help of internet and online media.<sup>13</sup> However, this method can be difficult for those teachers who are specialized in conventional teaching and are uncomfortable to use electronic gadgets. Also, students may not feel serious in online teaching as teachers have little control in online teaching.<sup>14</sup> Online learning has become a solution for the continuity of teaching and learning process during Covid-19 pandemic. After 12 weeks of only online learning with no face-to-face learning, we decided to analyze medical students' perception of this teaching approach. This knowledge is necessary to identify student's requirement during online learning to make this learning system beneficial for the students.

#### Objectives

1. To evaluate student's perception regarding online learning.
2. To evaluate student's view on the effectiveness of online learning.
3. To evaluate student's satisfaction regarding online classes.

#### Materials and Methods

We have designed this study to get opinion from 4th year MBBS medical students of Shaheed Monsur Ali Medical College, Dhaka regarding the perception on online learning during COVID -19 pandemic. This cross sectional survey study was done on 103 medical students after 12 weeks of initiation of their online classes. This online survey was carried out from 2nd August, 2021 to 10th August, 2021. A set of self designed questionnaire based on 5-point Likert scale was given to the students, to rank the effectiveness of online learning and their understanding with the satisfaction level on various parameters. The remaining items in the questionnaire comprised a mixture of question styles. The questionnaire was accessed online. There were no exclusion criteria. Each student was allowed to complete the questionnaire once. All respondents were fully informed about the objectives of the study and agreed to voluntarily participate.

#### Statistical analysis

Statistical analysis's were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were used for analysis of data. Frequency was expressed as percentage.

#### Result

In this survey, total 103 medical students of 4th year took part. Students were enquired whether they had attended any type of online classes before this pandemic. Out of 103 students, 95(92.23%) had not attended online classes earlier and only 8 students had already experienced. Among them 75.72% students used mobile, whereas 21.35% used laptop and 2.91% used computer for attending online classes. 66.01% students used wifi and 27.18% students used cellular data for attending the class. Only 6.79% students used both wifi and cellular data. 82.52% students had access to static internet and 27.18% of them had no internet facility at their own home. Majority of the students 93.2% felt that online classes should be continued during this pandemic. 88.34% of the respondents are satisfied from the online classes using ZOOM application (Table-1).

**Table-I: Online class related characteristics of respondents (n = 103)**

Variables	Number	Percentage (%)
<b>Ever received online class before COVID 19</b>		
No	95	92.23
<b>Type of Gadget used for attending online class</b>		
Mobile	78	75.72
Laptop	22	21.35
Computer	3	2.91
<b>Type of internet connection</b>		
Wifi	68	66.01
Cellular data	28	27.18
Combination of both	7	6.79
<b>Access to sound/static internet</b>		
Yes	85	82.52
No	18	17.47
<b>Access to internet facility at own home</b>		
yes	75	72.81
No	28	27.18
<b>Should online learning be continued during this pandemic?</b>		
yes	96	93.2
No	7	6.79
<b>Student's Perceived Level of Satisfaction from Online Classes using ZOOM</b>		
Strongly satisfied	70	67.96
Satisfied	21	20.38
Less satisfied	12	11.65

Tabl-II: shows the perception of students towards online classes. More than half of the students (54.36%) agreed that online learning system is easy to use. 72.81% students agreed that there is no need of specific preparation before attending online class. 22.32% of students disagreed that learning is the same in class and at home by using internet. 40.77% of students

strongly agreed that learners population does not affect learning in online classes.73.77% of them agreed that self-discipline is necessary during online studies. 43.68% of students strongly agreed that online learning improves their technical skill in using gadgets. More than half of the students (62.13%) agreed that there is need of face to face contact with teachers to learn effectively.78.64% of students disagreed that online learning is better than traditional learning. Among them 74.74% disagreed that there is low participation of students in online learning. 22.33% of students strongly agreed that recorded online class can be useful for future.

**Table-II: Perception of students towards online classes (n = 103)**

Statements	Strongly disagree (%)	Disagree (%)	Neutral (%)	Agree (%)	Strongly agree (%)
Online learning system is easy to use	7 (6.79 %)	15 (14.56 %)	25 (24.27 %)	43 (41.74 %)	13 (12.62 %)
It is easy to manage study time effectively	7 (6.79 %)	9 (8.73 %)	14 (13.59 %)	55 (53.39 %)	18 (17.47 %)
No specific preparation is needed	3 (2.91 %)	12 (11.65 %)	13(12.62 %)	60 (58.25 %)	15 (14.56 %)
Learning is the same in class and at home by using Internet	13(12.62 %)	10 (9.7 %)	15(14.56 %)	45(43.68 %)	20 (19.41 %)
Learning on the internet outside of class is more motivating than a regular class	28 (27.18 %)	35 (33.96 %)	25 (24.27 %)	10 (9.7 %)	5 (4.85 %)
There is easy sharing ideas with others in online learning	7 (6.79 %)	17 (16.50 %)	14 (13.59 %)	50 (48.54 %)	15 (14.56 %)
Learners population does not affect learning in online classes	0	3 (2.91 %)	13 (12.62 %)	45 (43.68 %)	42 (40.77 %)
Self-discipline is necessary during online studies	0	7 (6.79 %)	20 (19.41 %)	65 (63.10 %)	11 (10.67 %)
I can ask my teacher questions and receive a quick response during online class	2 (1.94 %)	5 (4.85 %)	16 (15.53 %)	60 (58.25 %)	20 (19.41 %)
Online learning improves technical skill in using electronic gadget	0	0	20 (19.41 %)	38 (36.89 %)	45 (43.68 %)
Face-to-face contact with teacher is necessary to learn	0	9 (8.73 %)	30 (29.12 %)	40 (38.83 %)	24 (23.30 %)
It is comfortable communicating electronically during online classes	9 (8.73 %)	13 (12.62 %)	38 (36.89 %)	33 (32.03 %)	10 (9.7 %)
Online learning is better than traditional learning	35 (33.98 %)	46 (44.66 %)	15 (14.56 %)	7 (6.79 %)	0
There is low participation of students in online learning	32 (31.06 %)	45 (43.68 %)	20 (19.41 %)	6 (5.8 %)	0
Online class cost is low	25(24.27 %)	45 (43.68 %)	20 (19.41 %)	8 (7.76 %)	5 (4.85 %)
Lack of concentration	28 (27.18 %)	38 (36.89 %)	22 (21.35 %)	10 (9.7 %)	5 (4.85 %)
Recorded online class can be useful for future	0	15 (14.56 %)	20 (19.41 %)	45(43.68 %)	23 (22.33 %)
Learning environment is better in college than at home	5 (4.85 %)	10 (9.7 %)	25 (24.27 %)	48 (46.60 %)	15 (14.56 %)

Table-III: shows the rank of effectiveness regarding online learning. Out of 7 parameters, in 2 parameters, students rated the online-classes to be equally effective, the parameters which are contributing to offering convenience and meeting individual learning needs. In 2 parameters, regarding building skills and knowledge, offering better understanding through recorded classes the students found it to be somewhat more effective. In other 3 parameters, regarding interaction level, contributing to effective communication and balancing of practical and theoretical knowledge, the students found it to be somewhat less effective.

**Table-III: Rank of effectiveness regarding online learning compared to regular classroom settings (n = 103)**

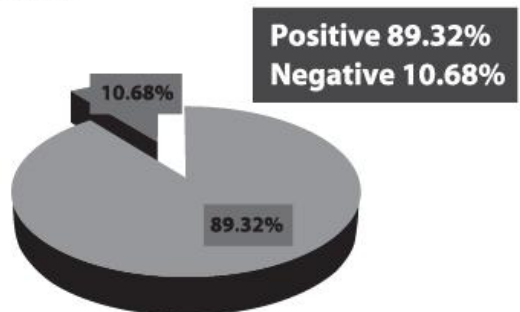
Parameters	Much less effective (%)	Somewhat less effective (%)	Equally effective (%)	Somewhat more effective (%)	Much more effective (%)
Offering convenience	3	20	40	35	5
Meeting individual learning needs	5	15	55	20	8
Contributing to effective communication	10	38	25	23	7
Building skills and knowledge	3	14	32	42	13
Offering better understanding through recorded class	10	12	36	40	5
Interaction level	20	38	23	20	2
Balancing of practical and theoretical experience	15	40	25	18	5

Table-IV: shows the satisfaction level of students with regard to online classes. With regard to class material provided to students they were strongly satisfied. Regarding in balancing the practical and theoretical knowledge and in availability of e-resources the students were not much satisfied.

**Table-IV: The satisfaction level of students with regard to online classes on five parameters (n = 103)**

Parameters	Strongly dissatisfied (%)	Dissatisfied (%)	Neutral (%)	Satisfied (%)	Strongly Satisfied (%)
How helpful was the class material provided to you?	5 (4.85 %)	9 (8.73 %)	13(12.62 %)	20(19.41 %)	56 (54.36 %)
How satisfied are you with the balance of practical and theoretical knowledge provided by these classes?	10(9.7 %)	35 (33.98 %)	25(24.27 %)	20(19.41 %)	13(12.62 %)
Availability of e-resources	8(7.76 %)	37(35.92 %)	15(14.56 %)	25(24.27 %)	18(17.47 %)

Figure-I: reveals the overall level of perception of students towards online classes. Most of the students (89.32%) had positive perception towards online classes.



**Figure-I: Overall perception of students regarding online learning**

**Discussion**

Medicine being a challenging profession, needs a lot of commitment, dedication, acquisition of clinical skills, and self-directed learning attitude by the students.

COVID-19 outbreak created a panic, distress among student community, and uncertainty about the normalization of the situation. Online classes were started throughout the medical colleges keeping in mind, the students perception. The present study assessed the perception of 4th year medical students towards online classes during the period of COVID -19 pandemic. The study found that most of the students (89.32%) had positive perception towards online classes. In this study, majority of the students 93.2% felt that online classes should be continued during this pandemic. 78.64% of students disagreed that online learning is better than traditional learning. A study conducted among Saudi pharmacy students showed that 72% preferred traditional in-class lectures over the online classes.<sup>15</sup> In this study, more than half of the students (62.13%) agreed that there is need of face to face contact with teachers to learn effectively. Similarly, a study conducted among Pakistani medical students showed that majority of the students (85%) preferred face to face teaching over online teaching.<sup>16</sup> More than half of the students (61.16%) agreed that learning environment is better in college than at home. Though 40.77% of students strongly agreed that learners population does not affect learning in online classes. 43.68% of students strongly agreed that online learning improves their technical skill in using gadgets. Among them 74.74% students disagreed that there is low participation of students in online learning. 43.68% of students agreed that recorded online class can be useful for future. 58.25% of students agreed that they can ask questions to teacher and can get quick responses. These data suggest that students prefer online classes during this pandemic.

A study also shows that to some extent, online learning might not compete with aspects of other learning, such as interactive knowledge building between teacher and students.<sup>17</sup> Such limitations could create opportunities for students to obtain self-learning methods through information technology. The results of this study were also similar to our survey which showed that the level of interaction of students with the faculty is less as compared to classroom teaching. The highly personalized content for learning can be improved by web-based learning. The students online expertise is possibly increased by diversity of skills and knowledge.<sup>18</sup>

The effectiveness of online learning, though less effective as compared to a normal classroom teaching and it varied for various categories of students. Our study shows that students rated the online-classes to

be equally effective, the parameters which are contributing to offering convenience and meeting individual learning needs. In this study, regarding building skills and knowledge, offering better understanding through recorded classes the students found it to be somewhat more effective. Regarding interaction level, contributing to effective communication and balancing of practical and theoretical knowledge, the students found it to be somewhat less effective. To avoid the potential limitation of online learning in undergraduate medical education, it should be worthwhile to combine the advantages of online teachings and classroom teachings called blended learning.<sup>19,20</sup> We could conclude from our study that e-education can supplement the process of education, but it cannot be a substitute for the established system of education.

