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Editorial

Climate Change Challenges

Introduction

Despite 20 years of intensive negotiations, the world's nations have yet to come to an agreement that would effectively prevent dangerous climate change. Global emissions of greenhouse gases (GHG) keep rising, which means that the world is headed for a 4°C temperature rise by 2100, if current trends continue.[1]

Five elements make it very challenging to find an agreement that is both effective and politically acceptable to the concerned parties:[2,3]

1. There is a close link between prosperity GDP, energy use, and GHG emissions. But a disconnection of GDP and GHG emissions has been achieved for sure; most economies cannot achieve never-ending reductions in GHG emissions in the short term without having negative impacts on GDP. Profound disconnection would require a basic transformation of energy generation and transport systems, which would take decades, large sum of money, infrastructure changes and development in in energy yielding technologies.
2. Local greenhouse-gas emissions have global effects. Local efforts on reducing GHG emissions will benefit the whole planet. It will not be effective unless other parts of the world make similar contributions as the atmosphere is a 'global commons'.
3. The impacts of GHG emissions are felt long time after they have been emitted. Rise in temperature occur decades after GHGs are emitted, sea levels rise takes a period more than centuries.
4. Some GHGs (mainly CO_2) remain in the atmosphere for a very long period. The impacts continues even when the of emissions GHGs have stopped. The climate change is a combined result of cumulative GHG emissions from the past two centuries as the industrially developed countries owe their infrastructure, technology and prosperity to their past energy use and GHG emissions.
5. Economically and technologically developed countries are less susceptible to the impacts of climate change. As a result sacrifices in financial developments, which are made to slow down climate changes, need to be increased to reduce the vulnerability of climate change.

There is high a risk that slow economic growth will make it increasingly difficult for economies and technologies required to change to a low-carbon for the benefit of environment. It is difficult to agree and participate by all the countries emitting GHGs on the distribution of reduction of GHGs.[4] Besides the largest historic GHG emitters have broadly agreed to be the contributor of climate changes. Furthermore, there is interdependence in production of goods and GHG emissions in one region; these goods are exported to and consumed in other parts of the world.

What we are actually doing ?

The global emissions increasing day by day. Emissions from the burning of fossil fuels and production of cement reached to a record of 36 billion tons of carbon dioxide in 2013 which was 2.3% above the 2012 level. Emissions are expected to grow by 2.5% and set a new record of 37 billion tons in 2014. The IPCC projections shows that emissions will lead to around five degrees of warming by the end of twenty first century.[5]

What we would need to do to stay below two degrees ?

The world has already warmed by 0.85 degrees Celsius above the pre-industrial average and if industries emit in the same quantities the temperature of the world will go higher by three to five degrees by the year 2100, according to the latest Intergovernmental Panel on Climate Change (IPCC) reports.[4] Nevertheless, it is possible to limit warming to two degrees as long as industrialization can stick within a fixed carbon budget, theoretically. This is the maximum amount we can emit from the beginning of the industrial revolution until the day we stop adding carbon to the atmosphere.[7]

Already emitted 1,900 billion tons of carbons have been emitted; remaining quota is of just 1,000 billion tons for the future. If the use is not curtailed the remaining quota will be used up within 21 years if reduced it might last for 33 years at current emissions rates.[8]

If the earth is less sensitive to emissions than it has been assumed, that would increase the quantity emission of more carbon too and still stay below two degrees. But at current rates extra allowances will be burnt in about a decade.[9]

Mitigation of climate change

Mitigation means action taken to limit dangerous climate changes, especially by reducing the emission of GHGs into the atmosphere. It is important to note that emissions from one part of the world contribute to climate changes for the entire planet.[10] On the contrary, mitigation efforts by one country benefit all others, whether they contribute or not. A country that unilaterally implements mitigation measures may be at an economic disadvantage compared with countries with lower economic demand.[11] As the EU (European Union) is only responsible for some 11% of global GHG emissions, EU mitigation action alone can reduce impact on global warming, compared efforts by other countries.[2]

Measures to reduce carbon emissions from energy use include promoting low-carbon energy sources (renewables, nuclear, natural gas), energy conservation and energy efficiency. Carbon capture and storage (CCS) can help reduce emissions from the continued use of fossil fuels, but some argue that CCS capacities should be preserved to build carbon-negative power plants (bio-energy with CCS) in the future.[12] The International Energy Agency proposes a decarbonization strategy based on energy efficiency, electrification of transport and heating, and low-carbon electricity generation. Emissions from existing high-carbon assets, which have a lifetime of many decades, must also be reduced, and subsidies for fossil fuels phased out.[5]

Outside the energy sector, reducing meat consumption can lead to reduced emissions, according to a recent Chatham House report. Land use, agriculture and forestry are other sectors that can achieve significant emissions reductions or even carbon removal.[5]

Nations around the world can take different approaches to dealing with climate changes. A number of organizations have analyzed the approaches and performance of individual countries. The Climate Change Performance Index ranks countries every year according to emissions level, emissions trend, renewable energy development, energy efficiency and climate policy. In the 2015 ranking, 11 of the 12 best-performing countries are European countries taking part in the EU ETS (Emission Trading System). Mitigation benefits arise from reduced climate impacts.[6] A 2013 study concludes that strong mitigation can reduce the impacts expected for the year 2100 by up to 65%. The Stern Review concludes that losses from climate impacts would amount to 5-20% of global GDP if GHG emissions are not reduced. Apart from reducing climate change, mitigation is considered to bring further benefits such as less air pollution (a major public health problem in China and India), technology leadership, 'green' jobs and reduced dependence on energy imports (for countries without primary energy resources).[12]

Conclusion

Given the scale of the multiple challenges set out above it is perhaps no surprise that some are saying it might be time to call game over for a two degrees world. Not everyone agrees, and more importantly the story doesn't end if we fail to limit warming to two degrees.[4] Already human being are exposed to increased warming less than a degree. The risks will increase as the planet warms further. Failure on reduction of temperature by two degrees implies that the desired limit warming to warming cannot be achieved. As voluntary contributions of the countries were not formally assessed or revised before the Paris conference, it is likely that they will not add up to the emissions reductions required to keep global warming below the internationally agreed limit of two degrees Celsius.[2] The process of taking voluntary national contributions Intended Nationally determined Contributions (INDCs) from all countries as a starting point has been characterized as 'first broad, then deep'. A process for the periodic assessment and strengthening of the national efforts will therefore have to become an important element of the Agreement, on the basis of transparency achieved through monitoring, reporting and verification.[13,14]

(Sir Salimullah Med Coll J 2015; 23: 44-46)

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Obstetrical Outcome of Grand Multiparous Women –A Study in A Tertiary Hospital

Novera Islam[1], Jaglul Haider Khan[2], Chowdhury Taslima Nasrein[3]

Abstract

This prospective study was carried out in Obstetrics ward of Rangpur Medical College Hospital (RMCH) among the 100 grandmultipara patients admitted to evaluate parity related complications during pregnancy and labour in grand multiparas and to see the outcome of pregnancy and labour and also to assess the maternal morbidity and mortality as well as fetal outcome in terms of perinatal mortality and morbidity.Grand multipara admission rate 2.56%. The mean age of the patients was 32.5 ± 2.7 years and the minimum and maximum ages were 26 and 40 respectively. About three quarter (77%) belong to poor class and 76% of the patients were rural residents, 62% primary level educated, and 71 % received ANC . Twentyone percent of the patients delivered babies before 37 weeks of gestation , 75% delivered fullterm baby and only 4% patient had postterm baby. 8% cases had past history of caesarean section (table-2). Hypertension found in 09 patients and GDM developed in 11% cases .UTI developed in 05 cases (table-3). Among the antepartum complications 9% of patients were encountered Preeclampsia, 5% eclampsia, another 5% oligohydromnios, 3% polyhydromnios, 3% IUGR,7 % placenta praevia, 4% abruptio placentae and 01 % post term. In terms of intrapartum complications, 16% of the patients had preterm labour, 13% malpresentation and 11% obstructed labour, Hand prolapse 4%, prolonged labour was 10%, rupture uterus was 5%, cord prolapsed 2% (table 6). Fourtyseven percent of the mothers experienced normal vaginal delivery (NVD), 43% caesarean delivery, 7% underwent laparotomy (subtotal hysterectomy 42.86% and repair of ruptured uterus 57.14%) and 2% breech delivery. Ventose extraction was done in 1 case .

Nine percent patients developed wound infection during postpartum period, 11% patients developed postpartum haemorrhage and 5% developed puerperal sepsis. Retained placenta 4%, postpartum eclampsia and UTI each was found in 2% of patients. Two Mothers died of complications (1 due to DIC and another due to septicemic shock). Ten babies was fresh still born 7 died on neonatal period and 5 intrauterine death (IUD) and 78% was alive. Among 85 patient 29.41% babies had APGAR score 6 or below at birth which reduced to 17.64 % at 5 minutes of birth.Three (3.52%) of babies were born with congenital anomalies, 25.88% had birth asphyxia, 23.52% with prematurity and 1.17% with postmaturity. Neonatal death occurred in 7 cases of which 2 (28.57%) due to birth asphyxia and 5(71.42%) due to LBW and prematurity Twenty (23.52%) babies were below 2.5 kg, 60(70.58%) were between 2.5-4.0 kg(70.58%) and 5 (5.88%) were above 4kg.

Key words: Obstetrical outcome, Multipara, Complication

(Sir Salimullah Med Coll J 2015; 23: 48-55)

Introduction

Grand multiparity (GMP), defined as a pregnancy preceded by five or more previous viable pregnencies[1].Pregnancy in grand multiparous women is viewed with anxiety especially by obstetrician in developing countries working with inadequate facilities. High parity is associated with serious consequence to the fetus, the mother, as

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well as the family and society also. The problem of grand multipara in developing country is compounded by a high prevalence of low socioeconomic status, poor female literacy and social deprivation and inadequate performance of family planning initiative[2].

Despite the Governments population policies which favour the small family size, high parity still remains a common feature of our obstetric practice in developing countries, with an overall incidence of 10-30%,with higher rate in Muslim countries, where there is a large family norm and poor acceptance of family planning methods. Considering the high maternal death in the developing countries,WHO conceived the idea of "Safe Motherhood Initiative" in the year 1987 at a conference in Nairobi, Kenya, to address the appalling high maternal death rates in developing countries, identified grand multiparity as a definite risk.[2]

In Bangladesh mortality declined from 322 in 2001(BMSS 2001) to 174 per 100,000 in 2016(BMSS 2016), a 40% decline in 15 years. The rate of decline was at an average of as out 5.5% per year, compared to the average annual rate of reduction of 5.4% required for achieving MDG-5. Committing to achieving the Millennium Development Goal (MDG) 5, Bangladesh's targets are to reduce the maternal mortality ratio to 143 per 100,000 live births by 2015 [3]. For this purpose high growth rate, especially grand multiparity should be prevented.

Grand multiparity (GMP) is considered as dangerous and high risk clinical entity as certain complication during pregnancy, labour and puerperium are thought to occur with increased incidence in these women. In terms of minimal risk concept: the safest babies to have are second, third and fourth. The hazards are greater for women in their fifth pregnancy and onwards[4].

Some complications that are classically associated with grand multiparaes include fetal malpresentation, dysfunctional labour, abruptio placentae, placenta previa, postpartum haemorrhage, ruptured uterus, macrosomic babies and anaemia. The incidence of abortion both spontaneous and induced due to unwanted pregnancy is very high in high parity women. It is one of the major causes of maternal deaths in contributing 11% to the maternal mortality. The risk of fetal chromosomal abnormalities, in particular- trisomy 21 or Down syndrome rises sharply with maternal age. Hypertensive vascular disease including PIH is found with increased frequency in grand multipara. Advanced maternal age, obesity, renal parenchymal disease, vascular disease and genetic predisposition which play important role in its development[5].