#### Conclusion

Advancement in biotechnology and internet technology has brought about a revolution in the field of medical sciences with the innovation of trinity of e-learning, e-teaching, and e-research constituting the superstructure of e-education. This will facilitate adaptive and collaborative learning by the learners and the teachers. It will lend support to the old system by extending the frontiers of knowledge and research. It will become effective means of communication provided it is supported by the state of art infrastructure and blended learning technology. Hence, blended learning should be started as soon as situation becomes normalized as it would lead to more development of professional skills and grooming of professional career.

#### References

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol.* 2020 Apr;92(4):401-402. doi: 10.1002/jmv.25678. Epub 2020 Feb 12. PMID: 31950516; PMCID: PMC7166628.
2. World Health Organization. WHO announces COVID-19 outbreak a pandemic. 2020. <https://bit.ly/35KytdL>
3. Johnson B. PM address to the nation on coronavirus: 23 Mar 2020. [Online] GOV.UK. Available: <https://www.gov.uk/government/speeches/pm-address-to-the-nation-on-coronavirus-23-march-2020> [Accessed 29th May 2020].
4. Hancock M. Controlling the spread of COVID-19: Health Secretary's statement to Parliament. [Online]

- GOV.UK. Available: <https://www.gov.uk/government/speeches/controlling-the-spread-of-covid-19-health-secretarys-statement-to-parliament> [Accessed 31 May 2020].
5. Stevens S, Pritchard A. Letter to chief executives of all NHS trusts and foundation trusts, CCG accountable officers, GP practices and primary care networks, and providers of community health services. [Online] NHS England and NHS Improvement. Available: <https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/urgent-next-steps-on-nhs-response-to-covid-19-lettersimon-stevens.pdf> [Accessed 29 May 2020].
  6. Sandhu P, de Wolf M. The impact of COVID-19 on the undergraduate medical curriculum. *Med Educ Online* 2020;25:1764740
  7. General Medical Council. Information for medical students. [Online] General Medical Council. Available: <https://www.gmc-uk.org/news/news-archive/coronavirus-information-and-advice/information-for-medical-students> [Accessed 27 May 2020].
  8. O'Doherty D, Dromey M, Loughheed J, et al. Barriers and solutions to online learning in medical education - an integrative review. *BMC Med Educ* 2018;18:s12909-018-1240-0.
  9. Harden RM. Trends and the future of postgraduate medical education. *Emerg Med J* 2006;23:emj.2005.033738:798-802.
  10. Moran J, Briscoe G, Peglow S. Current technology in advancing medical education: perspectives for learning and providing care. *Acad Psychiatry* 2018;42:s40596-018-0946-y:796-9.
  11. Lochner L, Wieser H, Waldboth S, et al. Combining traditional anatomy lectures with e-learning activities: how do students perceive their learning experience? *Int J Med Educ* 2016;7:69-74.
  12. Bentley Y, Selassie H, Shegunshi A. Design and evaluation of student-focused E learning. *Electronic Journal of E-Learning*. 2012;10(1):1-12. <https://bit.ly/34DKDWE>
  13. Eldeeb RA. Students' Perceptions to E-learning. *IOSR Journal of Research & Method in Education (IOSR-JRME)*. 2014;4(3):33-36.
  14. Zhang X. 4th International Conference on Culture, Education and Economic Development of Modern Society (ICCESE 2020) Atlantis Press; 2020. Thoughts on large-scale long-distance web-based teaching in colleges and universities under novel coronavirus pneumonia epidemic: a case of Chengdu University; pp. 1222-1225.
  15. Almoghaslah D, Ghazwani M, Alsayari A, Khaled A. Pharmacy students' perceptions towards online learning in a Saudi Pharmacy School. *Saudi Pharm J*. 2018 Jul;26(5):617-621. doi: 10.1016/j.jsps.2018.03.001. Epub 2018 Mar 5. PMID: 29991906; PMCID: PMC6036186.
  16. Abbasi S, Ayoob T, Malik A, Memon SI. Perceptions of students regarding E-learning during Covid-19 at a private medical college. *Pak J Med Sci*. 2020 May;36(COVID19-S4):S57-S61. doi: 10.12669/pjms.36.COVID19-S4.2766. PMID: 32582315; PMCID: PMC7306963.
  17. Bettinger EP, Fox L, Loeb S, Taylor ES. Virtual classrooms: How online college courses affect student success. *Am Econ Rev* 2017;107:2855-75.
  18. Nalini GK, Deepak P, Neelamma P, Sahana GN, Nagaral JV. Effectiveness of digital learning versus traditional learning among undergraduate students-prescription writing. *Natl J Physiol Pharm Pharmacol* 2020;10:9-14.
  19. Garrison DR, Vaughan ND. *Blended Learning in Higher Education: Framework, Principles, and Guidelines*. New York: John Wiley and Sons; 2007. p. 9-11.
  20. Dodiya D, Vadasmiya DS, Diwan J. A comparative study of flip classroom teaching method versus traditional classroom teaching method in undergraduate medical students in physiology. *Natl J Physiol Pharm Pharmacol* 2019;9:551-5.

Original Article

## Evaluation of Vitamin B<sub>12</sub> Deficiency in Newly Diagnosed Hypothyroid Female Patients in Dhaka City

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### Abstract:

**Background:** Vitamin B<sub>12</sub> deficiency may remain latent in the early phase of hypothyroidism. Symptoms of neuropathy may occur due to combination of deficiency of thyroxine & vitamin B<sub>12</sub> in newly diagnosed hypothyroid female patients.

**Objectives:** To assess the prevalence and clinical features of vitamin B<sub>12</sub> deficiency in newly diagnosed hypothyroid female patients in Dhaka.

**Methods:** This cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC) between July' 2015 to June' 2016 on 80 newly diagnosed hypothyroid female patients with clinical features of vitamin B<sub>12</sub> deficiency. Their serum TSH, FT<sub>4</sub>, FT<sub>3</sub> levels were estimated for assessment of thyroid function status by ELISA method. Vitamin B<sub>12</sub> level was also estimated to observe its level by using standard method. The statistical analysis was done by ANOVA test, paired, independent sample 't' test.

**Results:** In this study, a total 80 newly diagnosed hypothyroid female patients were evaluated among them 34 patients had low vitamin B<sub>12</sub> level. Generalized weakness, impaired memory, depression, numbness and decreased reflexes were more frequently noted in vitamin B<sub>12</sub> deficient patient. Additionally 16 subjects were complained of symptoms consistent with vitamin B<sub>12</sub> deficiency, but had normal range of vitamin B<sub>12</sub> level.

**Conclusion:** The present study revealed that there is a high (approx 42.5%) prevalence of vitamin B<sub>12</sub> deficiency in newly diagnosed hypothyroid female patients. Traditional symptoms are not a good guide to determining presence of vitamin B<sub>12</sub> deficiency. Screening for vitamin B<sub>12</sub> level should be undertaken in all newly diagnosed hypothyroid female patients.

**Key words:** Hypothyroidism, Thyroxine, Vitamin B<sub>12</sub>.

### Introduction

Hypothyroidism is a clinical condition resulting from reduced circulating levels of free thyroxine (FT<sub>4</sub>) and triiodothyronine (FT<sub>3</sub>).<sup>1</sup> However, the thyroid hormones increase the metabolic activities of almost all tissues of the body. The basal metabolic rate can increase 60 to 100 percent above normal when large amount of hormones are secreted.<sup>2</sup> The thyroid gland is not essential for life, but its absence or hypo function during fetal and neonatal life results in severe mental retardation and dwarfism.<sup>3</sup>

The prevalence of primary hypothyroidism is 10/1000 but increases to 50/1000 if patients with sub-clinical hypothyroidism (normal FT<sub>4</sub>, raised TSH) are included and the female: male ratio is approximately 6:1.<sup>4</sup>

However, hypothyroidism might be reversible at early

stages; on the other hand irreversible cases might have longer duration of diseases or might present etiologies other than hypothyroidism. Long term accumulation of mucinous tissue is the possible cause of irreversibility.<sup>5</sup>

Most of the hypothyroid patients complain some sensory symptoms like tingling sensation, numbness, paraesthesia, burning pain and some motor symptoms like weakness, muscle fatigability, stiffness and cramp.<sup>6</sup> Again, decreased tendon reflexes, decreased muscle strength, positive Phalen's test and Tinel's sign at the wrist (test for clinical diagnosis of carpal tunnel syndrome) were also found in some hypothyroid female.<sup>7</sup>

Some investigator revealed that, sensory and motor sign/symptoms such as tingling sensation, numbness, loss of vibration, pain, decreased muscle strength and

delayed tendon reflexes were still persisted in hypothyroid patients even after 1 year of thyroxine replacement therapy.<sup>8</sup>

In a follow-up study, some researchers demonstrated that these symptoms to be common among our hypothyroid patients & to evaluate vitamin B<sub>12</sub> levels in patients with primary hypothyroidism.<sup>9</sup>

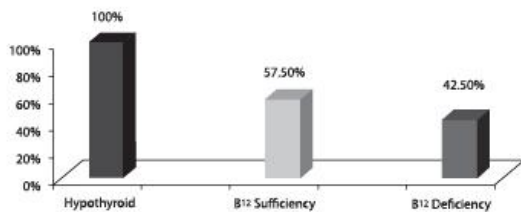
**Methods**

This cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC) between July' 2015 to June' 2016. In this study, 80 newly diagnosed hypothyroid female patients with symptom of peripheral neuropathy, age ranged from 20-45 years was selected. All the study subjects were selected from out patients department of SSMC and BSMMU. They were belonged to middle socioeconomic status. Subjects with hypertension, diabetic Mellitus, heart disease, kidney disease, hyperthyroidism, past history of neuropathy or neuromuscular diseases, use of drugs known to cause neuropathy or myopathy, malignancy or other serious diseases, pregnancy or lactation, history of gastric or ileal resection were excluded from the study. Their serum TSH, FT<sub>4</sub>, FT<sub>3</sub> levels were estimated for assessment of thyroid function status by ELISA method. Vitamin B<sub>12</sub> level was also estimated to observe its level by using standard method. The ethical permission was taken from the authority.

**Results**

In this study, 80 newly diagnosed hypothyroid female were evaluated, age ranges from 20-45 years, among them 34(42.5%) had vitamin B<sub>12</sub> deficiency (Figure: 01). Symptoms of numbness, paraesthesia were seen more commonly in B<sub>12</sub> deficiency patients compared to B<sub>12</sub> sufficient patients. The frequency of the commonly recognized symptom associated with vitamin B<sub>12</sub> deficiency among our hypothyroid patients is noted in table-I.

**Figure-I:**



**Table-I: Frequency of symptoms in hypothyroid patients with low & normal B<sub>12</sub> level**

Symptom	Total No.	vitaminB <sub>12</sub> <200pg/ml	vitaminB <sub>12</sub> >200pg/ml
Weakness	61/80	35 (43.75%)	26 (32.5%)
Numbness	22/80	14 (17.5%)	8 (10%)
Loss of vibration	11/80	8 (10%)	3 (3.7%)
Muscle weakness	33/80	21 (26.25%)	12 (15%)
Delayed tendon reflex	21/80	15 (18.75%)	6 (7.5%)
Decreased sensitivity	16/80	11 (13.75%)	5 (6.25%)

**Discussion**

Vitamin B<sub>12</sub> is known as cobalamin, was first isolated in 1948 & soon after found to be effective in treatment of pernicious anemia.<sup>10</sup> Prevalence of vitamin B<sub>12</sub> has been reported up to 15-25% in certain population groups particularly in elderly.<sup>11</sup> We have studied prevalence of vitamin B<sub>12</sub> in hypothyroid patients & found 34 out of 80 patients (42.5%) have low B<sub>12</sub> level.

Vitamin B<sub>12</sub> deficiency may occur as a result of autoimmune pernicious anemia, malabsorption, malnutrition or use of drugs including proton pump inhibitors, H<sub>2</sub> receptor antagonists or metformin.<sup>12</sup> Metformin may cause malabsorption secondary to its effects on ileal mucosa or membrane receptors.<sup>13</sup> Proton pump inhibitors & H<sub>2</sub> receptor antagonists causes gastric hypochlorhydria and malabsorption of vitamin B<sub>12</sub>. Untreated helicobacter pylori infection is occasionally associated with B<sub>12</sub> deficiency.<sup>14</sup> In our study we found no association between use of drugs and B<sub>12</sub> deficiency but we found frequent occurrence of B<sub>12</sub> deficiency in hypothyroid patients, it was not possible to determine the underlying etiology of this association.

Clinical signs of vitamin B<sub>12</sub> deficiency may take long to manifest & often affected patients as asymptomatic for several years. Occasionally, hematological or neuropsychiatric manifestations may presents as a early marker of deficiency but non specific complaints are attributed to aging.<sup>15</sup> The neuropsychiatric features include fatigue, weakness, numbness, loss of vibration, delayed tendon reflex, loss of memory, demensia and depression.<sup>16</sup> Hypothyroid & vitamin B<sub>12</sub> deficient patients often have common symptoms of weakness, lethargy, memory impairment, numbness and tingling.<sup>17</sup> We have noticed that several patients, despite being on adequate thyroxine replacement, had persistence of symptoms and subsequently we found to be B<sub>12</sub> deficient.

Our study showed vitamin B<sub>12</sub> deficiency to be common in the hypothyroid female patients. Screening for B<sub>12</sub> deficiency should be undertaken early in the diagnosis of hypothyroidism and periodically thereafter. Patients should be followed and evaluated for suggestive symptoms.

#### Conclusion

From the result of the study, it can be concluded that, peripheral neuropathy along with deficiency of vitamin B<sub>12</sub> was observed in newly diagnosed hypothyroid female before starting their treatment.

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#### References

1. Keele CA, Neil E, Joels N. Samson Wright's Applied Physiology, 13th ed. New York: Oxford University Press; 1982. 542-545.
2. Hall JE. Textbook of Medical Physiology, 12th ed. Elsevier India Private limited; 2016. 550-552.
3. KE Barman, SM Boitano, S Brooks. Review of Medical Physiology, 24th ed. New York: McGraw-Hill Company; 2010. 587-588.
4. Edwards CRW, Toft AD, Walker BR. 'Endocrine Disease' in Haslett C, Chilvers ER, Hunter JAA, Boon NA. Davidson's principle & practice of Medicine. 22nd ed. Churchill Livingstone. India; 2014. 568-571.
5. Kececi H, Degirmenci. Hormone replacement therapy in hypothyroidism and nerve conduction study. *Neurophysiol Clin* 2006; 35(2): 79-83.
6. Garg R, Bansal N, Singh N, Maria AK, Arora KS. Nerve conduction studies in newly diagnosed cases of Hypothyroidism. *Sch. Acad. J. Biosci.* 2015; 3(5): 479-488.
7. Mahadule AA, Jadhao PS, Phatak MS. Motor conduction parameters in recently diagnosed and untreated hypothyroidism. *Annals of Neurosciences* 2015; 22(1): 6-10.
8. Duyff RF, Bosch JVD, Laman DM, Loon BJPV, Linssen WHJP. Neuromuscular findings of thyroid dysfunction: prospective clinical electrodiagnostic study. *J Neurol Neurosurg Psychiatry* 2000; 68: 750-755.
9. Jabbar A, Yawar A, Wasim S, Islam N, Haque N, Zuberi L, et al. Vitamin B<sub>12</sub> deficiency common in J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 20-22 primary hypothyroidism. *J Pak Med Assoc* 2008; 54(5): 6-10.
10. Dharmarajan TS, Norkus EP. Approaches to vitamin B<sub>12</sub> deficiency, early treatment may prevent devastating complication. *Postgraduate Medicine* 2001; 99-106.
11. Wynn M, Wynn A. The danger of Vitamin B<sub>12</sub> deficiency in the elderly. *Nutrihealth* 1998; 12: 215-226.
12. Green R, Kinsella LJ. Current concepts in diagnosis of cobalamin deficiency. *Neurology* 1995; 45: 435-440.
13. Banman WA, Shaw S, Jayatilake E. Increased intake of calcium reverses vitamin B<sub>12</sub> malabsorption induced by metformin. *Diab Care* 2000; 23: 1227-1231.
14. Kaptan K, Beyan C, Ural U, Cetin T. Helicobacter Pylori is it a novel causative agent in vitamin B<sub>12</sub> deficiency. *Arch Intern Med* 2000; 160: 1349-53.
15. Serin E, Gumurula Y, Ozar B, Kayaseluk F, Yimaz U. Impact of helicobacter pylori on the development of vitamin B<sub>12</sub> deficiency in the absence of gastric atrophy. *Helicobacter* 2002; 7: 337-41.
16. Yaqoob J, Jafri W, Abid S. Helicobacter pylori infection and micronutrient deficiency. *World J Gastroenterol* 2003; 9: 2137-2139.
17. Lindenbaum J, Heaton B, Savage D. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Eng J Med* 1988; 318: 1720-1722.

Original Article

## Post Vaccination Immunity Status Against Hepatitis B Virus Infection-An Analytical Study

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### Abstract:

**Introduction:** Hepatitis B vaccine has shown to be highly efficacious in preventing hepatitis B virus (HBV infection). Immunization with this vaccine reduces the subsequent development of chronic hepatitis B in young children from perinatal or early childhood exposure to HBV.<sup>8,9</sup> However, the duration of satisfactory protection level conferred by hepatitis B vaccination is not well understood.<sup>10,11</sup> Previous thinking was that this vaccination would provide effective coverage for five to seven years.<sup>12,13</sup> But subsequently it has been proved that it offers long-term immunity.

**Methods:** This is a cross sectional observational study. All the patients were collected among the admitted patients of Paediatric ward, Dhaka National Medical College (DNMC) from January to December, 2019.

**Result:** This study reveals 49.12% children have developed adequate immunity i.e. Anti-HBs antibody level >100 mIU /ml, and 38.60% showed poor response (10-100 mIU /ml). Only 12.28 % are nonresponsive. Poor responders also having satisfactory immunity, may be for a shorter period. Difference of immunity level developed between two groups, 1 yr. - 6yrs and > 6 yrs. -12 yrs. is obvious. The reason is not very clear. More elaborate studies are required to probe on these facts.

**Conclusion:** Acquisition of acceptable immunity level following our vaccination schedule is satisfactory (87.72%). Larger study should be conducted to develop a consensus of opinion.

**Key words:** Hepatitis B Vaccination, Immunity, HBV.

### Introduction:

American physician Baruch Blumberg discovered what he called the "Australia Antigen" (now called HBsAg) in the serum of an Australian Aboriginal person in 1963.<sup>1</sup> In 1968, this protein was proved to be a part of the virus that causes "serum hepatitis" (hepatitis B) by virologist Alfred Prince.<sup>2</sup>

Hepatitis B vaccine was first approved by United States in 1981.<sup>3</sup> One recombinant version has become available in the market since 1986.<sup>4</sup> It is included in the World Health Organization's Essential Medicines list. These two versions were developed by Maurice Hilleman and his team.<sup>5,6,7</sup>

Hepatitis B vaccine (both plasma derived and recombinant) has been demonstrated to be highly effective in preventing hepatitis B virus (HBV) infection. Immunization with this vaccine if begins at birth has subsequently dramatically reduce the development of chronic hepatitis B in children of perinatal or early

childhood exposure to HBV.<sup>8,9</sup> However, the duration of protection conferred by hepatitis B vaccination is not well understood.<sup>10,11</sup> It was previously suggested that the vaccination would only provide effective coverage for five to seven years.<sup>12,13</sup> But subsequently it has been appreciated that long-term immunity derives from immunological memory and hence subsequent testing and administration of booster dose is unnecessary in successfully vaccinated immune-competent individuals.<sup>14</sup>

Following the primary course of three vaccinations, a blood test may be taken after an interval of 1-4 months to measure the response level.<sup>15</sup> World Health Organization (WHO) has recommended Hepatitis B vaccination along with DPT and Oral Polio vaccine<sup>16</sup> offered schedule for hepatitis B immunization of children consists of a dose within 24 hours of birth followed by a second and third dose of hepatitis B containing vaccines at intervals of at least 4 weeks<sup>17</sup>



Bangladesh included Hepatitis B vaccination since 2005 and pentavalent vaccination (DPT + Hepatitis B + Hib) since 2009 in national EPI schedule. The recommended schedule is at the age of 6, 10 and 14 weeks.<sup>18</sup>

This is a study of 57 children, those have been vaccinated as per national EPI schedule. We have undertaken the study to see the level of immunity against Hepatitis B virus among children in our perspective conferred by this immunization schedule.

**Materials & Method:**

This is a cross sectional observational study. All the patients were collected from the Paediatric in-patient department of Dhaka National Medical College (DNMC) during the year 2019, who had been admitted with different diseases. Total 57 children were included in this study by purposive random selection technique, those had been vaccinated for Hepatitis B virus infection as per national immunization schedule during first year of life. All of them received full 03 courses of vaccine.

The age range was from 01 year to 12 years, belongs to both sexes from urban and rural areas. Children below 01 year were non-cooperative and those above 12 years were excluded to maintain the harmonicas of age in the study group. We have tested them by EILISA method in the laboratory of Dhaka National Medical College (DNMC) for detection of Hepatitis B surface antibody (HBS antibody) in their serum. Children with any other chronic disease and severely malnourished were excluded from the study. Children, whose parent/s were non-cooperative, also not included.

**Result:**

Fifty-seven (57) children were include in the study, among them 29 were male and 28 were female.

**Table-I: (n=57) Sex distribution.**

Gender	Age (1 to 6 yrs.)	Age (>6 to 12 yrs.)	Total	Percentage
Male	13	16	29	50.88 %
Female	18	10	28	49.12 %
<b>Total</b>	<b>31</b>	<b>26</b>	<b>57</b>	<b>100%</b>

We have divided them into two groups to see the impact on immunity level if any.

**Table-II: (n=57) Antibody status.**

Serum level in our study population following pentavalent vaccination (DPT + Hepatitis B + Hib).

Gender	<10 mIU/ml	10-100 mIU/ml	100 mIU/ml
Male	04 (13.79%)	12 (41.37%)	13 (44.83%)
Female	03 (10.71%)	10 (35.71%)	15 (53.57%)
<b>Total</b>	<b>07 (12.28%)</b>	<b>22 (38.60%)</b>	<b>28 (49.12%)</b>

Immunity (HBS antibody) level according to age group

**Table-III: (n=57) Immunity (Hbs Ab) level according to age group.**

Age group	<10 mIU/ml	10-100 ml U/ml	>100 ml U/ml	P. value
(1 yr.- 6yrs)	05(16.13%)	12(38.71%)	14(45.16%)	0.595
(>6yrs.-12yrs.)	02(7.69%)	10 (38.46%)	14 (53.85%)	

**Discussion:**

The hepatitis B vaccine is a safe and effective and recommended for infants. This vaccine is also recommended for children, those have failed to be vaccinated during early infancy and for adults those are at higher risk for infection because of their job nature, lifestyle and living conditions.