According to the survey on perinatal mortality in hypertensive disorders were responsible for 12% of perinatal death which include 97% stillbirth and 3% neonatal death. There is a 5.6foid increased risk for placenta praevia in high parity group over the age of 40years.Rupture uterus is the gravest complication of high parity.[5]

Post partum haemorrhage is also common in multipara. In grand multipara it occurs due to uterine atony, lack of retraction. The chances of caesarean section are high due to malpresentation, malposition, cephalopelvic disproportion placental abruption and eclampsia. The perinatal mortality in grand multipara is also high due to various factors like preterm labour and prematurity[5].

Materials and Method

This is a prospective study conducted on 100 patients admitted at the department of Obstretics and Gynaecology of Rangpur Medical College Hospital from 1st January 2013 to 30th June 2013.

Inclusion criteria : It includes the patients-

a) Parity 5 or more

b) All grandmultipara admitted into RMCH during the study period with labour pain or without labour pain at last trimester (> 28 wks) of antepartum period.

Exclusion criteria :

- Parity less than 5.
- Gestation <28wks
- Pregnancy with complications like heart disease, chronic systemic illness like–DM, Hypertension, ARF, CRF, Chronic liver disease etc.

Method of collection of data:

Data was collected by using a structured questionnaire containing all the variables of interest. Written consent was taken from the patients or her legal guardian after proper counseling. Patients were selected according to inclusion & exclusion criteria. All collected questionnaire were checked very carefully to identify error in data. Data processing consisted of registration schedule editing computerization, preparation of dummy table, analyzing & matching of data.

Research instrument:

1. Structured data collection sheet were filled up at the time of admission after taking informed written consent from the patient and her legal guardian.
2. Structured follow up sheet were used during the period of hospitalization.

Results

During the study period, a total of 4520 patients were admitted in the Department of Obstetrics & Gynaecology, Rangpur Medical College Hospital. Of them, 116 (2.566%) were grand multipara. Out of 116 patients, 100 were included in the study according to inclusion and exclusion criteria. In this study about 19 percent of the patients were below 30 years, 52 % in the range of 30-35 years and the rest 29% were at 35 or more than 35 years. The mean age of the patients was 32.5 ± 2.7 years and the minimum and maximum ages were 26 and 40 respectively (table-I).

Socioeconomic status of the patients demonstrates that about three quarter (77%) belong to poor class, followed by 19% lower middle class and the remaining 4 % middle class. Residence status shows that over three quarter (76%) of the patients were rural residents, 20% urban and 4% slum residents. Educational level shows that 35% of the patients was illiterate, 62% primary level educated, 3% secondary and higher secondary level. 19% of patients received antenatal care regularly and 52 % irregularly. 21% of the patients delivered babies before 37 weeks of gestation (preterm) , 75% delivered fullterm baby and only 4% patient had postterm baby. 8% cases had past history of caesarean section (table-II).

Table-I

Sociodemographic profile of the patients

Varibles	No. of patients	Percentage
Age (years)		
<30	19	19
30-35	52	52
>35	29	29
Socioeconomic status		
Poor	77	77
Lower middle	19	19
Middle	04	04
Residence		
Rural	76	76
Urban	20	20
Slum	04	04
Educational level		
Illiterate	35	35
Primary	62	62
Secondary	03	03

Table-II

Distribution of patients by obstetric profile

Obstetric profiles	Frequency	Percentage
ANC received		
Regular	19	19
Irregular	52	52
None	29	29
Gestational age		
<37 Weeks	21	21
37-40 Weeks	75	75
>41 Weeks	04	04
Parity		
5	66	66
6	30	30
7	03	03
8	01	01
Gravidity		
6	64	64
7	31	31
8	04	04
9	01	01
Past history of C/S	08	08

82 patients(82%) were anaemic of which 75 were mild to moderately anaemic (91.46%) and 7 were (8.53%) severe anaemic. Among 100 cases, Gross oedema present in 15 cases (15%). Hypertension found in 09patients (9%) and GDM developed in 11 cases (11%).UTI developed in 05 cases (table-III)

Table-III

Clinical presentation associated with pregnancy

Clinical presentation associated with pregnancy	Frequency	Percentage
Anaemia	82	82
Mild to moderate	75	91.46
Severe	07	8.53
Gross Oedema	15	15
GDM	11	11
HTN	09	09
UTI	05	05

Antepartum complications depicts that 9% of patients were encountered Preeclampsia, 5% eclampsia, another 5% oligohydromnios, 3% polyhydromnios, 3% IUGR,7 % placenta praevia, 4% abruptio placentae and 01 % post term. In terms of intrapartum complications, 16% of the patients had preterm labour, 13% malpresentation and 11% obstructed labour. Hand prolapse 4%, prolonged labour was 10%, rupture uterus was 5 %, cord prolapsed 2% (table-VI) Among 13 malpresentation cases, 5 were breech, 3 were shoulder, 2 face 1 brow and 2 with compound presentation (figure-1) Table VI shows that 47% of the mothers experienced normal vaginal delivery (NVD), 43% caesarean delivery, 7% underwent laparotomy (subtotal hysterectomy 42.86% and repair of ruptured uterus 57.14%) and 2% breech delivery. Ventose extraction was done in 1 case (1%).

Table VII showed that 9 patients developed wound infection during postpartum period, 11 patients developed postpartum haemorrhage and 5% developed puerperal sepsis. Retained placenta,4%, postpartum eclampsia and UTI each was found in2 % of patients. Two Mothers died of complications (1 due to DIC and another due to septicemic shock). Table VIII shows that 10.% of babies was fresh still born ; 07% died on neonatal period and 5 % had intrauterine death (IUD)and 78% was alive. Among 85,babies 25(29.41 %) babies had APGAR score 6 or below 6 at birth which reduced to 17.64 % at 5 minutes of birth.3.52% of babies were born with congenital anomalies, 25.88% had birth asphyxia, 23.52% with prematurity and 1.17% with postmaturity. Neonatal death occurred in 7 cases of which 2 (28.57%) due to birth asphyxia and 5(71.42) due to LBW and prematurity.

Table-IV

Distribution of patients by antepartum complications

Antepartum complications	Frequency	Percentage
Preeclamsia	09	09
Eclampsia	05	05
Oligohydromnions	05	05
Polyhydromnions	03	03
IUGR	03	03
Post-term	01	01
Placenta praevia	07	07
Abruptio placenta	04	04

Table-V

Distribution of patients by intra–partum complications

Intrapartum complications	Frequency	Percentage
Pre term labour	16	16
Malpresentation	13	13
Obstructed labour	11	11
Hand prolapsed	04	04
Prolonged labour	10	10
Rupture uterus	05	05
Cord prolapsed	02	02

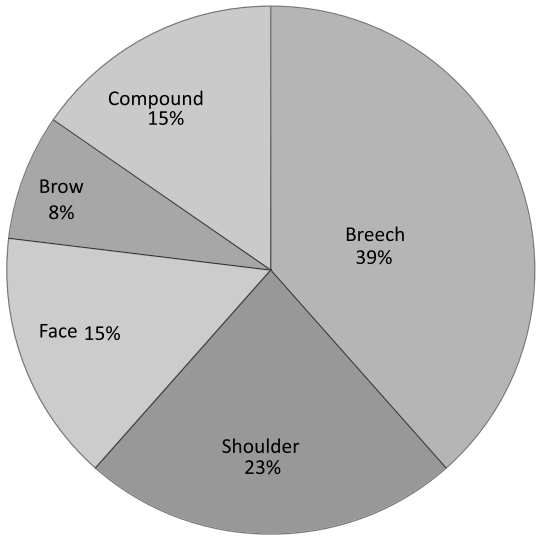

Fig.-1: *Types of malpresentation*

Fig 2 demonstrated that 20 (23.52 %) babies were below 2.5 kg, 60(70.58%) were between 2.5-4.0 kg(70.58%) and 5 (5.88%) were above 4kg

Table-VI
Mode of delivery

Mode of delivery	No. of patients	Percentage
NVD	47	47
Caesarean section	43	43
Laparotomy	07	79
Repair of uterus	05	57.14
Subtotal hysterectomy	02	42.86
Breech	02	02
Ventose	01	01

Table-VII
Distribution of patients by postpartum complications

postpartum complications	No.	Percentage
Wound infection	09	09
PPH	11	11
Retained placenta	04	04
Puerperal sepsis	05	05
Post-partum eclampsia	02	02
UTI	02	02
Maternal death	02	02

Table-VIII
Neonatal outcome

Neonatal outcome	Frequency	Percentage
Perinatal outcome(n=100)		
Still birth	10	10
IUD	05	05
Neonatal death	07	07
Alive	78	78
APGAR at birth		
<6	25	29;41
>6	60	70.58
APGAR at 5 minutes		
<6	15	17.64
>6	70	82.35
Congenital anomalies	03	3.52
Birth asphyxia	22	25.88
Prematurity	20	23.52
Post maturity	01	1.17
Neonatal death(n=07)		
Birth asphyxia	02	28.57
LBW and Prematurity	05	71.42

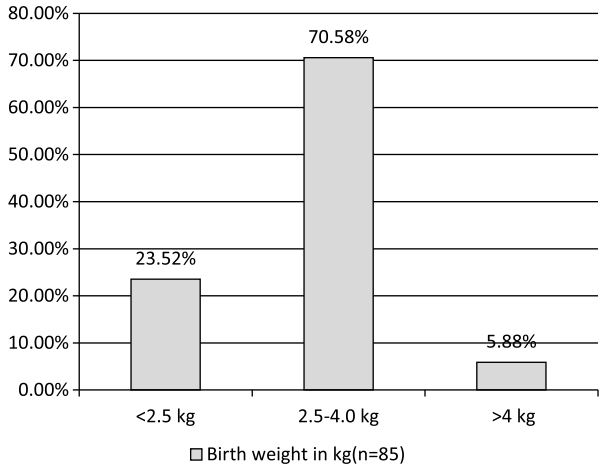

Fig.-2: *Distribution of neonate according to weight (in kg)*

Discussion

The results from this study demonstrated that half of the patients were between 30-35 years old age(52%) and second highest above 35 years old (29%).The mean age is 32.5±2.7.About three-quarter (77%).belonged to lower socioeconomic class and rural resident (76%).About 35% were illiterate, 62% primary level and very few were (3%) secondary level.

A study performed by Rayamajhi [6] demonstrated nearly two-thirds of grand multiparas (65.1%) were 35 - 39 years, 10.9% between 30 - 34 yrs, 16.9% were between 40-44 years. A study done by A.Omole Ohonsi[2] in Aminu Kano Teaching Hospital ,Nigeria found 48.60% in between 25-29 years and 34.80% were in 30-34 years and 8.7% in35-39 years age; mean age being 29.72±2.09 years. A study done by Rokeya[7] in DMCH 2007 found 52.6% belong to 31-35 years old followed by 22.8% in between 36-40 years; mean age being 33.71±3.94.

Mazhar[8] and Roman et al[9] showed mean age as 30.45±5.46 and 34.8±4.8 years respectively. Another study in Pakistan military hospital by Rozina shahid[5] showed that about 85% patients were between 31-40 years age. Hundred consequtive cases of GMP were included in the study. Frequency of GMP was more in low and middle socioeconomic class (85%). It is uncommon in higher social class because of trend of small family and adequate practice of contraception. Sixty percent patient were above 35 years of age.

In another study by Mor-Yosef[10] compared obstetric outcomes between grand multiparous from high and low socioeconomic classes and demonstrated a significantly higher risk in those from lower socioeconomic group.