All the children included in our study were vaccinated as per our national EPI schedule i.e.at the age of 6, 10 and 14 weeks. They were vaccinated in the National Medical College EPI center and also from neighboring Upo-Zilla Health Complexes.

Out of them 50.88% were male and 49.12 % were female.

The study reveals 49.12% children have developed adequate immunity level i.e. HBS antibody level is >100 mIU /ml, and 38.60% showing poor response (10-100 mIU /ml). The rest 12.28 % are non-responsive. Satisfactory immunity level should occurs in about 85–90% of vaccinated people. In our series 87.72% children have developed acceptable level of immunity. The children with poor response confer acceptable immunity level against Hep B virus infection but may require a booster dose to ensure long term immunity.

Following the course of three vaccinations, test should be done to establish if there is an **adequate response**, which is defined as anti-hepatitis B surface antigen (anti-Hbs) antibody level above 100 mIU/ml. Antibody level between 10 and 100 mIU/ml is considered as **poor response**, and these individuals although possessing sufficient immunity level should receive single booster dose vaccination, but do not require retesting.<sup>19</sup>

People who are non-responsive (anti-Hbs antibody level below 10 mIU/ml) should be checked for recent or past Hepatitis B infection. If so, give a repeat course of three vaccinations, followed by further testing 1–4 months

after finishing second course. Those who still do not respond to a second course of vaccination may respond to intradermal administration<sup>20</sup> or to a higher dose vaccine<sup>21</sup> or to a double dose of a combined hepatitis A and B vaccine.<sup>22</sup>

Poor responses are related with obesity, celiac disease, and mostly people who are suffering from immunosuppression.<sup>23,24</sup> One study suggests that hepatitis B vaccination is less effective in patients having HIV.<sup>25</sup> Hep B vaccine is sensitive to low temperatures and can be damaged by freezing. On the other hand, it is quite heat stable and use with a vaccine vial monitor (VVM) allows greater flexibility in transportation and storage. According to the WHO multi-dose vial policy (WHO/V&B/00.09), opened multi-dose vials of hepatitis B vaccine may be reused in subsequent immunization sessions for up to four weeks in fixed health facilities if all the following conditions are met:

- 1) The expiry date has not passed.
- 2) The vial has been stored under appropriate cold chain conditions (i.e. refrigerated between 2 °C and 8 °C).
- 3) The vaccine vial septum (where the needle is put in to withdraw doses) has not been submerged in water (to prevent this from happening, well-sealed ice packs should be used in vaccine carriers and water should not be allowed to accumulate where the vials are stored).
- 4) An aseptic technique has been used to withdraw all doses.
- 5) The vaccine vial monitor (VVM), if attached, has not reached the discard point.<sup>26</sup>

Vaccine those are not well maintained properly cannot conserve its efficacy and potency. This might be the crucial factor for immunization failure.

The Indian Academy of Pediatrics (IAP) Committee on Immunization has strongly recommended that the first dose of Hepatitis B vaccine should be given as early as possible after birth and preferably within 24 hours. The second dose may be given along with DPT at 6 weeks and third dose at 14 weeks. But administering the vaccine earlier makes it easier and more ensured to achieve high immunization coverage. Hepatitis B vaccination at birth give protection to perinatal HBV infections. A variety of schedules have been advocated for hepatitis B immunization globally targeted, different age groups, may be based on local epidemiological

conditions and logistic supports. There is no current evidence to support the idea that higher titers following vaccination with a particular schedule provide longer and higher protection from the disease.<sup>27-32</sup>

Newborn or infant vaccination aims to address the babies who would otherwise be affected perinatally or in early childhood, when the chance of becoming Chronic Hepatitis is highest, 90% among infants of HBsAg and hepatitis B antigen (HBsAg)-positive mothers, infected during the first year after birth, develop chronic infection, compared to 30% of children infected in between 1st and 4th years of age and less than 5% of infected adults.<sup>33</sup>

The risk of HBV infection among infants born from HBsAg-positive mothers were found to be eight times higher when the first dose was administered 7 days after birth, compared to when it was administered within the first 72 hours after birth. Those countries where mothers usually deliver in a hospital or clinic, adequate first-dose HBV vaccine coverage can be achieved when the vaccine is given at birth, which facilitates potential of increased compliance for subsequent doses. Studies in the USA indicate that children who have received the first dose of hepatitis B vaccine during their first month of life (the birth dose) are more likely to complete the hepatitis B vaccination series as well as other immunizations.

In our series difference of immunity developed between two groups, 1 yr. - 6yrs and >6 yrs. -12 yrs. (Table-3) is obvious and p value is also close to be significant. The reason is not very clear. More elaborate studies are required to probe on these facts.

As cure is not possible with available therapy, the aim is long-term viral suppression. Emphasis should be put on health education of the general people, high-risk populations, and also health workers to increase knowledge on avoiding unsafe injection practices, high-risk sex, unnecessary blood transfusion and providing appropriate screening of blood products. These should be combined with screening and aggressive vaccination.<sup>34</sup>

### Conclusion

This study was done among admitted patients in the Paediatric department of a single hospital. Acquisition of adequate immunity level following our vaccination schedule, found optimally satisfactory. Multicenter based larger studies should be conducted to develop a consensus of opinion.

## References

1. Blumberg BS, Alter HJ, Visnich S. "A "New" Antigen In Leukemia Sera". *JAMA* 1965, 191 (7): 541–6. doi:10.1001/jama.1965.03080070025007. PMID 14239025.
2. Howard, Colin; Zuckerman, Arie J. (1979). *Hepatitis viruses of man*. Boston: Academic Press. pp. 16–18. ISBN 978-0-12-782150-4.
3. Moticka E (25 November 2015). *A Historical Perspective on Evidence-Based Immunology*. p. 336. ISBN 9780123983756.
4. World Health Organization . "Hepatitis B vaccines: WHO position paper – July 2017". *Wkly. Epidemiol. Rec.* 2017, 92 (27): 369–92. hdl:10665/255873. PMID 28685564. Lay summary (PDF).
5. Tulchinsky, Theodore H. (2018). "Maurice Hilleman: Creator of Vaccines That Changed the World". *Case Studies in Public Health*: 443–470. doi:10.1016/B978-0-12-804571-8.00003-2. ISBN 9780128045718. PMC 7150172.
6. Oransky, Ivan "Maurice R Hilleman". *The Lancet*. 2005,365 (9472): 1682. doi:10.1016/S0140-6736(05)66536-1. ISSN 0140-6736. PMID 15912596. S2CID 46630955.
7. Offit, Paul A. (2007). "Chapter 8: Blood". *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases* (PDF). HarperCollins. pp. 115–126, 136–140.
8. MastEE, AlterMJ, MargolisHS. Strategies to prevent and control hepatitis B and C virus infections: a global perspective, *Vaccine* . 1999 Mar 26;17(13-14):1730-3. doi: 10.1016/s0264-410x(98)00415-0. CrossrefPubMed
9. MastEE, MargolisHS, FioreAE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents, *MMWR Recomm Rep* . 2005 Dec 23;54(RR-16):1-31. PMID: 16371945
10. DentingerCM, McMahon BJ, ButlerJC, et al. Persistence of antibody to hepatitis B and protection from disease among Alaska natives immunized at birth, *Pediatr Infect Dis J* . 2005 Sep;24(9):786-92. doi: 10.1097/01.inf.0000176617.63457.9f. Cross ref. PubMed
11. McMahon BJ, BrudenDL, PetersenKM, et al. Antibody levels and protection after hepatitis B vaccination: results of a 15-year follow-up, *Ann Intern Med*. 2005 Mar 1; 142(5):333-41. doi: 10.7326/0003-4819-142-5-200503010-00008. Cross ref. PubMed
12. Krugman S, Davidson M (1987). "Hepatitis B vaccine: prospects for duration of immunity". *Yale J Biol Med*. 1987 Jul-Aug; 60(4): 333–339. PMC 2590237. PMID 3660859.
13. Petersen KM, Bulkow LR, McMahon BJ, Zanis C, Getty M, Peters H, Parkinson AJ (July 2004). "Duration of hepatitis B immunity in low risk children receiving hepatitis B vaccinations from birth". *Pediatr Infect Dis J* . 2004 Jul;23(7):650-5. doi: 10.1097/01.inf.0000130952.96259.f. PMID 15247604. Archived from the original on 5 June 2015.
14. Gabbuti A, Romanò L, Blanc P, Meacci F, Amendola A, Mele A, Mazzotta F, Zanetti AR, "Long-term immunogenicity of hepatitis B vaccination in a cohort of Italian healthy adolescents". *Vaccine*. 2007,25 (16): 3129–32. doi:10.1016/j.vaccine.2007.01.045. PMID 17291637.
15. Joint Committee on Vaccination and Immunisation." Chapter 18: Hepatitis B". *Immunisation Against Infectious Disease 2006 ("The Green Book")* (3rd edition (Chapter 18 revised 10 October 2007) ed.). Edinburgh: Stationery Office. p. 468. ISBN 978-0-11-322528-6. Archived from the original(PDF) on 7 January 2013.
16. Dey SK, Nahar z, Chowdhury s, Shahidullah M, Rahman SA . Immune response to Hepatitis B Vaccine in Term and Preterm Babies Received as per EPI schedule., *Bangladesh J Child Health*, 2009 ; 33(1): 1-5.
17. WHO Immunization schedule for Children (web site)
18. Karim R, Rahman MS, Uddin MS, Immune response against Hepatitis B virus after Pentavalent Vaccination in Children . *Mymensingh Med J*. 2018 Apr; 27(2):294-297. PMID: 29769493
19. Joint Committee on Vaccination and Immunisation (2006). "Chapter 18: Hepatitis B". *Immunisation Against Infectious Disease 2006 ("The Green Book")* (3rd edition (Chapter 18 revised 10 October 2007) ed.). Edinburgh: Stationery Office. p. 468. ISBN 978-0-11-322528-6. Archived from the original (PDF) on 7 January 2013.

- J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 23-27
20. Filippelli M, Lionetti E, Gennaro A, Lanzafame A, Arrigo T, Salpietro C, La Rosa M, Leonardi S (August 2014). "Hepatitis B vaccine by intradermal route in non responder patients: an update". *World J. Gastroenterol.* (Review). 20 (30): 10383–94. doi:10.3748/wjg.v20.i30.10383. PMC 4130845. PMID 25132754.
  21. Levitz RE, Cooper BW, Regan HC (February 1995). "Immunization with high-dose intradermal recombinant hepatitis B vaccine in healthcare workers who failed to respond to intramuscular vaccination". *Infection Control and Hospital Epidemiology.* 16 (2): 88–91. doi:10.1086/647062. PMID 7759824.
  22. Cardell K, Akerlind B, Sällberg M, Frydén A (August 2008). "Excellent response rate to a double dose of the combined hepatitis A and B vaccine in previous nonresponders to hepatitis B vaccine". *The Journal of Infectious Diseases.* 198 (3): 299–304. doi:10.1086/589722. PMID 18544037.
  23. Filippelli M, Lionetti E, Gennaro A, Lanzafame A, Arrigo T, Salpietro C, La Rosa M, Leonardi S. "Hepatitis B vaccine by intradermal route in non responder patients: an update". *World J. Gastroenterol.* (Review). 2014, 20 (30): 10383–94. doi:10.3748/wjg.v20.i30.10383. PMC 4130845. PMID 25132754.
  24. Roome AJ, Walsh SJ, Cartter ML, Hadler JL. "Hepatitis B vaccine responsiveness in Connecticut public safety personnel". *JAMA.* 1993, 270 (24): 2931–4. doi:10.1001/jama.270.24.2931. PMID 8254852.
  25. Pasricha N, Datta U, Chawla Y, Singh S, Arora SK, Sud A, Minz RW, Saikia B, Singh H, James I, Sehgal S (March 2006). "Immune responses in patients with HIV infection after vaccination with recombinant Hepatitis B virus vaccine". *BMC Infectious Diseases.* 6: 65. doi:10.1186/1471-2334-6-65. PMC 1525180.
  26. Hepatitis B, WHO/V&B/01.31, 2001, Page 22.
  27. Gupta ML, Sharma U, Saxena S, Sharma ML, Pokharna DS. Vertical transmission of Hepatitis B surface antigen from asymptomatic carrier mothers. *Indian Pediatr* 1985; 22: 339-342.
  28. Nayak NC, Panda SK, Zuckerman AJ, Bhan MK, Guha AK. Dynamics and impact of perinatal transmission of hepatitis B. *J Med Virol* 1987; 21:137-145.
  29. Kulkarni ML, Reddy PV. Prevalence of HBsAg in asymptomatic carrier mothers and vertical transmission. *Am J Dis Child* 1988; 142: 124-125.
  30. World Health Organization. Global Program for vaccines and immunization. Expanded program on immunization: Immunization policy, WHO GPV/GEN/95.03Rev.1, 1995.
  31. Kumar TS, Abraham P, Raghuraman S, Cherian T. Immunogenicity of indigenous recombinant hepatitis B vaccine in infants following 0, 1, 2-month vaccination schedule. *Indian Pediatr* 2000; 37: 75-80.
  32. Gomber S, Sharma R, Ramchandran VG, Talwar V, Sinha B. Immunogenicity of Hepatitis B vaccine incorporated into Expanded Program of Immunization Schedule. *Indian Pediatr* 2000; 37: 411-413.
  33. WJ Edmunds, GF Medley, DJ Nokes, AJ Hall, HC Whittle. The influence of age on the development of the hepatitis B carrier state, *Proc Biol Sci*, 253 (1993), pp. 197-201 View Record in Scopus Google Scholar
  34. World Health Organization, Practices to improve coverage of the hepatitis B birth dose vaccine, WHO (2013).  
HYPERLINK "[http://apps.who.int/iris/bitstream/10665/78616/1/WHO\\_IVB\\_12.11\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/78616/1/WHO_IVB_12.11_eng.pdf)" \t "\_blank" Available

Original Article

## Burden of the Care Giver Serving the Mentally ill Patients

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### Abstract:

**Introduction:** Care giver burden are actually an expression of addressing the adverse consequences of the care provided to the mentally ill patients. Review of the previous studies reveals a higher rate of burden among the care giver as compared to the general population.

**Objective:** To find out the burden of care giver of mentally ill patient attended NIMH of Dhaka and to the association of duration of mental disorder on the burden of care giver of mentally ill patient attended NIMH of Dhaka.

**Methods and materials:** This cross sectional descriptive type study was conducted at the National Institute of mental health (NIMH), Sher-e-Bangla Nagar Hospital of Dhaka in Bangladesh. The period of study was from July 2015 to June 2016. A total 300 respondent were included care givers of mentally ill patients. After pre tested written questionnaires and face to face interview and care giver burden measure by using ZBI (Zarit burden interview scale) for subjective burden and Montgomery Borgatta care giver burden scale for objective burden.

**Result:** Majority 185(61.67%) of caregiver duration of care 0-10 years followed by 76(25.33%) of them 11-20 years and 39(13%) of them 21-30 years. More than three fourth (77.3%) of caregiver were moderate and 22.7% were mild objective burden. Almost two third (66%) of care giver were moderate subjective burden and rest(34%) were mild subjective burden (p<0.05).

**Conclusion:** Study shows caregivers burden depends on the disease duration as well as some socio demographic factors. To provide a total care to the patients with mental disorders it is necessary to mitigate the caregiver's burden. For this reason clinicians need to review periodically the status of caregiver's burden. Further exploration is needed in future to assess the caregiver burden in community based, multi centered approach in long term follow up with a large sample size.

### Introduction

Bangladesh is a developing country located in South Asia, is home to approximately 160 million people living in an area of 147,570 sq. km. It estimates that 10% of the population i.e. 16 million peoples are living with a disability that need assistance from a caregiver or family member and mentally illness patient is one of the common cause of this disability.

Mental illness not only affect the survivor; it also affects their family or caregiver as the survivors and caregivers suffer from depression.<sup>1</sup> Survivors require help from family members or from the close friends who become a valuable resource for the patient.<sup>2</sup>

The World Health Organization has predicted that by 2030, more people will be affected by depression than any other health problem. Recently published findings

from a study on mental illness among healthy adults age 40 years and older in rural Bangladesh reveal that elderly individuals and women of poor socio-economic status are at highest risk of mental illness.<sup>3</sup>

As mental illness causes serious and long term disability, impacting their ability to perform activities of daily living independently thus they are dependent on their family members which are known as caregivers. Family members already have a lot of responsibilities in the family, but when a family member acts as a caregiver role, they have to take on additional responsibilities of the mental illness besides other responsibilities of family. So, these additional responsibilities seem unbearable or a burden for them. On the part of the family caregivers, the adjustment to the new challenges poses the necessity of learning to cope with various potentially stressful problems in everyday life.<sup>4</sup>

**Methodology**

A descriptive cross sectional study conducted at National Institute of mental health (NIMH) situated at Sher-e-Bangla Nagar, of Dhaka from July 2015 to June 2016. The population of this study were the caregivers of mentally ill in door and outdoor patients attended of National Institute of mental health (NIMH) Sher-e-Bangla Nagar, Dhaka in Bangladesh. Convenient sampling technique were used to select the subject during the period. Inclusion criteria: Family member living and caring with mental illness patient. The caregivers who did not suffer from mental illness. Exclusion criteria: Participants who were not taking part in patient care, Participants who were younger than 15 years old, because usually who are younger than 15 not able to take care of others and themselves are in need for care giver. Data collection technique: Data were collection face to face interview by questionnaires method respondents were found care giver mental illness patient of National Institute of mental health (NIMH) Sher-e-Bangla Nagar Dhaka Bangladesh. After pre tested written questionnaires and face to face interview and care giver burden measure by using ZBI (Zarit burden interview scale) for subjective burden and Montgomery Borgatta care giver burden scale for objective burden and scoring the mild moderate and severe. The questionnaire contained. First section was for collecting information socio demographic variables e.g. age, level of education, occupation, monthly income, family characteristics etc. Second section was for collecting information to know the level of burden by measuring scale. Data processing-

After collections of each day the data were checked and to main followed by editing & cleaning to detect error or omission to maintain consistency and validity then the data were entered into the computer for analysis with SPSS software version 20. Data analysis-Data were analyzed by computer using SPSS 20 version software according to appropriate variables. Then various tables were made and analyzed according to the objectives, frequency distribution, mean value with standard deviation was calculated, presented in the table where necessary, Significant test were done by chi-square tests.

**Result**

**Table-I: Distribution of the respondents by their feeling excess stress and responsibility**

Feeling excess stress	Number of frequency	Percentage
Never	45	15.0
Rarely	155	51.7
Some time	41	13.7
Frequently	42	14.0
Nearly always	17	5.7
<b>Total</b>	<b>300</b>	<b>100</b>

**Table-I:** Shows 51.7% were rarely, 15% never, 13.7% some time, 14% frequently and 5.7% nearly always feeling excess stress and responsibility.

**Table-II: Distribution of the respondents by feeling angry to take care of their patient.**

Feeling angry to take care of their patient	Number of frequency	Percentage
Never	72	24.0
Rarely	7	2.3
Some time	164	54.7
Frequently	51	17.0
Nearly always	6	2.0
<b>Total</b>	<b>300</b>	<b>100</b>

**Table-II:** Shows 24% were never, 2.3% rarely, 54.7% some time, 17% frequently and 2% nearly always feeling angry to take care of their patient.

**Table-III: Distribution of the respondents by feeling excessive help requests for their patients.**

Feeling excessive help requests for their patients	Number of frequency	Percentage
Never	58	19.3
Rarely	56	35.0
Some time	107	35.7
Frequently	66	22.0
Nearly always	13	4.3
<b>Total</b>	<b>300</b>	<b>100</b>

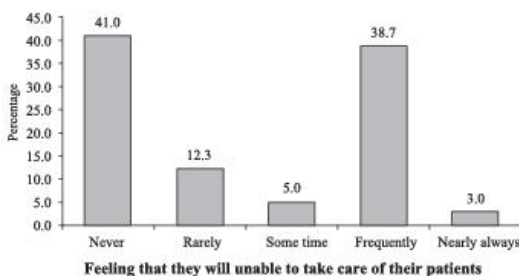
**Table-III:** Shows that 19.3% were never, 35% rarely, 35.7% some time, 22% frequently and 4.3% nearly always feeling excessive help requests for their patients

**Table-IV: Distribution of the respondents by thinking that they did not enough money to care of their patient.**

Thinking that they did not enough money to care of their patient	Number of frequency	Percentage
Never	49	16.3
Rarely	137	45.7
Some time	20	6.7
Frequently	74	24.7
Nearly always	20	6.7
<b>Total</b>	<b>300</b>	<b>100</b>

**Table-IV:** Shows that 16.3% were never, 45.7% rarely, 6.7% some time, 24.7% frequently and 6.7% nearly always thinking that they did not enough money to care of their patient.

**Figure-I: Distribution of the respondents by feeling that they will unable to take care of their patients.**



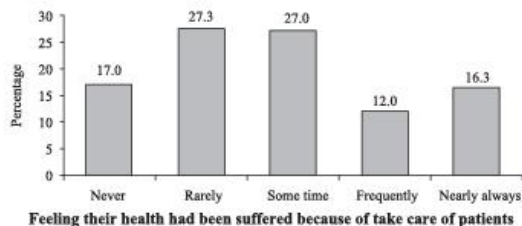
**Figure-I:** Shows 41% were never, 12.3% rarely, 5% some time, 38.7% frequently and 3% nearly always feeling that they will unable to take care of their patients.

**Table-V: Distribution of the respondents by their feeling that they had just to leave to take care of patient.**

Feeling that they had just to leave to take care of their patient	Number of frequency	Percentage
Never	98	32.7
Rarely	116	38.7
Some time	18	6.0
Frequently	47	15.7
Nearly always	21	7.0
<b>Total</b>	<b>300</b>	<b>100</b>

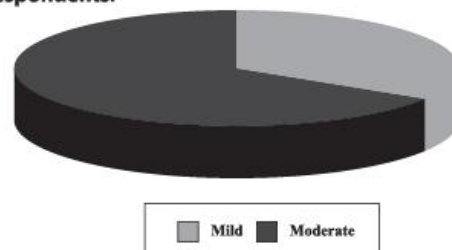
**Table-V:** Observed that 32.7% were never, 38.7% rarely, 6% some time, 15.7% frequently and 7% nearly always feeling that they had just to leave to take care of their patient.

**Figure-II: Distribution of the respondents by feeling their health had been suffered because of take care of patients.**



**Figure-II:** Shows 17% were never, 27.3% rarely, 27% some time, 12% frequently and 16.3% nearly always feeling their health had been suffered because of take care of patients.