In our study, only 19% patients received antenatal care regularly; 52% irregularly and 29% didn't receive any antenatal check up. A study done by A. Omole Ohonsi[2] found prevelance 10.20% for booked grand multipara and also such report from United Arab Emirates and Riyad which are predominantly muslim communities like ours. This may be because of the higher prevalence of early marriage, a large family norm, poor acceptance of modern family planning methods in muslim communities and illiteracy.Over 90% of the pregnancies were unplanned or unwanted which indicates the need for making contraceptives not only available but also affordable.

Rayamajhi[6] documented that 26.4% of the grand multipara had no antenatal care and 20.8% with 3- 5 antenatal visits. Nazneen[11] found in her study that only 17% patients received ante natal care regularly and 33% irregularly. Fifty percent mothers didn't receive any antenatal care.

Parity distribution of women admitted to RpMCH during the study showed that 64% women had up to 5 children and 31% had 6 children. A study done by Rokeya[7] in DMCH found 68.4% women had 5 children; 70% in a study by shahida[12] and 74 % in a study by Mazher[8]. A study by Ozumba and Igwegbe[13] showed parity 5-6 in 90% patients and a study done by Roman et al[9] showed mean parity as 6.Gil A et al[14] showed 33% women with parity 6 and 23.4% had 7.

Majority (82%) of the patients presented with anaemia of which 91.46% presented with mild to moderate anaemia and 8.53% with severe anaemia, most of them didn't require blood transfusion.15% patients developed gross oedema. GDM found in11% patents and pregnancy induced hypertension in 9%. 5% patient suffered from UTI .

Shahid[5] reported anaemia as one of the common (45%) medical problem found in grand multipara; pregnancy induced HTN in 8% cases and the frequency of diabetes was 5%. As antenatal attendance of grand multiparaous patients was poor so most cases of diabetes and HTN were not previously diagnosed or treated. However, Shamshad[15] found a comparatively low incidence of anaemia (26%).

Gil A Goldman et al[14] found in their study that about GDM developed in 6.9% and pregnancy induced hypertension in 8.4% cases. Kavitaha D'souza et al[16] found in their study that 59% patients presented with anaemia; pregnancy induced hypertension occurred in 21% cases and 5% patients presented with UTI. A. Omole Ohonsi[2] found in their study that only 2.3% patients presented with anaemia, 11.1% patients presented with GDM and 8.8% presented with pregnancy induced hypertension.

Common antepartum complications that the women experienced in this study were Preeclampsia (9%), eclampsia (5%), placenta praevia (7%) and oligohydromnions (5%), polyhydromnions (3%) IUGR(3%), abruptio placentae(4%) and postterm (01%) baby.

The study done by Gil A.Goldman et al[14] revealed that, patients with preeclampsia(3.3%), placenta praevia(3.7%) and oligohydromnions(1.6%), polyhydromnions (1.9%) IUGR(1.5%), abruptio placentae(1.9%) . Rozina shahid[5] in her study found that 4% patients presented with eclampsia, 9% with preeclampsia, 5% with placenta preavia and 8% with abruptio placenta and also IUGR 6%. Kavitha D'souza[16] showed the frequency of placenta preavia was 3% and abruptio placenta was 8%. A study done by Nazneen[11] in CMCH found preeclampsia (16%). Eclampsia, placenta praevia and oligohydromnios were the second most common complications (around 6% each). IUGR, abruption placentae and postterm were 3rd in ranking order (around 4% each), HELLP syndrome was negligible (1%).

In terms of intrapartum complications, 16% of the patients had preterm labour, 13% malpresentation and 11% obstructed labour. Hand prolapsed 4% , prolonged labour was 10%, rupture uterus was 5 %, cord prolapsed 2%.

In the study of Rozina Shahid[5], the frequency for preterm labor was 15%, for malpresentation was 16% and 2% for ruotured uterus. Al Sibai[17] and Bibinszki et al[18] showed a high incidence of preterm labour which is similar to our study .Nazneen[11] found in her study that 23% of patients

have had preterm labor, 13% had malpresentation, 12% had obstructed labor and 6% with ruptured uterus. Hand prolapse, prolonged labour each was 6% and multiple pregnancy was found in 4% of patients.

Nearly half 47% of the mothers delivered their babies normally, 43% needed caesarean section and 7% required laparotomy. After laparotomy subtotal hysterectomy performed in 42.86% cases and ruptured uterus repaired in 57.14% cases. Breech delivery performed in 2% cases. . A very negligible percentage of patients delivered with ventose extraction.

A study done by Kavitha D'souza[16] showed 90% patients delivered by NVD and 10% underwent caesarean section. Another study by Gil A.Goldman[14] found 84% delivered normally,6.8% underwent caesarean section and in 5.6% forceps delivery performed. Rozina shahid[5] in her study found the frequency of NVD in 58% cases and 23% underwent c/s. Mor-Yosef[10] showed a high incidence of normal vaginal delivery and caesarean section is similar to our study. Nazneen[11] in her study showed that nearly half (48%) of the mothers delivered their babies normally, 41% needed caesarean section and 6% required laparotomy; Three percent experienced breech delivery and a negligible percentage of patients delivered with ventose extraction and craniotomy.

During postpartum period wound infection occurred in 9% patients, 11% developed PPH and 5% with puerperal sepsis.Frequency of Retained placenta 4%, postpartum eclampsia and UTI revealed same and that was 2% .Two mothers died with postpartum complications - one due to DIC and another due to septicemic shock.

Tanbo and Bungum[19] in their study observed wound infection in 21% cases, PPH in 11% cases, postpartum eclampsia in 2% and retained placenta in 1%. Kavitha D'souza[16] in their study found that 12% developed PPH, 5% developed UTI, 1% developed puerperal sepsis and there was no maternal death in their study. Rozina Shahid[5] in her study showed that PPH occurred in 9% patients, retained placenta in 2% and perineal tear in 2% cases.Rokeya[7] in her study in DMCH revealed 15.2% suffered from PPH and 12.9% experienced of puerperal sepsis followed by retained placenta in 11.1% cases and postpartum eclampsia in 2.3% cases. Nazneen[11] in her study found that wound infection during postpartum period was 18%, 9% with postpartum haemorrhage and 4% with puerperal sepsis. Retained placenta, postpartum eclampsia and UTI each was found in 3% cases.

In this study, 10% babies were fresh still born, 7% died on neonatal period and 5% had intrauterine death (IUD)and 78% was alive . Birth weight of baby revealed that 20 (23.52 %) baby were below 2.5 kg, 60(70.58%) were between 2.5-4.0 kg and 5 (5.88%) were above 4kg.Among 85, 20(23.521 %) babies had APGAR score 6 or below 6 at birth which reduced to 25(29.41) % at 5 minutes of birth. Birth asphyxia was the commonest(25.88%) complication followed by (23.521%) prematurity , (1.17%) postmaturity and (3.52%) congenital anomalies(macrosomia and hydrocephalous with meningomyocole). Neonatal death occurred in 7 cases of which 2 (28.57%) due to birth asphyxia and 5 due to LBW and prematurity .

Gil A. goldman[14] found that 9.5% were preterm baby,11.5% were postterm , perinatal death occurred in 2.3% cases .Rozina shahid[5] in her study revealed that alive number of baby was 83% and dead baby was 17%.Frequency of LBW babies was 15%,14 cases being premature and 2 cases with IUGR. Macrosomic babies were 10%. About 80% of these were having APGAR score between 8-10 and 8% babies had an APGAR score below 5 and all of these had neonatal dead. In this study, healthy babies were delivered in 73.043% cases and 84.9%, 75% and 69% respectively in 3 other studies in Bangladesh[7,8,12]. Neonatal death found in our study was 11.34% compared to 7.2% and 3% in recent two studies on grandmultiparous women. Rayamajhi[6] demonstrated that 5.7% babies with LBW, 4% congenital anomaly, 11%birth asphyxia, 5% prematurity and 2% with postmaturity.

Conclusion

It is concluded from results of this study that grand multiparity is still a major obstetric hazard in our setup with higher frequency of complications. The combination of several factors, good antenatal care and delivery services, increased patient's awareness through adequate counseling, an efficient social welfare service and an efficient blood banking system can avoid adverse effects of grand

multiparity on the mother and newborn. Emphasis on qualitative antenatal care and hospital deliver as well as education, and acceptance of modern family planning methods to prevent grand multiparity should be intensified in our community, if Millennium Development Goals 4 and 5 are to be achieved.

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Prevalence of Feelings of Women during and after Sustaining Mental Trauma due to Domestic Violence among Rural Women of Reproductive age

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Abstract

Patriarchal social system is ruling the world hence there is a lack of power balance between females and males. A cross-sectional, descriptive study was carried out in different households in rural areas of Keraniganj Upazilla of Dhaka district between March 2016 and June 2016. The study population comprised of married women of reproductive age group (15-49 years) with a sample size of 201. Purposive sampling technique was applied. An interviewer administered structured questionnaire was developed and used after pre-testing to collect primary data. Data was collected by face to face interview of the respondents by the researchers during data collection period. After collection, data were checked and verified. Omission and errors were corrected properly. Data were analyzed by using Social Package for the Social Sciences (SPSS version 22). The study found that, most of the respondents (56%) felt sad during the period of violence followed by 34% percent of the respondents felt scared. About 30% of the respondents felt like crying with 26% started crying. The standard deviations (SD) in the table indicates that the data points had spread out over a wider range of values. Most of the women 58.7% try not to remember the violence and 41.3% felt scared when they remembered the violence. Unscrupulous feelings causes grave consequences to all the battered women therefore brings adverse conditions in the society. To combat this both the females and males need to have formal and casual educations to develop mutual respect.

Key Words: *Feelings, Prevalence, Sustaining Mental trauma, Domestic violence.*

(Sir Salimullah Med Coll J 2015; 23: 56-59)

Introduction

Violence against women (VAW) is materialization of a historic unequal power relation between sexes. It is a form of discrimination and mistreatment of women which results is physical, psychological and socioeconomic trauma to women and therefore to the society. This is as well termed as a global epidemic.[1] Violence against women leads to accidents that causes deaths of women of reproductive age. And is one of the most disgraceful expressions of human rights violation across the world women in the study areas experience physical and sexual spousal violence in their lifetime ranged from 15% to 71%. In Bangladesh, violence against women is a very common practice. It leads to inequality in distribution of power, deprives women equal opportunity of work and decision making. This culminates loss of social security, self-esteem, dignity in the family and in the society as a whole.[2] Trauma is often the result of an overwhelming amount of stress that exceeds one's ability to cope or integrate the emotions involved with that experience. A traumatic event involves one experience, or repenting events with the sense of being overwhelmed that can be delayed by weeks, years, or even decades as the person

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struggles to cope with the immediate circumstances, eventually leading to serious, long-term negative consequences, often overlooked ever by mental health professionals: "If clinicians fail to look through a trauma lens and to conceptualize client problems as related possibly to current or past trauma, they may fail to see that trauma victims, young and old, organize much of their lives around repetitive memories, reminders, and affects." [2]

Methods

A cross-sectional, descriptive study was carried out in different households in rural areas of Keraniganj Upazilla of Dhaka district between March 2016 and June 2016. The study population comprised of married women of reproductive age group (15-49 years). The sample size was 201, the number of the sample was so because of the situations, ability and the provision of time. Only married women of reproductive age group were taken to make the sample more specific. Women beyond reproductive age, widowed and unmarried women were excluded from the study. Purposive sampling technique was applied. An interviewer administered structured questionnaire was developed and used after pre-testing to collect primary data. Data was collected by face to face interview during data collection period. After collection, data were checked and verified. Omission and errors were corrected properly. Data were analyzed by using Social Package for the Social Sciences (SPSS version 22), an IBM software and was represented in tables.