**Figure-III: Shows subjective burden of the study respondents.**



**Figure-III:** Shows 34% had mild burden and 66% had moderate burden.

**Table-VI: Distribution of the respondents by objective burden.**

Objective burden	Number of frequency	Percentage
Mild	232	77.3
Moderate	68	22.7
<b>Total</b>	<b>300</b>	<b>100.0</b>

**Table-VI:** Shows objective burden of the respondents, it was observed that 77.3% had mild burden and 22.7% had moderate burden.

**Discussion**

In current study found that female family caregivers perceived less social support and experienced higher degrees of caregiver burden compared to male family caregivers.<sup>5</sup> According to burden types mean values; standard deviation and the response degree of the study sample responses were calculated. The results show the distribution of burden types; it illustrates that subjective burden, while (34%) had mild burden, (66%) had moderate. Regarding objective burden, (77.3)

had mild burden, while (22.7%) had moderate, (15%) had moderate burden. Nevertheless the development of community mental health services in Palestine is still in progress and needs further support and long term commitment to ensure the provision of comprehensive services and support to sufferers and their families.<sup>6</sup> Similar findings were found in Israel that the burden of Israeli family members of mentally ill individuals was moderate.<sup>7,8</sup> In another study found that burden and emotional well-being among Cypriot families' caregivers of schizophrenic patients illustrated a high level of burden among family caregivers where (43%) of the participants scored above 24/42 in the family burden Scale.<sup>9,10</sup> At present study there were significant differences between males and females in regard to subjective burden and these differences were for females (P value 0.0003). There were also significant differences between males and females in regard to objective burden and these differences were for females (P value 0.001). These results were in agreement with who found that there was a significant difference in gender in term of their burden, which was explained by social gender role and hormonal factors.<sup>11</sup>

Women were predominant in care giving and spent more time in care giving than men. In terms of hormonal, oxytocin hormone contributed in distress and women's need to nurture. When caring for patient women experienced distress, her oxytocin level and nurture need will increase, but at the same time she had to pay more attention to the patient. Therefore women felt more burden than men.<sup>12</sup>

### Conclusion

This study extends knowledge about the level of burden experienced by the caregivers of mental illness patient in terms of general strain, isolation, disappointment, emotional involvement and environment. The study findings revealed that most of the caregivers faced moderate burden where they were highly disappointed rather than isolated or emotionally upset. The environment did not create any burden for them, possibly due to the Bangladeshi culture where country people are more hospitable. Caregivers think that caring for their near ones is their responsibility and they take this responsibility enthusiastically rather than

feel burden. Through this study it was also found that the degree of burden depends on several aspects, such as caregiver's social and demographic characteristics: age, sex, relationship, care giving duration of mental illness. The study also discovered that there is a possibility to have higher. This study suggests the health professional to focus on the care giving situation to provide a better support to them.

### References:

1. Han, B & Haley, w. (Family caregiving for patient with stroke. Review and analysis, stroke,30, 1999,;1478-1485
2. Anderson,CS,Linto, j &Stewart-wynne,EG A population based assessment of the impact and burden of care giving for long –term stroke survivors: Stroke1995; vol26,pp.843-849.
3. Das,S,Hazra,A ray, BK, Ghosal.M,Banerjee,Tk, ROY, T, chaudhuri, A, Raut, DK&Das, Sk, Burden Among stroke caregivers: results of a community- based study from Kolkata,india strike, 2010;vol, 41,pp-2965-2968.
4. Gangulykk, CHaddark.SinghTB Caregiver Burden and Coping in Schizophrenia and Bipolar disorder. The American journal of psychiatry. 2010;161(5),850-856.
5. Ampalam P, Gunturu S, Padma V. A comparative study of caregiver burden in psychiatric illness and chronic medical illness. Indian J Psychiatry. 1012; 54(3), pp. 239–243.
6. Abu SwayR,Mental Health Service Deveilopment in Palestine. This week inpalestine issue No.150,2010:
7. Rudnick,A Burden of caregivers of Mentally ill individuals in Israel:A family Participatory study. International Journal of psychosocial Rehabilillititation,2004; 9(1),147-152
8. Ukpong,D, Burden and psychological distress among Nigerian family caregivers of schizophrenic patients the roie of positive and negative symptom, Turkish journal of psychiatry.23(1).40.
9. Papastavrou,E, charalambous,Tsangari, H&.,Karayiannis,G The cost ofcaring the relative with



- Schizophrenia. Scandinavian journal of caring science. ..2010 ;24(5)817-23.
10. Prafulla,S.Murthy,s&Rama presad.D. Family Burden and Rehabilitation need of beneficiaries as of a rural mental health Camp in a southern state of India. International journal of Psychosocial Rehabilitation 2010; 15(2).5-11.
  11. Schneider,M,Steele,R, Cadell, S.& Hemsworth, D, Differences in psychosocial outcomes between male and female caregivers of children with life limiting illness. Journal of pediatric Nursing.2010;30, 1-14.
  12. Akpınar,b.Kucukguelu,o&yener,G9.Effect of gender on burden among caregivers of Alzheimer's patients. Journal of nursing scholarship,2011,43(3),248-254.

**Case Report**

## **Patient with Spastic Ataxic Quadripareisis-Case of Arnold Chiari Type-1 Malformation**

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**Abstract:**

A 22 years old patient presented with complaints of weakness in all four limbs and ataxia for 2 months. He had also history of slurring of speech and inclining to right side during walking. His gait was wide based and spastic ataxic. Patient was spastic quadriparetic with subtle right sided cerebellar sign and dissociated sensory loss in both upper limb and right Hemithorax. MRI of the brain and cervical spine revealed tonsillar herniation > 12 mm in cervical canal with large syrinx from cervical cord to thoracic region. Finally, the case was diagnosed as a Chiari Type-1 Malformation. Early diagnosis and intervention by Neurosurgeon actually halted the further syrinx extension and reduce neurological deficit with improvement of daily life activities.

**Introduction**

Chiari-1 Malformation as defined by tonsillar ectopia located below the foramina magnum, is being increasingly identified as a result of advance of MR imaging.<sup>1</sup> The malformation appears to be complex in its presentation, cause and natural history.<sup>2</sup>



**Figure-1:** Showed tonsillar herniation and large syringohydromyelia.

This and associated anomalies were first described by Chiari (1981, 1896).<sup>3</sup> Arnold name is often attached to the syndrome but recently this malformation divided into Type-1 to IV- i.e. Chiari malformation, Types-I-IV, refer to spectrum of congenital hind brain abnormalities affecting the structural relationship between the cerebellum, brainstem, upper cervical cord

and the bony canal base.<sup>4,5</sup> Numerous factors contribute to the development of such malformation. Currently there are over 20 different practiced operation directed at improving the aberrant CSF dynamics thought to be a major concept of malformation<sup>2,6,7</sup> but the pathogenesis is best explained by a molecular genetic analysis, Ectopic expression of a segmentation of gene in the rhombomeres explain not only the Chiari malformation but also the brainstem anomalies and defective basioccipital and supra occipital bone formation that result in a too small posterior fossa.<sup>8</sup>

Mostly Chiari Type-I shows the caudal displacement of Cerebellar tonsils below plane of foramina magnum (+ syringomyelia 20-75%).<sup>9</sup> Prompt clinical suspicion and early MR evaluation and neurosurgical intervention improve CSF dynamic and modify the disease process and disability.

**Case report**

Twenty-two years aged, normotensive non-diabetic, right handed person presented on 10th May-2015 with history of weakness in all four limbs (right sided weakness more than the left), difficulty in walking, imbalance and neck pain for two months. He also complained of intermittent stiffening of both lower limbs during walking and apnoea during sleep with occasional neck deviation (torticollis). He had also history of recurrent fall and inclining to right side during walking. His speech was slurred and tremor in both upper limbs. He did not give any history of fever, vomiting, head or spine injury or any alternation of

consciousness or convulsion. He did not give any history of the bladder and bowel involvement and no family history of such neurological problem. Personal history revealed no history of addiction or history of exposure. On examination, he looked ill and assume abnormal posture. Pulse was 88/min, BP-100/65 mmHg, Temperature was normal, and others general parameters were normal. Various skeleton abnormalities such as high arch palate, short neck and scoliosis were also seen. On systemic examination, all the systems seem to be normal except nervous system which revealed: -Patient was conscious and oriented, slurred-speech syllable by syllable, gait was spastic ataxic with wide stance and swaying, that increased by eye closure. All the cranial nerves were intact. Muscle power was reduced in all four limbs, grade 4 in Upper limb and grade-III in lower limbs. All DTR were increased in all 4 limbs, coordination was defective in both lower limbs and right upper limb. Romberg test was positive, and vibration was impaired in both lower limbs. Planter extensor in right side and Hoff-man sign positive in right upper limb. Bilateral horizontal nystagmus was seen in both eye and occasional downbeat nystagmus. Sensory examination revealed loss of pain and touch sensation in both upper limb and right half of the trunk. Fundoscopy revealed no abnormalities. Relevant investigations showed, T-11180, N-63%, HB-13.1 gm/dl, PBF-Non-specific morphology, RBS-9.2 mm/L, S. creatinine-0.90 mg/DL, S. electrolytes-No abnormalities, VDRL-Non-reactive, Vit-B<sub>12</sub> assay-524 pg/ng, X-Ray-Skull and Cervical spine, Chest PA view revealed no abnormalities, ECG was normal. MRI of the brain revealed post contrast, T1W1 showed elongated pointed, low lying cerebellar tonsil which displaced inferiorly through the foramina magnum into upper cervical spinal canal. Tonsillar herniation in the spinal canal is more than 12 mm below the foramina magnum and MRI of cervical spine showed that enlargement of cervical cord with a hypointense central fluid filling cavity (syringohydromyelia) extending from the level of C<sub>2</sub> down to thoracic region. Above MRI features were suggestive of Chiari Malformation. We immediately started symptomatic treatment by pain killer, baclofen, gabapentin and referred the patient to Neurosurgeon for PF decompression and syringotomy with duroplasty. Operations were done and patient improved his gait and further follow-up revealed no progression of disease.

#### Discussion

Although Chiari malformation is still listed as a rare disease by the office of rare disease of the National

Institute of Health, this categorization is based on outdated data from before the MRI era. With routine use of MRI, Chiari Malformation is discovered with increasing frequency. For Chiari-I, Prevalence rate of 0.1--5% with a slight female predominance are suggested by recent study.<sup>10</sup> Based on analysis of familial aggregation, a genetic basis of chain has been suggested.<sup>11</sup> Recent study suggested linkage to chromosome 9 and 15.<sup>12</sup> In type 1 Chiari malformation (without meningocele or another sign of dysraphism), neurologic symptom may not develop until adolescent and adult life.<sup>3</sup> Our case presented after the age of 22 years. The symptoms are increased intracranial pressure mainly headache, Progressive Cerebellar ataxia, Progressive spastic quadriparesis, downbeating nystagmus, Syringomyelia.<sup>3</sup> In figure-1 this case showed the tonsillar herniation and large syrinx extending from cervical to thoracic region.

In another study<sup>13</sup> analyzed for 17 case of Chiari malformation, younger than 20 years of age. The initial symptoms were skeleton abnormalities (71%), Such as scoliosis (11 patient), Pes cavas (1 Patient), Pain or Numbness (24%), and motor weakness (6%). Frequently seen signs on admission were sensory difficulty (100%), Scoliosis (85%), muscle weakness (6.4%) Muscle atrophy (35%) and Lower cranial nerve (35%) The characteristic neurological findings were unilateral sensory with motor weakness (65%) with decreased or absent DTR on the same side.