Results

Table I

Feelings of victim at the time of violence (n=184)

Feeling at the time of violence	Frequency	Percentage
Feel scared	63	34.2
Feel sad	103	56.0
Feel like crying	55	29.9
Feel anxious	18	9.8
Start crying	48	26.1
Develop low self-esteem	17	9.2
Become stunned	4	2.2
Feel like ending up her life	9	4.9
Think of committing suicide	7	3.8
Attempt to commit suicide	3	1.6

*Multiple responses

Women who ever experienced domestic violence had different type of types of feeling at the time of violence. The study found that, most of the respondents (56%) felt sad during the period of violence followed by 34% percent of the respondents felt scared. About 30% of the respondents felt like crying with 26% started crying. Those who felt anxious were and developed low self-esteem 10% and 9% respectively. Around 4.9% felt like ending up their lives, 3.8% thought of committing suicide and 1.6% attempted to commit suicide. A negligible number of the respondents (2.2%) became stunned.

Table II

Association of feelings of victim at the time of violence with age (n=184)

Feeling at the time of violence	Frequency (%)	Age (mean ± SD)
Feel scared	63 (34.2)	26.78 ± 6.79
Feel sad	103 (56.0)	28.86 ± 7.23
Feel like crying	55 (29.9)	26.89 ± 6.55
Feel anxious	18 (9.8)	31.50 ± 7.39
Start crying	48 (26.1)	30.23 ± 9.14
Develop low self esteem	17 (9.2)	27.94 ± 6.36
Become stunned	4 (2.2)	27.50 ± 7.59
Feel like ending up her life	9 (4.9)	26.89 ± 5.53
Think of committing suicide	7 (3.8)	30.57 ± 7.48
Attempt to commit suicide	3 (1.6)	29.00 ± 9.64

The standard deviations (SD) in the table indicate that the data points for each or the responses had spread out over a wider range of values.

Table III

Feelings after the violence (n=184)

Feeling after the violence	Frequency	Percentage
Feel scared when she remembers the violence	76	41.3
Try not to remember the violence	108	58.7

Most of the women 58.7% try not to remember the violence and 41.3% felt scared when they remembered the violence.

Discussion

This is a cross-sectional type of descriptive study was carried out in rural area of Keraniganj Upazilla under district of Dhaka. The purpose of study was to find out magnitude of domestic violence causing mental trauma among married women of reproductive age (15-49 years). The objectives of the study was to assess the feeling of the victims at the time of mental violence, association of these feelings to age of the victims, and feeling of the victims after the violence. Small study period forced the sample size to be 201 only. This topic is very sensitive and respondents were shy to express their opinions openly and willingly, thoughts of damaging self-images and that of families. Chance of recall bias is very high in any study based on the self-reporting. [3]

Victims of domestic violence suffering from mental trauma try to lessen and refute the abuse. They feel scared and sad. Some of the women feel like crying on the other hand some of them start crying. These women block the abusive events from their memory and become stunned. Majority of the victims develop low self-esteem. Developing anxiety, apprehension or panic because of persistent trauma is a regular phenomenon. Victims try very hard to avoid dealing with the situations whereas some of them develop persistent flashbacks of episodes of domestic violence. Henceforward victims develop precise fears and repeatedly scrutinize for signs of additional harm. [4] Around 80% of women who experienced mental or physical violence by an intimate partner reported significant effects including posttraumatic stress disorder (PTSD) for a short or a long time.[5] Women who have experienced violence are liable to suffer from PTSD three times more than who did not.[6] Women who have experienced violence or survivors of domestic violence have nearly double the risk for developing depressive symptoms, and three times the risk for developing major depressive disorder.[7] Mothers who experience Violence are nearly twice as likely to develop post-partum depression compared to mothers who have not been abused by an intimate partner. Mothers reporting IPV intimate partner violence (IPV) are more likely to have a current diagnosis of depression.[8]

In addition to depression and PTSD strongly suggests that experiencing IPV increases the risk of other mental health conditions, including deliberate self-harm which is three times more likely to happen than non-abused women. Factors such as PTSD, numbing symptoms or more severe sexual violence associated with current deliberate self-harm.[9]

Suicidality is a common outcome of violence.[10] Attempts to commit suicide as well is very common outcome.[11] Women who reported partner violence at least once in their lifetime are nearly three times as likely to have suicidal thoughts and nearly four times as likely to attempt suicide, compared to women who have not been abused by a partner.[12]

Conclusion

A battered woman is vulnerable and along with her she brings more vulnerability to the society. The consequences of the anxiety, sadness and poor self-esteem are grave. These women develop post-traumatic stress disorders. Thought of self-harm, substance abuse, attempt to commit suicide and committing suicide are frequent outcomes of domestic violence. All these can be reduced if the prevalence of domestic violence is reduced which can be brought forward by balancing the patriarchal society.

Recommendations

Males dominate over females due to power imbalance in the society. This has been going on from the very beginning of the civilization. Women are abused although women are stigmatized to be the social symbol of goodliness. To overcome all these glitches education of women and men are compulsory. Not only formal educations but knowledge of moral values, social norms and mutual respect for the opposite gender can play vital role to reduce the domestic violence and unscrupulous consequences related to it.

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Evaluation of Ultrasonography (USG) as a Diagnostic Modality for Urinary Bladder Mass with Histopathological Correlation

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Abstract

Background: *Bladder cancer is the most common tumor of the urinary system. Though the incidence of bladder cancer in Bangladesh is not known.*

Objectives: *To evaluate the diagnostic usefulness of gray scale ultrasonography in the diagnosis of urinary bladder mass; to evaluate the findings of gray scale ultrasonography and histopathology of urinary bladder mass; to calculate the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of gray scale ultrasonography in the diagnosis of urinary bladder mass.*

Methods: *This cross-sectional study was conducted to evaluate the diagnostic accuracy of Gray Scale Ultrasonography in the diagnosis of urinary bladder mass enrolling 47 patients of 29 to 76 years of age range during the period of January 2013 to December 2014in the department of Radiology and Imaging of Sir Salimullah Medical College and Mitford Hospital, Dhaka. After taking informed consent, data was collected in a pre-tested questionnaire by taking history, examining the patients clinically, the finding and interpretation of the Ultrasonography and histopathological reports. Histopathological diagnosis was considered as gold standard of diagnostic criteria.*

Results: *Among 47 patients included in this study the age ranged between 29-76 years. Mean age was 55.84 ± 13.67 (mean ± SD) years. Majority of the respondents (42.55%) were found between 41-60 years of age. There were 31 men (65.95%) and 16 women (34.05%).*

The most common symptom associated with bladder mass was haematuria (93.61%). 41 subjects (87.23%) had anemia, 38 subjects (80.85%) had suprapubic pain, 53.19% had urgency, 38.29% had burning micturition, 34.04% had increased frequency, 27.65% had anorexia, 12.76% had pelvic pain, 10.63% had pain in flank, 6.36% had abdominal pain and 4.25% subjects presented with abdominal mass.

Most of the malignant lesions involved mostly base (79.48%) and lateral wall (46.15%) with irregularly (79.48%) walled isoechoic lesion (51.28%) with extension into perivesical tissue. Benign lesions showed involvement of lateral wall of urinary bladder (87.5%). These lesions revealed as irregularly margined (87.5%) mass lesion affecting base (62.5%) & lateral wall (87.5%).

At histology, 21 cases (44.68%) were diagnosed as Transitional Cell carcinoma and 13 (27.67%) cases as Squamous cell carcinoma. 5 cases (10.63%) were Adenocarcinoma. Cystitis and adherent blood clot to wall were found as 4 (8.51%) cases each. Among 47 cases, 39 cases (82.79%) were diagnosed as malignant and rest 8 (17.21%) cases were benign, found in histopathology. In USG, 38 (80.85%) were malignant and rest 9 (19.15%) were benign. Considering histopathological diagnosis as gold standard test accuracy, sensitivity, specificity, PPV, NPV and accuracy of USG in diagnosis of malignant bladder mass were 97.44%,97.43%, 87.5%, 97.43% and 87.5% respectively.

Conclusion: *Ultrasonography is a non invasive available, radiation free procedure which is used as a first line preliminary diagnostic procedure. The gray scale ultrasonography is a useful diagnostic tool for diagnosis of urinary bladder mass.*

(Sir Salimullah Med Coll J 2015; 23: 60-66)

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Introduction

Bladder cancer is the most common tumor of the urinary system. Though the incidence of bladder cancer in Bangladesh is not known, it was estimated that 68,810 new cases were diagnosed and 14,100 deaths were caused by bladder cancer in the United States in 2008. The lifetime risk for men is 3.4% and for women, 1.2%. Although bladder cancer can be detected at any age, more than 70% of new cases are diagnosed in patients who are 65 years of age or older.[1,2] In addition, up to 70% of patients treated for bladder cancer will experience a recurrence after treatment. Bladder cancer rates are nearly four times higher in men than in women.[3,4,5,6], TCC accounts for approximately 90% of all bladder tumors. The second most common cell type is squamous cell cancer (8%), followed by adenocarcinoma. Other rarer subtypes such as small cell carcinoma account for less than 1% of the cases.[3,4] Patient symptoms are all nonspecific. The most common presenting symptom is gross hematuria, although microscopic hematuria may be detected at urinalysis. Patients may also experience voiding symptoms such as increase frequency, dysuria, and pelvic pain and pressure[4].

Tumors arising from the epithelial lining of the urinary tract—that is, the renal collecting system, renal pelvis, ureter, bladder, and urethra—are called urothelial tumors. The most common type, accounting for roughly 95% of all malignant urothelial tumors, is TCC. Bladder cancers and those in the proximal urethra are commonly considered lower urinary tract urothelial tumors to distinguish them from ureteral, renal pelvic, and calyceal urothelial tumors, which are collectively referred to as upper urinary tract tumors.[3]

The goal of cancer screening is to detect cancer at an early stage when it is treatable and curable. The major factors influencing prognosis and treatment of bladder tumor are histological cell type, grade of malignancy, tumor size, growth pattern, depth of bladder wall infiltration and the presence of metastases in lymph nodes and blood borne sites. Depth of infiltration refers to the spread of tumour through the layers of the bladder wall and has a major impact on treatment choice.[7] Cystoscopy is the conventional procedure for monitoring the bladder and taking biopsy from the lesion.[8] Cystoscopic evaluation and biopsy reveals the growth pattern, histological cell type and grade of malignancy.[7] However this procedure exhibits four major problems. First, it is painful; hence, many patients refuse the exam. Second, it increases the risk of urinary tract infection. Third, it does not easily show the diverticula and the bladder neck, especially in males. Fourth, it only shows the inner surface of the bladder wall; the interior of the wall and the neighboring structures are not visible.[8] So, reliable, noninvasive, image-based method has been needed to be established for detection of bladder cancer.[5] USG has proved to be an accurate imaging modality for various cancers.[9]

Patients with suspected bladder abnormalities were examined by noninvasive suprapubic sonography to define the accuracy of ultrasound for detecting and staging bladder carcinomas by.[10] In 103 patients, 65 tumors were found by cystoscopy, of which sonography detected 61 (94%). Four lesions less than 2–3 mm were missed at the bladder dome, the ventral wall, and side wall. The sonographic staging was correct in 83% of all tumor stages with the lowest value of 69% for T_2/T_{3a} tumors; excluding recurrent tumors, the overall accuracy increased. From these results, suprapubic sonography was considered to be a reliable noninvasive technique for detecting bladder tumors and for preoperative local staging. The staging results were comparable with reports in the literature on the accuracy of intravesical sonography.

Conventional and contrast-enhanced sonographies were performed on 34 consecutively registered patients with bladder tumors.[11] All examinations were reviewed by two independent sonologists. At gray-scale sonography, interruption of the hyperechoic bladder wall was considered the main diagnostic criterion for differentiating superficial and infiltrating tumors. At contrast-enhanced sonography, a tumor was considered superficial when the hypoenhancing muscle layer of the bladder wall was intact; disruption of the muscle layer by enhancing tumor tissue was considered diagnostic of infiltration. A level of confidence in the diagnosis of tumor infiltration of the muscle layer was assigned on a 5-degree scale. Receiver operating characteristic analysis was used to assess

overall confidence in the diagnosis of muscle infiltration by tumor at both conventional and contrast-enhanced sonography. Histologic diagnosis was obtained for all patients. Final pathologic staging revealed 25 superficial tumors (Ta–T1 disease) and nine muscle-infiltrating tumors (> T1). Conventional sonography depicted five of nine muscle-infiltrating tumors, and contrast-enhanced sonography depicted all nine. The diagnostic performance of contrast-enhanced sonography approached that of the reference standard as well as the diagnostic performance of gray-scale ultrasound.

Although, CT scan, MRI[12], PET-CT scan are better modalities than USG in detecting and staging bladder mass with more diagnostic accuracy than USG. But these modalities are invasive, use contrast media of radio-pharmaceuticles and have potential radiation hazards. On the contrary, USG is a non-invasive, readily available, relatively cheap method. If care is given during sonography, a radiologist can accurately detect bladder mass which would be comparable with other imaging methods. Sir Salimullah Medical College and Mitford Hospital is one of the busiest hospital situated in the capital city, Dhaka. This hospital provides both the Department of Urology and the Department of Radiology and Imaging well-equipped with modern technology. In this hospital USGs are performed under the direct supervision of highly specialized and experienced radiologists with minimum cost. This is the reason for which the investigator selected the Department of Radiology and Imaging of SSMC as an ideal place of study.

Methods

This cross-sectional study was carried out in the department of Radiology and Imaging of Sir Salimullah Medical College And Mitford Hospital, Dhaka enrolling 47 patients who were referred to Radiology and Imaging department by Urology department of Sir Salimullah Medical College and Mitford Hospital, Dhaka as a clinically suspected urinary bladder mass for USG of abdomen, during the period of January 2013 to December 2014.

Prior to the commencement of this study, the research protocol was approved by the Institutional Review Board of SSMC, Dhaka. It was assured that all information and records would be kept confidential and the procedure would be helpful for both the surgeons and the patients in making rational approach of the case management. All USG examinations were performed with Logiq P5 GE (General Electronics). All the relevant collected data were compiled on a master chart first and was then organized by using scientific calculator and standard statistical formulae. The diagnostic value of USG in the diagnosis of urinary bladder mass was determined by calculating sensitivity, specificity, accuracy, positive and negative predictive values.

Results

Among 47 patients included in this study the age ranged between 29-76 years. Mean age was 55.84 ± 13.67 (mean ± SD) years. Majority of the respondents (42.55%) were found between 41-60 years of age. Five (10.63%) subjects were found below 40 years of age. There were 31 men (65.95%) and 16 women (34.05%).

Table I
Distribution of the patients by demographic characteristics

Demographic characteristics	No. of patients	Percentage
Age		
21- 30	01	2.12
31 -40	04	8.51
41- 50	14	29.78
51- 60	20	42.55
61- 70	03	6.38
71- 80	05	10.63

Most of the malignant lesions involved mostly base (79.48%) and lateral wall (46.15%).Margin was irregular in (79.48%) and regular in (20.51%) cases. Lesions were isoechoic (51.28%), hypoechoic (32.30%) and hyperechoic (13.89%) with extension into peri vesical tissue. Benign lesions showed involvement of lateral wall (87.5%) & base (62.5%) of urinary bladder. Margin was irregular in (37.50%) & regular in (62.50%).Lesions were hypoechoic in (50%) & hyperechoic in (50%) cases.

Table II

Distribution of Site of involvement of the urinary bladder masses (n=47)

Type of lesion	Neoplastic	Non- Neoplastic
USG finding (%)	n=39	n=08
Involvement of base of urinary bladder	79.48	62.50
Involvement of lateral wall of urinary bladder	46.15	87.50
Involvement of both base & lateral wall	24.30	15.24

* Multiple responses were elicited and results were expressed in percentage.

Table III

Distribution of echogenicity of lesion of the urinary bladder masses (n=47)

Type of lesion	Neoplastic	Non- Neoplastic
USG finding (%)	n=39	n=08
Isoechoic	51.28	00
Hypoechoic	32.30	50
Hyperechoic	13.89	50
Mixed echogenic	02.53	00

At histopathology, 21 cases (44.68%) were diagnosed as Transitional Cell carcinoma and 13 (27.67%) cases as Squamous cell carcinoma. 5(10.63%) cases were Adenocarcinoma, Cystitis and adherent blood clot to wall were found as 4 (8.51%) cases each.

Among 47 cases, 39 cases (82.79%) were diagnosed as malignant and rest 8 (17.21%) cases were malignant found in histopathology. In USG, 38 (80.85%) were malignant and rest 9 (19.15%) were benign. Out of the 47 study subjects, 39 were histopathologically confirmed as malignant mass. Among the confirmed 39 subjects, 38 (True positive) were diagnosed as malignant mass in USG accurately, while in 01 (False negative) subjects, USG failed to clearly diagnose malignant mass. One subject was false positively considered as bladder carcinoma. 07 (True negative) subjects had other than bladder carcinoma as diagnosed by both USG and Histopathological diagnosis.

Table IV

Histopathological diagnosis of urinary bladder mass (n=47)

Findings	No. of patients	Percentage
Transitional Cell carcinoma	21	44.68
Squamous Cell carcinoma	13	27.67
Adenocarcinoma	05	10.63
Cystitis	04	08.51
Adherent blood clot to wall	04	08.51
Total	47	100

Table V

Comparison between transabdominal sonography with histopathological diagnosis as a gold standard test for diagnosis of malignant bladder mass

USG Diagnosis	Histopathological diagnosis		Total
	(+) ve for malignancy	(-) ve for malignancy	
(+) ve for malignancy	38(True positive=TP)	01(False positive=FP)	39
(-)ve for malignancy	01(False negative=FN)	07(True negative=TN)	08
Total	39(TP+FN)	08(FP+TN)	47 (TP+FP+TN+FN)

Considering histopathological diagnosis as gold standard test sensitivity, specificity, PPV, NPV and accuracy of USG in diagnosis of malignant bladder mass were 97.43%, 87.5%, 97.43%, 87.5% and 97.44% respectively.

Table VI

Sensitivity, Specificity, Positive predictive value, Negative predictive value and Accuracy of USG for diagnosis of malignant bladder mass considering Histopathology as gold standard test

Diagnostic parameter	Value (%)
Accuracy	97.44
Sensitivity	97.43
Specificity	87.50
Positive predictive value	97.43
Negative predictive value	87.50

Discussion

Bladder cancer which is the most common malignancy of the urinary tract can be detected at any age, more than 70% of new cases are diagnosed in patients who are 65 years of age or older. Up to 70% of patients treated for bladder cancer would experience a recurrence after treatment. Reliable and noninvasive image-based methods for bladder cancer detection are ultrasonography, CT scan and MRI. Although, Cystoscopy and histopathology remain the reference standard for bladder cancer detection, both are invasive procedure and are uncomfortable in some patients. Ultrasonography is non invasive, radiation free modality for the first assessment of any abdominal pathology. Though CT scan, MRI, PET, cystoscopy play better role than USG in depicting the detail anatomy and extension of the masses of urinary bladder, it is not available at all levels. USG remains the initial modality of diagnosis of urinary bladder pathology. USG has proved to be an accurate imaging modality for various cancers.[9] Although ultrasonography has limitations in detail demonstration of mass lesion as compared to other imaging modalities. It is not easy to identify bladder wall thickness unless the bladder is adequately distended. In addition, invasion of surrounding structures and pelvic lymph nodes could not be well delineated due to bowel gas. But, if adequate time with detail knowledge about characteristics of bladder masses is given during USG of bladder mass, it is not difficult to give a correct diagnosis about the characteristics and nature of the bladder mass.

This cross-sectional study was conducted to evaluate the diagnostic accuracy of Gray Scale Ultrasonography in the diagnosis of urinary bladder mass enrolling 47 patients of 29 to 76 years of age range during the period of January 2013 to December 2014in the department of Radiology and Imaging of Sir Salimullah Medical College and Mitford Hospital, Dhaka. After taking informed consent, data was collected in a pre-tested questionnaire by taking history, examining the patients clinically, the finding and interpretation of the Ultrasonography and histopathological reports. Histopathological diagnosis was considered as gold standard of diagnostic criteria. The findings of the study are discussed on basis of related previous studies concerning the objective of the study.

Among 47 patients included in this study the age ranged between 29-76 years. Mean age was 55.84 ± 13.67 (mean ± SD) years. Majority of the respondents (42.55%) were found between 41-60 years of age. Five (10.63%) subjects were found below 40 years of age. There were 31 men (65.95%) and 16 women (34.05%). In previous study, Crawford et al. 1997 reported that the incidence of urinary bladder tumors accounting for 5.5% of all the cancer cases in men. In women, it is accounting for 2.3% of all cancers .The male to female ratio is 3.8:1 and has peak incidence at the age of 65.

Current study showed that most common symptom associated with bladder mass was haematuria (93.61%). 41 subjects (87.23%) had anemia, 38 subjects (80.85%) had suprapubic pain, 53.19% had urgency, 38.29% had burning micturition, 34.04% had increased frequency, 27.65% had anorexia, 12.76% had pelvic pain, 10.63% had pain in flank, 6.36% had abdominal pain and 4.25% subjects presented with abdominal mass. Wong-You–Cheong et al. (2006)[4] observed that the most frequent presentations of bladder mass lesion were haematuria, Urinary tract infections, Irritative symptoms such as urinary frequency, dysuria, and urgency.

Most of the malignant lesions involved mostly base (79.48%) and lateral wall (46.15%) with irregularly (79.48%) walled isoechoic lesion (51.28%) with extension into perivesical tissue. Benign lesions showed involvement of lateral wall of urinary bladder (87.5%). These lesions revealed as irregularly margined (87.5%) mass lesion affecting base (62.5%) & lateral wall (87.5%). These were

the common findings of bladder masses found in previous studies.[4]

In present study it was seen that at histology, 21 cases (44.68%) were diagnosed as Transitional Cell carcinoma and 13 (27.67%) cases as Squamous cell carcinoma. 5(10.63%) cases were Adenocarcinoma, Cystitis and adherent blood clot to wall were found as four (8.51%) cases each. Among 47 cases, 39 cases (82.79%) were diagnosed as malignant and rest 8 (17.21%) cases were malignant found in histopathology. In USG, 38 (80.85%) were malignant and rest 9 (19.15%) were benign. Vikram, Sandler and Ng (2009)[3]; Wong-You–Cheong et al (2006)[4] observed that TCC accounts for approximately 90% of all bladder tumors. The second most common cell type is squamous cell cancer (8%), followed by adenocarcinoma. Other rarer subtypes such as small cell carcinoma account for less than 1% of the cases. Tubin et al, (2005)[13], also described that SCC is the second most common malignant tumour of urinary bladder. SCC appears as solid predominantly hypo echoic, flat infiltrative lesion. Often associated stone is seen. Sometimes it appears as poorly defined, irregular solid mass. Berlac et al, (1992)[14] reported that Adenocarcinoma of urinary bladder is rare tumour and often related with history of chronic cystitis. It is hypo to hyper echoic mass with presence of calcification. They are homogeneous to heterogeneous mass with poorly defined margin. Sometimes it shows central necrosis. Adherent blood clots are common benign urinary bladder mass in a patient with haematuria. They are ill-defined hyper echoic mass commonly found in base and lateral wall. Repeated sonography shows decreased in size or dislodgement of the mass from primary site.[13]. Cystitis appeared as focal thickening to polypoid hypo echoic mass lesion arising from lateral wall and base of urinary bladder. Mucosal edema and irregularity are associated features. They are usually associated with contraction of bladder.[15]

In current study, Considering histopathological diagnosis as gold standard test accuracy , sensitivity, specificity, PPV, NPV and accuracy of USG in diagnosis of malignant bladder mass were 97.44%,97.43%, 87.5%, 97.43% and 87.5% respectively. Stamatiou et al. (2009)[16] prospectively evaluated 173 patients presenting to the outpatient department with painless hematuria by transabdominal ultrasound and cystoscopy. For ultrasonography, the sensitivity (92%), specificity (98.1%), positive predictive value (94.4%) and negative predictive value (95.4%) were seen.