Our case presented mainly difficulty in walking and gait abnormalities as spastic quadriparesis and cerebellar sign on both upper limbs. Dissociated sensory loss in both upper limb and right hemithorax. Some cases of syringomyelia are associated with trauma and tumour. Our case did not show any evidence of trauma or tumour. This patient also showed the sleep apnoea and neck deformity that may occur if lower brain stem is involved, which leads to difficulty in feeding and respiratory distress.<sup>9</sup> The most common differential diagnosis is Multiple Sclerosis, Lower brainstem stroke, foramina magnum tumour, SCD, basillar impression and related conditions were excluded by relevant clinical examinations and investigations. MRI of the spine and brain is the most useful and most widely used imaging study for diagnosis of Chiari malformation- in addition to detecting the anatomy of cervicocranial junction, it provides useful information about associated abnormalities such as syringomyelia and hydrocephalus.<sup>14</sup> Contrast enhanced MRI should be obtained to search for abnormal enhancement from an associated spinal Cord tumour.<sup>15</sup> Our case typically

showed the feature of Chiari Type-I and syringomyelia without spinal cord tumour. Preoperatively those with little or no neurological deficit, symptomatic primarily with pain, can expect an excellent outcome. A systemic review of decompressive surgery in adult for Chiari I malformation with syringomyelia revealed that syrinx may persist after surgery at an average rate of 6.7% (range 0-22%).<sup>16</sup>

#### Conclusion

It is generally accepted that if the causative pathology is identified and treated, the long-term improvement and resolution of syrinx is good. Prognosis is also largely depended on the prognosis of the primary pathologic that result in the syrinx. So, it is concluded that early clinical suspicion and diagnosis with neurosurgical intervention overall improve the disease course and reduced disability.

#### References

1. Barkovich AJ, Lippold, FJ, Sharmann JL, et.al. Significance of Cerebellar Tonsillar Position on MR AJNR 1976; 7:795-799.
2. Milhorat TH, Chum W, Trinnidad EM, et. al. Chiari I malformation define clinical, radiographic, and genetic feature in 364 symptomatic patients Neuro Surgery 1999; 44:1005-1017.
3. Adam RD, Victor M, Rooper AH. Developmental disease of nervous system. In; Principle of Neurology 7th edn, MC grawwhill Book Company, New York 2001; 1064-65.
4. Greenberg MS. Chiari malformation Hand book of Neuro Surgery, New york; Theme; 2006; 6:103-109.
5. Abd-El Barr MM, Strong CI, Groff MW. Chiari malformation: Diagnosis, Treatment and Failures J neuro surg Sci 2014 Dec 58 (4); 215-21.
6. Heiss JD, Patronas N, Devroom HL, et al. Elucidation the Pathophysiology of Syringomyelia J Neuro Surg 1999; 91: 553-562.
7. Dyste GN, Meneres AH, Vangilder JC. Symptomatic Chiari malformation, An analysis of Presentation, management and long-term outcome J Neuro Surg 1989; 71:159-168.
8. Bradley WG. Developmental disorder of the Nervous system. In: Bradley WG, Fenicle GM, JANKOVIC J (eds) Neurology in clinical practice, 4th ed. Butter-worth-Heinmenn, A imprint of Elsevier, Philadelphia. 2004, 399, 591.
9. Huges E, Cros JH. Disorder of Central Nervous System development. In: Fowler TJ, Scadding JW (eds), J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 33-35 Clinical Neurology 3rd ed, Arnold 2003, 431-32.
10. Speer MG, Enterline DS, Mehlreter L, Manmock P, Joseph J, Dickson M et.al. Chiari Type I malformation with or without syringomyelia prevalence and genetics. J Genet Focus. 2003, 12: 297-311.
11. Speer MC, George Tm, Enter line DS, Frankling A, Wolperrt CM, Milhorat TH, A genetic hypothesis for Chiari I malformation with or without syringomyelia. Neuro Surg Focus. 2000 March 15, 8(3): E 12.
12. Boyless AI, Enter line DS, Hammock PH, Sigel DG, Slifer SH, Mehlterter L et.al. Phenotypic definition for Chiari type I malformation Coupled with high density SNP genome screen shows significant evidence for linkage to region chromosome 9 and 15. Am J. Med Genet A. 2006 Dec 15; 140(24): 2776-85.
13. Toyohiko I, Youshiuohu I, Minoru A, Hiroshi A. Hydrosyringomyelia associated with a Chiari I malformation in Children and Adolescents. Neuro Surg 1990; 26(4): 591-97.
14. MC vige JW, Leonmdo J. Neuro Imaging and Clinical manifestation of Chiari type I (CMI), Curr Pain Headache Rep. 2015 June, 19(6): 18.
15. Hoser SL. Diseases of the spinal cord. In: Brawdnowald E, Faucias Kasper DL, Hauser SL, Longo DL, Jameson JL (eds), Harison Principle of Internal Medicine. 15th Ed. MC Graw-Hill Book Company, New York, 2001; 2432.
16. Schuster JM, Zhang F, Norvell DC, Hermsyeeyn JT. Persistent recurrent syringomyelia after Chiari decompression-Natural History-management Strategy: A Systemic review. Evid based spine care J. 2013 (Oct) 4(2): 116-125.

Review Article

## Ectopic Pregnancy

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### Abstract:

Ectopic pregnancy remains a major gynecological emergency. Currently it remains a major problem in contemporary gynecological practice and continues to be an important cause of morbidity and mortality in women. Prevalence of ectopic pregnancy is 1-3% worldwide. The true current incidence of ectopic pregnancy is difficult to estimate because many patients are treated in an outpatient setting where events are not tracked and national surveillance data on ectopic pregnancy have not been update. Nearly all ectopic pregnancies are implanted within the fallopian. Ectopic implantation can also occur outside of the fallopian tube, within the cervix, ovary, abdomen, uterine cornua, and cesarean scars. The classic triad of symptoms, amenorrhea, abdominal pain, and abnormal bleeding varies greatly among individuals. Serial evaluation with transvaginal ultrasonography, or serum beta human chorionic gonadotrophin (hCG) level measurement or both often is required to confirm the diagnosis. The most common complication is rupture with internal bleeding which may lead to hypovolemic shock leads to death. So, a timely, early diagnosis can help patients obtain better pregnancy out-comes. The decision for surgical management or medical management of ectopic pregnancy should be guided by the initial clinical, laboratory and radiologic data as well as patient informed choice based on a discussion of the benefits and risks of each approach.

**Key words:** Ectopic pregnancy.

### Introduction

Ectopic pregnancy is a complication of pregnancy in which the embryo attaches outside the uterus.<sup>1</sup> Ectopic pregnancy is defined as any intra or extra uterine pregnancy in which the fertilized ovum implants at an aberrant site which is inconducive to its growth and development.<sup>2</sup> Ectopic pregnancy is a common diagnosis and implantation location varies. Although 97% of ectopics are implanted within the fallopian tube, associated with commonly recognized risk factors, ectopic implantation can occur in other pelvic and abdominal locations that may not have such predisposing risk factors. When ectopic pregnancy is diagnosed early, before rupture, regardless of location, conservative, fertility-sparing treatment options can be successful in terminating the pregnancy. Predisposing risk factors and treatment options can vary and can be ectopic-location specific.<sup>3,4</sup> The classic triad of symptoms, amenorrhea, abdominal pain, and abnormal bleeding varies greatly among individuals and ectopic pregnancies

frequently are confused with other conditions such as ovarian cyst, pelvic inflammatory disease and spontaneous abortion.<sup>5</sup> It is the major cause of

maternal mortality during the first trimester of pregnancy which accounts for 10-15% of all maternal deaths.<sup>6</sup>

### Incidence

Prevalence of ectopic pregnancy is 1-3% worldwide.<sup>7</sup> The incidence in the United States has increased greatly in the last few decades from 4.5 per 1000 pregnancies in 1970 to an estimated 10.7 per 1000 pregnancies in 1992.<sup>8-10</sup> In multicentric case control study in india, the incidence of ectopic pregnancy rate was 3.12 per 1000 pregnancies or 3.86 per 1000 live births.<sup>11</sup> reported an incidence of 2.46 per 1000 deliveries. It is also reported incidence of 16 per 1000 deliveries, found an incidence of 1:399 pregnancies in Mysore, India.<sup>12</sup> In developing countries, a majority of hospital based studies have reported ectopic pregnancy case fatality rate of around 1-3%, 10 times higher than those reported in developed countries.<sup>13</sup> In Bangladesh it was found Incidence of ectopic pregnancy in Bangladesh was 7.4/1000 deliveries.<sup>14</sup> However, the true current incidence of ectopic pregnancy is difficult to estimate because many patients are treated in an outpatient setting where events are not tracked and national surveillance data on ectopic pregnancy have not been update.

### Site of Ectopic Pregnancy

Nearly all ectopic pregnancies (97%) are implanted within the fallopian tube, and a common factor for the development of such ectopics is the presence of a pathologic fallopian tube. Causes of such pathology include genital tract infection caused by gonorrhea and chlamydia, tubal surgery including tubal sterilization, previous ectopic pregnancy, and in utero exposure to diethylstilbestrol.<sup>15,16</sup> Tubal ectopic pregnancy within the tubal ampulla, 70% of all ectopics, and fimbriae, 11% of all ectopics.<sup>17</sup> Ectopic implantation can also occur outside of the fallopian tube, within the cervix, ovary, abdomen, uterine cornua, and cesarean scars. These extra tubal implantations may not be associated with tubal pathology or the expected preexisting risk factors for tubal ectopic implantation. Regardless of location, however, when diagnosed early, before symptoms of rupture, many ectopic pregnancies can be successfully treated conservatively. Up to 12% of ectopics are implanted within the isthmic, or proximal portion of the fallopian tube.<sup>18</sup>

It was found more than 96 percent of ectopic pregnancy occur in the fallopian tubes. Only 4% cases were non tubal pregnancy and most of the patients presented with ruptured tubal pregnancy. Only in 19% of cases tubes were found unruptured and 14% of cases were diagnosed as to be tubal abortion. It was also observed that the commonest site of location of the ectopic pregnancy was in the ampulla of the fallopian tube which is in comparison with others.<sup>19</sup> The sites of ectopic pregnancy were ampullary 52%, isthmic 32%, interstitial 12%, rudimentary horn of a bicornute uterus 2%.<sup>20</sup>

### Risk factors

Ectopic pregnancy can occur at any time during the child bearing age of the woman. It was also found majority of cases were in 21-30 years age groups. The range varies between 16-38 years. Similar findings were found in India, Nigeria and Pakistan.<sup>20-23</sup> In different studies found that 45% of their patients were between 25-35 years.<sup>24-26</sup>

Ectopic pregnancy is closely related with low parity. Although about 11% of the patients were Nulli parous. The peak incidence was among the patients with para-1-2. The incidence is low among those who are para>4. Similar studies found 82.9% were multiparas and 17-20% were Primiparas. However, there was conflicting result from studies by others. It was also

showed there is increased risk of ectopic pregnancy in primigravida. Risk of ectopic pregnancy amongst single women and students than married women.<sup>27-30</sup>

Past history of menstrual regulation, infertility & past history of ectopic pregnancy constitutes the main bulk of the risk factors. Pelvic infection, history of abortion & history of IUCD cases had middle risk factor. IUCD prevents intrauterine pregnancy but not tubal or ovarian pregnancy. History of any operation also had some risks and abortion was the commonest risk factor.<sup>31,32</sup> Post abortal infection leads to tubal damage and thus increases the chances of ectopic pregnancies. Other risk factors included infertility, tubal surgery, previous D&C, previous ectopic pregnancy, appendectomy, previous ectopic and use of OCPs.<sup>33</sup>

### Clinical Presentation

The commonest presenting complaints of a ectopic were abdominal pain, amenorrhea and abnormal vaginal bleeding.<sup>34</sup> Clinical signs included abdominal tenderness, cervical excitation and adnexal tenderness.<sup>35</sup> The commonest presenting symptoms were abdominal pain which was presents in 100% cases, 76% with period of amenorrhoea and 50% with per-vaginal bleeding.<sup>36</sup> In 95% cases presented with abdominal pain, 65% with period of amenorrhoea and 07 % cases with irregular per-vaginal bleeding. In 90% of cases had history of amenorrhea, 87.5% reported pain abdomen, bleeding per vagina encountered in 67.5%.<sup>37</sup> The most frequent clinical presentation was amenorrhea, abdominal pain followed by vaginal bleeding and also shock (22%). It was found that 90% cases had history of abdominal pain, 72% had H/O amenorrhoea, 54% had vaginal bleeding, 34% had syncopal attack. The most common physical sign was abdominal tenderness present in 66% cases and cervical excitation test in 46% cases.<sup>38</sup>

### Diagnostic Evaluation

After taking a very careful history with particular screening of the menstrual, obstetric and contraceptive history, a thorough physical examination was performed and ectopic pregnancy was diagnosed clinically in a large number of cases. Currently, Doppler ultrasonography is not considered to significantly contribute to the diagnosis of ectopic pregnancy.<sup>33</sup> The minimum diagnostic evaluation of a suspected ectopic pregnancy is a transvaginal ultrasound evaluation and confirmation of pregnancy. Serial evaluation

with transvaginal ultrasonography, or serum beta human chorionic gonadotrophin (hCG) level measurement or both often is required to confirm the diagnosis.

#### **Fatal Complications**

The most common complication is rupture with internal bleeding which may lead to hypovolemic shock. Death from rupture is the leading cause of death in the first trimester of the pregnancy.<sup>34</sup> The incidence of pelvic inflammatory disease has increased among the young women. Infection following induced abortion is the major cause of Pelvic inflammatory disease and the risk of ectopic pregnancy 10 times higher in areas with a high incidence of illegal abortion.<sup>35</sup> Kumer et al<sup>36</sup> found risks for ectopic pregnancy are higher in women with damage to fallopian tubes because of pelvic infections, pelvic surgery or previous ectopic pregnancy and smokers. Fatalities due to ectopic pregnancies generally are associated with patient delay, failure to make an accurate diagnosis or delay or ineffective treatment.<sup>10</sup>

#### **Treatment Protocol**

Medical management with methotrexate can be considered for women with a confirmed or high clinical suspicion of ectopic pregnancy who are hemodynamically stable, who have an unruptured mass, and who do not have absolute contraindications to methotrexate administration<sup>37</sup> These patients generally also are candidates for surgical management. The decision for surgical management or medical management of ectopic pregnancy should be guided by the initial clinical, laboratory and radiologic data as well as patient informed choice based on a discussion of the benefits and risks of each approach. Khatun et al<sup>20</sup> showed in her study, the laparotomy was done all patients. The ectopic tubal pregnancy was ruptured or grossly damaged in most of the cases. Among them salpingectomy with or without contralateral tubectomy was (88%) done. Only in 5 cases salpingo-oophorectomy was performed. One case was done excision of the cornu of the uterus. Jesmin et al<sup>38</sup> found 93%, Kulsum et al<sup>22</sup> 91%, Perveen et al<sup>28</sup> 86%

J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 36-40 patients undergone salpingectomy. The most common surgeries performed by Yeasmin et al<sup>16</sup> were partial/total salpingectomy, salpingo-oophorectomy and salpingostomy. Conservative surgery is superior to radical surgery at preserving fertility. Islam et al<sup>21</sup> done unilateral salpingectomy (58%), salpingectomy with contralateral tubectomy in 18% cases, salpingo-oophorectomy in 8% cases, resection of bicornuate uterus and total abdominal hysterectomy was done in 4% cases.

#### **Conclusion**

Abdominal pain and amenorrhea are the most consistent features of ectopic pregnancy. Rupture ectopic pregnancy is the most serious gynaecological emergency due to internal haemorrhage, shock and sepsis which leads to maternal morbidity and mortality. Emphasizes the early diagnosis by clinical suspicion, better investigation which also modify the mode of treatment. Prompt conservative surgical or medical management which will not only help in reducing maternal mortality and morbidity rates but which also helps to preservation the tube and future fertility.

#### **References**

1. Crochet JR, Bastian LA, Chireau MV. "Does this woman have an ectopic pregnancy?: the rational clinical examination systematic review". JAMA. 2013; 309 (16): 1722-9.
2. Howard W, John A, Rock, Ectopic pregnancy. Telinde's Operative Gynaecology. 11th ed. Philadelphia, Lippincott Williams and Wilkins; 2015:798.
3. Fylstra DL. Ectopic pregnancy not within the (distal) fallopian tube: etiology, diagnosis, and treatment. AJOG. 2012; 289-99.
4. MMWR. Ectopic pregnancy—United States, 1990-1992. Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep 1995; 44:46-8.
5. Nancy C, Osguthore. Ectopic pregnancy. Journal of Obstetric, Gynecology & Neonatal Nursing 1987; 16:36-41.

- J. Dhaka National Med. Coll. Hos. 2020; 26 (02): 36-40
6. Mahboob U, Mazhar SB. Management of ectopic pregnancy : a two-year study. *Ayub Med Coll Abbottabad*. 2006; 18:37-7.
  7. Shetty SK, Shetty AK. A clinical study of ectopic pregnancies in a tertiary care hospital of Mangalore, India. *Innovative journal of Medical and Health Science* 2014; 4 (1):305-30.
  8. Goldner TE, Lawson HW, Xia Z, Atrash HK. Surveillance for ectopic pregnancy - United States, 1970-1989. *MMWR CDC Surveillance Summaries*. 1993; 42:73-85.
  9. Current trends ectopic pregnancy-United states, 1990-1992. *MMWR Morb Mortal Wkly Rep* 1995; 44:46-8.
  10. *MMWR-CDC Surveillance Summaries*. Ectopic pregnancy in the US, 1979-1980. 1984; 33:155-75S.
  11. ICMR Task Force Project: multicentre case control study of ectopic pregnancy in India. *J Obstet Gynaecol India*; 40; 425-30.
  12. Guta R, porwal S, Swarnkar M, Sharma N, Maheshwari P. Incidence, trends and risk factors for Ectopic pregnancies in a tertiary care hospital of Rajasthan. *JPBMS*. 2012; 16 (07): 1-3.
  13. Raina A, Bajpal M. Experience with ectopic pregnancy in a hospital in India. *Indian journal of Applied Research*. 2015; 5 (4):535-37.
  14. Gaddagi RA, Chandrashekhar AP. A Clinical Study of Ectopic Pregnancy. *Journal of Clinical and Diagnostic Research*. 2012; 6(5):867-69.
  15. Kumar P, Malhotra N. Ectopic Pregnancy. *Jefeoat's principles of Gynaecology*. 8th ed. 2008; 142-159.
  16. Yeasmin MS, Uddin MJ, Hasan E. A Clinical Study of Ectopic pregnancy in a Tertiary care Hospital of Chittagong, Bangladesh. *Chattagram Maa- O-Shishu Hospital Medical College journal*. 2014; 1-4.
  17. Ankum WM, Mol BWJ, Van der Veen F, Bod- duynt PM. Risk factors for ectopic pregnancy: a meta-analysis. *Fertil Steril* 1996; 65:1093-99.
  18. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of ectopic pregnancy after tubal sterilization: US Collaborative Review of Sterilization Working Group. *N Engl J Med* 1997; 336:762-70.
  19. Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Site of ectopic pregnancy: a 10 year population-based study of 1800 cases. *Hum Reprod* 2002; 17:3224-30.
  20. Khatun MHA, Anwar-ul-Azim AKM, Haque E. An analysis of 50 cases of Ectopic pregnancy in Dhaka National Medical Institute Hospital. Bangladesh. *Private Medical Practitioners Journal* 2006; 12(2):61- 65.
  21. Islam N. Diagnostic clues and management of ectopic pregnancy in sir salimullah medical college and Mitford, Dhaka. *Bangladesh J Obstet Gynaecol*. 2018; 33:49-53.
  22. Kulsum SU. Study of ectopic pregnancy: a prospective study of 100 cases. *Bangladesh College of Physicians and Surgons*. 2003; 47:59.
  23. Shah N, Khan NH. Ectopic pregnancy: pregnancy and risk factor. *JCPSP* 2005; 15:535-35.
  24. Majhi AK, Roy N, Karmakar KS, Banerjee PK. Ectopic pregnancy- an analysis of 180 cases. *Indian Med Assoc*. 2007; 105:308-312.
  25. Shaikh NB, Shaikh S, Shaikh F. A Clinical study of Ectopic pregnancy. *J Ayub Med Coll Abbottabd*. 2014; 26:178-81.
  26. Etuknwa BT, Azuonyemaechiokpara P, Imo PA. Ectopic pregnancy: A Nigeria Urban Experience. *Korean Obstet Gynecol*. 2012; 55:309-14.
  27. Siddiqua S, Alam MM, Khan TMA. Ectopic pregnancy-Adiagnostic dilemma. *Bangladesh J Obstet Gynaecol*. 2004; 119:7-10.
  28. Parveen U. Varied clinical presentation of ectopic pregnancy in tertiary care hospital. *Bangladesh College of physicians and Surgons*. 2006; 52:67.
  29. Majhi AK, Roy N, Karmakar KS, Banerjee PK. Ectopic pregnancy- an analysis of 180 cases. *Indian Med Assoc*. 2007; 105:308-312.
  30. Islam A, Fawad A, Shah AA, Jadoon H, Sarwar I, Abbasi. Analysis of Two Years Cases of Ectopic Pregnancy. *J Ayub Med Coll Abbottabad* 2017; 29: 65-67.
  31. Etuknwa BT, Azuonyemaechiokpara P, Imo PA. Ectopic pregnancy: A Nigeria Urban Experience. *Korean Obstet Gynecol*. 2012; 55:309-14.



32. Sindhura M, Sailatha R, Famida A. Trends in ectopic pregnancy: a retrospective clinical study of 79 cases. *Int J Reprod Contracept, Obstet Gynecol.* 2017;6:3009-3013.
33. Kirk E, Bottomley C, Bourne T. Diagnosing ectopic pregnancy and current concepts in the management of pregnancy of unknown location. *Human reproduction update.* 2014;250-61.
34. Ectopic pregnancy (<http://nhp.gov.in/disease/gynaecology-and-obstetrics/ectopic-pregnancy>). Retrieved 4 December 2018.
35. Breen JL. A 21 year surgery of 654 ectopic pregnancies. *Am J Obstet Gynaecol.* 1970; 106: 1007.
36. Kumer V. Tubal ectopic pregnancy. *BMJ Clin Evid.* 2015;2015:1406
37. Medical treatment of ectopic pregnancy: a committee opinion. Practice committee of American Society for Reproductive Medicine. *Fertil Steril.* 2013; 100:638-44.
38. Jesmin S. An analysis of 60 cases of tubal ectopic pregnancy in RMCH. *Bangladesh College of Physicians and Surgeons.* 2003;55:62.



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