Conclusion

Ultrasonography is a non invasive available, radiation free procedure which is used as a first line preliminary diagnostic procedure. In present study it was observed that considering histopathological diagnosis as gold standard test accuracy, sensitivity, specificity, PPV, NPV and accuracy of USG in diagnosis of malignant bladder mass were 97.44%. 97.43%, 87.5%, 97.43% and 87.5% respectively. It was concluded that gray scale ultrasonography is a useful diagnostic tool for diagnosis of urinary bladder mass.

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A Study on Clinical and Aetiological Pattern of Chronic Diarrhoea in a Tertiary Care Hospital

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Abstract

Chronic diarrhoea is one of the most common conditions facing both primary care clinicians and gastroenterologists The present study was a cross-sectional study conducted on 100 patients at the Department Medicine and Gastroenterology of Sir Salimullah Medical College, Mitford Hospital, Dhaka. Patients with chronic diarrhoea of at least 4 weeks duration were enrolled in the study. Data were collected using a structured questionnaire. The mean age was 39.14± 14.74 years with a range of 18 to 70 years. The male to female ratio was roughly of 2:1. Among the female 24% were housewives. Equal percentages of patients had abdominal pain, anorexia & significant weight loss (64%). Other clinical features were anemia (34%) fever and rectal bleeding (24%). The leading diagnoses were irritable bowel syndrome (34%), ulcerative colitis (18%), intestinal tuberculosis (12%), chronic pancreatitis (6%), carcinoma colon, intestinal lymphoma, non specific colitis & Crohn's disease (4% each). Endoscopy of upper GIT was done in 14% patients, colonoscopy 66%, double balloon enteroscopy 6% and specific histological diagnosis found in 56%, 10% was non-specific, 6% was diagnosed by ultrasound and 1% by stool routine examination. It was found that IBS, inflammatory bowel disease and intestinal tuberculosis are the leading cause in our country. Aetiology of chronic diarrhoea can be diagnosed by good history, clinical examinations and an appropriate investigation of which colonoscopy is most useful.

Key words: *Aetiology, Chronic diarrhoea.*

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Introduction

Diarrhoea may be defined in terms of stool frequency, consistency, volume, or weight. Patients' conceptions of diarrhoea often focus around stool consistency [1], other criteria, such as the passage of more than three stools per day or stool weight, provide alternative means of definition. A stool weight of 200 g/day is often regarded as the upper limit of normal [2], but this can be misleading as stool weights vary greatly and "normal" stool volumes can exceed this value, particularly when non-Western diets are encountered. A pragmatic definition incorporates these elements: diarrhoea is the abnormal passage of loose or liquid stools more than three times daily and/or a volume of stool greater than 200 g/day. Faecal incontinence in particular is commonly misinterpreted as diarrhoea [3]. Most physicians will accept that symptoms persisting for longer than four weeks suggest a non-infectious aetiology and merit further investigation [4]. In two population surveys, Talley *et al* reported a prevalence of "chronic diarrhoea" of between 7% and 14% [5, 6].

Causes of chronic diarrhoea: Colonic- colonic neoplasia, ulcerative and Crohn's colitis, microscopic colitis. Small bowel- intestinal TB, coeliac disease, Crohn's disease, Other small bowel enteropathies, bile acid malabsorption, disaccharidase deficiency, small bowel bacterial over growth, mesenteric ischemia, radiation enteritis, lymphoma, giardiasis, Pancreatic-chronic pancreatitis, pancreatic carcinoma, cystic fibrosis, Endocrine-hyperthyroidism, diabetes, hypoparathyroidism, Addison's disease, Hormone secreting tumours, "Surgical" causes (e.g. small bowel

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resections, internal fistulae), Drugs, Alcohol, Autonomic neuropathy .

Presence of iron deficiency is a sensitive indicator of small bowel enteropathies particularly coeliac disease [7], frequently presenting with diarrhoea due to steatorrhoea and malabsorption. Serological screening studies using IgA antiendomysium antibodies (EMA) have shown a prevalence of between 1:200 and 1:559 in European and North American populations [8–12]. The prevalence is considerably higher when there is an associated autoimmune disease present or in patients with Down's syndrome[13]. The recent identification of tissue transglutaminase (tTG) as the auto antigen of EMA32 has led to the development of commercial ELISA kits for the detection of anti-tTG antibodies[14].

Protozoal infections, such as giardiasis and amoebiasis can result in chronic infections. Examination of three fresh stools for ova, cysts, and parasites remains the mainstay of diagnosis and has a sensitivity of approximately 60–90% for detection of these organisms. The use of a stool ELISA (92% sensitivity and 98% specificity) has largely replaced the need for intestinal biopsies and wet preparations [15–17]. Serological testing is not effective in cases of suspected giardiasis but can be useful in amoebiasis where positive serology by an indirect haemagglutination test or ELISA can differentiate invasive disease from the asymptomatic carrier state [18].Diarrhoea may be caused by colorectal neoplasia. In addition to neoplasia, colonoscopy also has a diagnostic yield for other conditions ranging from 7% to 31%, with inflammatory bowel disease and microscopic colitis being most commonly found [19, 20–22]. Routine ileoscopy further adds to the value of colonoscopy. In patients in whom a diagnosis of inflammatory bowel disease is suspected, the value of ileoscopy and biopsy is further enhanced: 36% of patients with a normal colonoscopy and diarrhoea had terminal ileal disease[23] .Colonoscopy is also the preferred modality to exclude or confirm microscopic colitis. Lymphocytic and collagenous colitis (collectively called microscopic colitis) are conditions with a similar natural history and often (in 25–30%) overlapping features [23,24].

Colonoscopy is a more sensitive test than barium enema and given this, and the need to obtain histology to exclude colitis, the former investigation is recommended [25, 26].Small bowel enteroscopy has been evaluated as a complementary investigation to small bowel barium follow through, either as a means to distinguish small bowel abnormalities or to assess further the small bowel after a negative radiological investigation [27].

Malabsorption may occur as a result of defective luminal digestion due to lack of pancreatobiliary enzymes, or from failure of absorption due to mucosal disease or structural disorders. Pancreatic exocrine insufficiency is the usual cause of severe and dominant steatorrhoea where faecal fat excretion exceeds 13 g/day. Loss of endocrine function generally occurs late in the course of chronic pancreatitis, although an impaired glucose tolerance test and even frank diabetes mellitus may be found in early or mild disease [27, 28]. ERCP is, at present, the "gold standard" for the diagnosis of chronic pancreatitis and uses the presence of abnormal duct morphology for the detection of chronic pancreatic disease[29]. Diarrhoea in diabetic patients has often been ascribed to abnormalities of small bowel motility due to autonomic neuropathy. Its prevalence is estimated at 2–10% predominantly occurring in type 1 diabetics with other manifestations of autonomic neuropathy.

Chronic diarrhoea patients in our country is often misdiagnosed and not properly treated. Often people blame various foods for this reason and avoid many nutritious foods. So my study may produce awareness among all level of medical practitioners about the aetiology, patterns of presentation and ways of diagnosis of chronic diarrhoea and thus helping the management of such case in future.

Methods

The present cross-sectional observational study was carried out in department of Medicine and Gastroenterology, Sir Salimullah Medical College Mitford Hospital, Dhaka from January 2014 to June 2014. Patients attending at indoor and outpatient department (OPD) of Medicine and Gastro-enterology with chronic diarrhoea were the study population. A total of 100 patients of chronic diarrhoea were selected for the study. chronic diarrhoea was defined by diarrhoea persisting more than four weeks.IBS was defined acccording to

ROME III criteria.A semi structured questionnaire was prepared after pre-testing containing patient profile. This was used for collection of information by interviewing & examining patients & their reports. Patient's age less than 18 year were excluded. Complete blood count, random blood sugar, Stool routine examination and Ultrasonography of whole abdomen were done in all patients some special investigations like endoscopy of upper gastrointestinal tract, colonoscopy, double balloon enteroscopy, anti-tTG antibodies were done in selected patient.

Results

A total of 100 patients of chronic diarrhoea were selected for the study. The purpose of the study was to find out aetiological pattern of chronic diarrhoea. Over one-third (36%) of the patients was of 41-50 years old, followed by 50% below 40 years old; 10% between 51-60 years and the remaining 4% above 60 years of age. The mean age was 39.14 ± 14.74 years and the minimum and maximum ages were 18 and 70 years respectively. Sixty six patients (66%) were male and the rest thirty four (34%) were female. The male to female ratio was roughly of 2:1.

Table-I

Distribution of patients by Signs associated with chronic diarrhea (n=100)

Signs	Percent
Anemia	34
Edema	12
Ascites	6
Abdominal mass	6
Hepatosplenomegaly	4

Out of 100 patients, ,24% were service holder, 20% businessmen 16% farmer, 8% student and and 8% were involved in other professions. Women were mainly housewives (24%).Most of the patients had abdominal pain, anorexia and weight loss (64% each).Rectal bleeding and fever were present in 24% the patients, 14% cases experienced vomiting.Anemia was present in 34% case while edema 12%,ascites 6%,abdominal mass 6% and hepatosplenomegaly in 4% cases.

Tabl-II

Distribution of patients by selective investigations (n=100).

Investigations	Cases	Abnormality found	Normal
Colonoscopy	66	56(84.8%)	10(15.4%)
USG of abdomen	54	14(25.9%)	40(74.1%)
Endoscopy of upper GIT	14	8(57.1%)	6(42.9%)
Double balloon enteroscopy	6	6(100%)	0

Colonoscopy was done in 66%, USG of abdomen in 54% endoscopy of upper GIT done in 14%, double balloon enteroscopy was done in 6% cases,Anti-Ttg was done in 10%. Biopsy material was taken in 8% of endoscopy of upper GIT done, 56% of colonoscopy done, 6% of double balloon enteroscopy done. Eight biopsies were taken through endoscopic procedure and 2 had confirmed specific diagnosis by histology examination. In colonoscopic and enteroscopic specimens 52 and 2 Specific histological diagnosis were found respectively. Out of 100 patients 8% got specific treatment, 72% got non-specific treatment, 20% got no treatment before study

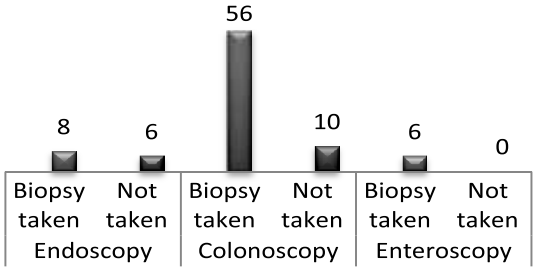

Fig.-1: *Distribution of patient on biopsy material taken or not (n=100)*

Table-III

Aetiological pattern of chronic diarrhoea (n=100)

Aetiology	Percent
Irritable bowel syndrome	34
Ulcerative colitis	18
Intestinal TB	12
Cause could not be ascertained	8
Chronic pancreatitis	6
Carcinoma colon	4
Lymphoma	4
Non specific colitis	4
Chron's Disease	4
Colonic polyp	3
Ca Rectum	2
Amoebiasis	1

Out of 100 patients 34% was diagnosed as irritable bowel syndrome,18% ulcerative colitis, 12% intestinal tuberculosis, 6% chronic pancreatitis, 4% carcinoma colon, 4% intestinal lymphoma, 4% non specific colitis, 4% Crohn's disease, 3% colonic polyp, 2% carcinoma rectum, 1% amoebiasis, and in 8% aetiology could not be ascertained.

Discussion

Diarrhoea is made up of two Greek words 'dia' and 'rhein' meaning 'through' and 'to flow' respectively. Hippocrates (460-370 B.C.) gave his clinical and epidemiological description of the entity of diarrhea [30]. The present study was conducted to find out the aetiological pattern, presentation and demographic pattern of sufferers of chronic diarrhoea in Bangladesh.

The mean age of patients was 39.14 ± 14.74 years. Half of the patients (50%) were below 40 years of age while 36% were 41-50 years old. In similar studies in USA Raj et al.[31] and Kenneth et al. [32]showed that the mean age of the patients of chronic diarrhoea were 51 years and 49 years respectively which are higher than our study population. In this study 50% of the patients were below 40 years as IBS is the commonest cause in our study which occurs in young age [33] In this study sixty six patients (66%) were male and thirty four (34%) were female. The male to female ratio was roughly of 2:1. A recent study[34] done on chronic diarrhoea in Bangladesh shows that over 60% of the patients were male and male to female ratio was roughly of 3:2 though IBS is more common in female. In this study 8% was student, 24% was service holder, 16% farmer, 20% businessmen, 24% housewives and 8% involved in other diverse professions indicates that majority of patients came from urban community .

Most of the patients had abdominal pain, anorexia and weight loss (64% each). Anemia was present in 34% case while rectal bleeding and fever were present in 24% cases. However, Rashed [35] in his study showed that 20% had abdominal pain and 91.4% had bleeding per rectum. Raj et al.[31]reported that 43% of the patients had abdominal pain while Rashid [34] showed that 92% had abdominal pain. Abdominal pain is therefore very common symptom of chronic diarrhoea. In this study anemia was present in 34% case. Rashid[34] and Raj et al.[31] showed in their study anemia were 40%and15% respectively, so anemia is the commonest sign in chronic diarrhoea cases.

In this study colonoscopy done in 66% cases. Not all patients underwent routine colonoscopy because appropriate investigation was done depending upon history and clinical examination. In a recent study Rashid [34] had done colonoscopy in 100% cases but biopsy materials were taken in 60% cases as in 40% colonoscopy were normal. In our study out of 66 cases 56(84.8%) had pathology. Endoscopy of upper GIT done in14 case and 8(57.1%) had pathology. So colonoscopy is therefore most useful investigation. Ian et al.[36] reported in a study that 35% of gastroenterologists almost always perform rectal biopsy. Double balloon enteroscopy done in patients with normal colonoscopy and endoscopy of upper GIT but suspected to have pathology. Double balloon enteroscopy done in 6 cases and 100%had pathology. Ultrasonography of abdomen was done in 54 cases and pathology found in14 (25.9%). Ultrasonography of abdomen helps in diagnosis of chronic pancreatitis and other cause of chronic diarrhoea.

In this study Biopsy material was taken in 56 cases among colonoscopy done, 8 cases among endoscopy of upper GIT done, 6 cases among double balloon enteroscopy done. Eight biopsies were taken through endoscopic procedure and 2 had confirmed specific diagnosis by histology examination. In colonoscopic and enteroscopic specimens 52 and 2 Specific histological diagnosis were found respectively. More than half (56%) of the patients had a specific histological diagnosis, 10% had a histological of nonspecific colitis. Rashid [34] showed in their study nearly half (48%) of the patients had a specific histological diagnosis, 10% had a histological of nonspecific colitis. Ian et al.[36]in their study showed that 87% the histology was entirely normal. In 28 cases (8%) there were non-specific histological abnormalities. A further search may be needed for this non specific colitis as microscopic colitis increasingly been identified as a cause of diarrhoea in patients with macroscopically normal mucosa [33].

In this study, before diagnosis 8% got specific treatment, 72% got non specific treatment like antidiarrhoeal 16%, antispasmodics 47%, and antihelminthic 41%, 20% got no treatment. This indicates that majority of chronic diarrhoea cases in our country are misdiagnosed and wrongly treated or untreated.

Thirty four percent patients were diagnosed as irritable bowel syndrome,18% ulcerative colitis, 12% intestinal tuberculosis, 6% chronic pancreatitis, 4% carcinoma colon, 4% intestinal lymphoma, 4% non specific colitis, 4% Crohn's disease, 3% colonic polyp, 2% Rectal polyp, 2% carcinoma 1% amoebiasis, rectum. In 6% cases aetiology could not be ascertained. Mohammed et al.[37] states that Crohn's disease in 38% and ulcerative colitis was the commonest from accounting for 48% of the patients. Rashed in the study showed that 27.4% had polyps. Raj et al. reported 6 % infectious diarrhoea, 1.9% NSAID associated colitis. 34% patients were diagnosed as having irritable bowel syndrome (IBS). A study conducted by Gonvers et al.[38] showed that 21.4% of the patients with IBS. Raj et al.[31] reported on 84 consecutive patients of chronic diarrhoea with final diagnoses that 55.9% of the patients ha IBS, 5.9% infection, 3.6% lactose intolerance, 2.4% bacteria overgrowth, 1.2% medication associated diarrhoea, 3.6% pancreatic insufficiency and 4.8% diabetic diarrhoea. In this study 12% is intestinal tuberculosis and prevalence of tuberculosis is more in our country. In this study our findings is IBS, IBD and intestinal tuberculosis is the most common cause chronic diarrhea which should be kept in mind among all doctors while dealing with chronic diarrhea case.

Conclusion

This study summarizes a practical approach to find out aetiology of chronic diarrhoea. Aetiology of chronic diarrhoea can be diagnosed by good history, clinical examinations and an appropriate investigation. It was found that irritable bowel syndrome, inflammatory bowel disease and intestinal tuberculosis are the leading cause in our country. Colonoscopy is the most useful tool for diarrhea patients.

Limitations

Like all other research work the current study also had some limitation. The study included only a single centre with a relatively small sample size which limits generalizability. There was limitation of time period. All investigations were not always feasible. Study was done in a tertiary hospital so the results do not reflect community scenario.

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Predictive Factors for Conversion of Laparoscopic Cholecystectomy into Open Cholecystectomy

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Abstract

Background: *Laparoscopic cholecystectomy (LC) has become the goldstandard in the treatment of symptomatic cholelithiasis. It has revolutionizedminimally invasive procedures. Laparoscopic cholecystectomy may berendered difficult by various problems encountered during surgery.Previous studies evaluating predictive factors for conversion from laparoscopic to opencholecystectomy have drawn conflicting conclusions. We evaluated preoperative variables as predictive factors for conversion of laparoscopic cholecystectomy.*

Purpose: *The aimof this study was to evaluate predictive factors for conversion of laparoscopic cholecystectomy into open cholecystectomy using the clinical, biochemical and ultrasonographic criteria.*

Methods: *A cross sectional study was carried out. Twelve variables were subjected to bivariate and multivariateanalysis to identify parameters that independently predict conversion to open cholecystectomy.*

Results: *Laparoscopic cholecystectomy was attempted on 500 patients for gall stone disease over 6 month period. Male (17%) and female (83%) ratio was 1:4.88. Total 47 (9.4%) cases needed conversions to open cholecystectomy. The most frequent reasons for conversion were dense and extensive adhesion adhesions (19.14%), friable, oedematous tissue in calot's triangle(19.14%), contracted small fibrotic adherent gall bladder (23.40%), uncontrolled bleeding (8.51%) and injury of billary tract(14.89%).Preoperative findings were co-releated with reasons for conversion to identifypredictive factors for conversion. Male gender, acute cholecystitis, Chronic cholecystitis with > 3 attack, previous upper abdominal surgery, diabetes mellitus, elevated whiteblood cell count,elevated serum alkaline phosphatase, elevated total bilirubin, ultrasound finding of pericholecystic fluidas well asgall bladder wall thickness ≥3 mm were foundas predictors of conversion. Among these, male gender, elevated WBC count, diabetes mellitus, elevated serum alkaline phosphatase, elevated serum bilirubin and ultrasound findings of pericholecystic fluid were found independently predictors of conversion on multivariate analysis and were associated with clinical diagnosis of acute cholecystitis.*

Conclusions: *These results demonstrate that conversion to open cholecystectomy can be predicted basedon parameters available preoperatively. Conversion is more likely in patients who have acutecholecystitis. Improvements in the ability to determine the risk for conversion have important implications forsurgical care.*

Key words: *Laparoscopic cholecystectomy, open conversion, predictive factor.*

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Introduction

Gall stone disease is a global health problem[1]. It is the most common biliary pathology. It may be either asymptomatic or symptomatic. Symptomatic gall stone diseases are acute and chronic cholecystitis with complications of acute cholecystitis such as empyema, perforation and gangrene. Surgical treatment of gall stone disease

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is cholecystectomy either open or laparoscopic. Carl-Langenbuch performed first ever cholecystectomy on 15 in July 1882 in Berlin on a 42 years old man. Laparscopic cholecystectomy first of all performed by Philipe Moret in Lyon, France in March 1987 has in fact revolutionized the treatment of cholelithasis[2]. Laparoscopic cholecystectomy has replaced open cholecystectomy as the therapeutic modality in the treatment of cholelithiasis.[3,4,5] It has become the gold standard in the treatment of symptomatic gall stone. Its benefits over open cholecystectomy include less patient discomfort, better cosmetic result, shorter hospitalization and more rapid return to full activities postoperatively.[6,7,8,9] Although laparoscopic cholecystectomy is attempted in majority of the cases but at times conversion to open procedure is needed.[10,11] Conversion to open cholecystectomy has been associated with increased overall morbidity surgical site and pulmonary infection, longer hospital stays and increase financial burden.[12,13] The ability to accurately identify an individual patient's risk for conversion based on preoperative information can result in more meaningful and accurate preoperative counseling , improved operative room scheduling and efficiency, stratification of risk for technical difficulty, and appropriate assignment of resident assistance, may improve patient safety by minimizing time to conversion, and help to identify patients in whom a planned open cholecystectomy is indicated. The aim of this study was to determine predictive factors of conversion in patients undergoing Laparoscopic cholecystectomy for various indications in elective and acute settings in a tertiary level of hospital.

Patients and method

This cross sectional study was conducted at department of surgery, Sir Salimullah Medical College Mitford Hospital from 30th September 2013 to 29th March 2014 over 6 months period. Patients were enrolled in our study from inpatient department of Sir Salimullah Medical College Mitford Hospital, Dhaka Medical College Hospital, Shaheed Suhrawardy Medical College Hospital and some other private hospitals in Dhaka, who were diagnosed to have gall stone disease on the basis of history, clinical examination and base line investigations along with USG of whole abdomen with special attention to hepatobiliary system. The inclusion criteria were symptomatic and asymptomatic gall stone disease with age > 18 years. Eexclusion criteria were co-morbid disease except Diabetes mellitus, biliary tract malignancy,obstructive jaundice with dilated common bile duct except due tocholedocholithiasis. All preoperative variables were recorded in data collection sheet from focused history, clinical examination and investigations. All patients were treated by experienced surgeons not below the position of Assistant Professor. Per operative findings were recorded including causes of conversion to open cholecystectomy. Total 500 patients with gall stone disease undergoing laparoscopic cholecystectomy wereobserved. These 500 samples were taken by purposive manner meeting the inclusion criteria (confidence level 95%).Statistical analysis for predictive factors, rate and causes of conversion were done with chi square test (χ^2). A p value <0.05 was considered statistically significant.

Result

Among 500 cases 85 were male (17%) and 415 were female (83%) with the ratio of 1:4.88, 65.2% was within 18 to 50 years age group, 24.8% was from 50 to 65 years and > 65 years were only 15%.Laparoscopic cholecystectomy could be carried out successfully in 90.6% and total 9.4% patients needed conversion to open cholecystectomy.The most frequent reasons for conversion were dense and extensive adhesion adhesions (19.14%), friable, oedematous tissue in calot's triangle(19.14%), contracted small fibrotic adherent gall bladder (23.40%), uncontrolled bleeding (8.51%) and injury of billary tract (14.89%). Acute cholecystitis were 25.2% among which 40.43% needed open conversion. In contrast, chronic cholecystitis were 49.8% among which > 3 attack were 67 (26.90%) and 44 patients were in conversion group (93.61%)Asymptomatic gall stone were 25% among which 6 patients needed conversion (12.77%) which was not statistically significant and history of

jaundice was also not significant.History of previous upper abdominal and lower abdominal surgery were 8 and 56 respectively. 7 out of 8 patients with previous upper abdominal surgery needed open conversion which was 14.89%.133 patients had elevated total leukocyte count (26.6%) and their conversion rate was 55.32% with p value 0.00006.Among 106 patients having elevated serum bilirubin (21.2%) 22 patient (46.81%) were in conversion group with p value 0.0001.183 patients (36.6%) had increased alkaline phosphatase. Among 47 open converted patients 36(76.59%) patients had elevated alkaline phosphatase. Diabetes mellitus was a predictive co-morbid disease and 93 patients (18.6%) having diabetes mellitus 20 (42.55%) patients were in converted group with p value < 0.001.Ultrasound findings of pericholecystic fluid, gallbladder wall thickness ≥ 3 mm were found to be predictive factor for conversion.

Twelve preoperative parameters were co-related with causesof conversion from laparoscopic to open cholecystectomy and ten were significant on bivariate analysis.

Table-I

Demographic characteristics

Frequency			Percent
Total patients		500	100%
Sex	Male	85	17%
	Female	415	83%
Age	18 to 50 years	326	65.2%
	50 to 65 years	124	24.8%
	>65 years	75	15%

Table-II

Sex distribution of the Laparoscopic cholecystectomy and open conversion of laparoscopic cholecystectomy.

Sex	OC(n-47)	LC (n-453)	p value
Male	14(29.8%)	71(15.7%)	0.01
Female	33(70.2%)	382(84.3%)	

OC : Open conversion

LC : Laparoscopic cholecystectomy

Table-III

Patients charecteristics with % of conversion

	Conversion number	Percentage(%)	p value*
Male	14	29.79	0.01
Female	33	70.21	> 0.05
Previous upper abdominal surgery	08	77.78	0.001
Previous lower abdominal surgery	02	4.25	>0.05
History of jaundice	07	14.89	0.16
Acute cholecystitis	19	40.43	0.01
Chronic cholecystitis with >3 attacks	44	93.62	<0.001
Asymptomatic gall stone	06	12.77	0.06
Elevated total leukocyte count	26	55.32	0.00006
Elevated Serum bilirubin	22	46.81	0.0001
Elevated serum alkaline phosphatase	36	76.60	<0.001
Diabetes mellitus	20	42.55	<0.001
Pericholecystic fluid	18	38.30	0.01
Gall bladder wall thickness ≥ 3 mm	17	36.17	0.04

Table-IV

Factors independently predictive of conversion to open cholecystectomy on multivariate analysis

Predictive factor	Odd ratio*	Risk ratio†	95% confidence interval
Male gender	2.28	2.07	9.12-23.81
Elevated total leukocyte count	4.0	3.42	2.08-7.74
Pericholecystic fluid	2.37	2.15	9.97-22.16
Diabetes mellitus	3.85	3.24	13.81-29.18
Elevated Serum bilirubin	3.87	3.27	1.99-7.51
Elevated serum alkaline phosphatase	6.81	5.67	3.23-14.66

* Odd ratio >1 significant
† Risk ratio > 1 significant

This study demonstrated that male gender, acute cholecystitis, choroniccholecystitis with >3 attacks, previous upper abdominal surgery, the presence of diabetes mellitus, elevated WBC count, elevated alkaline phosphatase, elevated total bilirubin, ultrasound findings of pericholecystic fluid and gall bladder wall thickness ≥ 3 mm were independent predictors of conversion.

Among these 10 factors 6 were more frequently identified in patients who had a diagnosis of acute cholecystitis. Factors evaluated but not found to be significant on bivariate analysis included asymptomatic gall stone disease on preoperative ultrasound, previous lower abdominal surgery, gall bladder wall thickness <3 mm, Chronic cholecystitis with d" 3 attack and previous history of jaundice.

Discussion

Gender is a prominent risk factor: women have a greater risk of gallstone disease (and undergoing cholecystectomy) than men at all ages and in the majority of studies. Women predominate, particularly when young (20-30 years of age), with a range of female-to-male ratio from 10:1 in Pima Indians to 2-3:1 in Europeans women; this ratio declines after the fifth decade.[14, 15]Female sex hormones are the obvious basis for this gender difference. It is thereforenot surprising to find that parity is a risk factor.[16] During pregnancy, biliary sludge(consisting of cholesterol crystals, calcium bilirubinate and mucin) develops in up to30%,[17] while gallstones form in 1-3%.[18] The link may be biliary sludge, a potential precursorto cholesterol gallstone formation. Following delivery, sludge disappears in overhalf, even as 30% of small stones (<10 mm diameter) vanish.[17]Such a return to normal, likely accounts for parity being only a modest risk factor. Estrogen is the culprit.[19] The current use of low-dose (compared to high dose >50 mg) oral contraceptives presents quite a modest risk that may even decrease with time.[20] In contrast, postmenopausal women on oestrogen replacement therapy have a definitely increased risk.[21]Preoperative and intraoperative factors that predict or contribute to conversion have been evaluated previously, but no consensus has emerged. A recent review by Tang and Cuschieri[22] identified 109 publications addressing this issue over 15 years. Among these studies, 4 scoring systems have been developed to predict conversion to open cholecystectomy.[23] This scoring systems have demonstrated variable and conflicting results and are affected by a small number of factors evaluated, inclusion of subjective variables, and collection of data early in the experience of laparoscopic cholecystectomy. None of these systems has been widely incorporated into surgical practice. Besides the only study to be validated prospectively had a negative predictive value of 100%, but the positive predictive value was only 43%.[24] Open conversion rate reported in literature is 2.2% to 13.9%.[25]Men have been identified to have a greaterincidence of conversion to open cholecystectomythan women.[26] Inflammation and dense adhesionsare frequently cited as reasons for conversion inmen.[26] Van der Steeg et al 169-173 showed 20.4% conversion rate in men and we have found conversion rate in men 29.79% which is slightly higher and had a significantly greater

incidence of acutecholecystitis. The pathophysiologic differences betweenmen and women with cholecystitis remain unclear. The presence of acute cholecystitis has been shown to predict conversion to open cholecystectomy.[27]In this study six factors that independentlypredicted conversion to open cholecystectomywere found significantly more frequently in patientswith clinical diagnosis of acute cholecystitis and among these five factors were found significant in the study by Lipman et. al. 556-65.The etiology of this associationis unclear. Chronic cholecystitis with > 3 attacks had higher conversion rate with significant result. The pathologic basis of this is unknown. Possibly frequent attack may cause more fibrosis and adhesion creating the anatomy unclear. Studies have demonstrated that previous upper abdominal operations increase the risk for conversion to open cholecystectomy.[28] This may be due to increased adhesion formation. It also makes the anatomy unclear and increases the possibility of injury of surrounding structure. However, we did not evaluate the specific location of the previous operation because the location of the incision may not entirely predict the area of adhesion formation or chronic inflammatory changes.[28] Diabetic patients undergoing laparoscopic cholecystectomyhave been found to have significantly increased rates of conversion.[28] The cause for the greater conversion rate in this group ofpatients is unclear. One explanation may be thepresence of more severe inflammation among diabeticpatients with acute cholecystitis comparedwith nondiabetics.[29] Because of autonomic and peripheralneuropathy; some diabetic patients maynot develop symptoms of gallbladder disease untillater in the course of their illness. This may lead todelayed diagnosis, which can result in more advanceddisease and a greater risk for conversion.[30] The association between an elevated WBC andconversion has been reported previously.[31,32] This parameter likely reflects the inflammatory responseassociated with more acutediseases and ismore commonly present with acute cholecystitis which is reflected well in this study.An elevated bilirubin has been previously recognizedas a significant predictor of conversion toopen cholecystectomy in acute cholecystitis.[28] Hyperbilirubinemia is most likely a marker for inflammationin this setting rather than an indicatorof biliary obstruction. Elevated bilirubin is also associatedwith Mirizzi syndrome, the presence ofwhich may increase the probability of conversion[33] though in this study we did not found any case of Mirizzi. Patients with elevated serum alkaline phosphatase had proved to be predictive factor and more frequently associated with acute cholecystitis. In acute cholecystitis and in CBD stone alkaline phosphatase raises due to inflammation of cholangiols. Pericholecystic fluid results from the translocationof fluid from the surrounding tissues owing tosevere inflammation of the gallbladder. This factorhas been previously demonstrated to predict conversion.[28] Inthis study, pericholecystic fluid and gall bladder wall thickness ≥ 3 mm werethe radiographic findings predictive of conversion. The most frequent reasons for conversion were dense and extensive adhesion adhesions (19.14%), friable, oedematous tissue in calot's triangle (19.14%), contracted small fibrotic adherent gall bladder (23.40%), uncontrolled bleeding (8.51%) and injury of billary tract(14.89%). Although our study has favorable characteristics to predict conversion from laparoscopic to open cholecystectomy, it has some limitations listed in limitation heading below. For patients with a high predicted rate of conversion, it may be advantageous to proceed with open cholecystectomy. This would negate the potential for trochar injuries, problems due to pneumoperitoneum peritoneum, and other complications specifically associated with laparoscopy. A high presumed risk for conversion was frequently cited as a reason for the use of a planned open approach. Because patients undergoing open cholecystectomy were not included in our analysis, the complication rate in patients who had conversion to open operation may be lower than would have been seen if all cholecystectomies were initially approached laparoscopically. These results demonstrate that an accurate and easily derived estimation of risk for conversion from laparoscopic to open cholecystectomy can be obtained from readily available preoperative data. Recognizing when a patient is at increased risk for conversion would improve preoperative counseling, assist with appropriate allocation of resources in the operating room, may increase safety by limiting delay in conversion to open cholecystectomy, and can

identify patients who might benefit from a planned open approach.

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Serum Homocysteine Levels in Metabolic Syndrome Subjects - An Original Article

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Abstract

Metabolic syndrome (MS) is not only the problem of western countries but also hidden burden for Bangladeshi population and other developing countries. Several complications of MS are Coronary artery disease, cardiovascular disease, cerebro vascular disease, peripheral vascular disease. Hyperhomocysteinemia worsen the complications of metabolic syndrome. Evaluation of serum Homocysteine level in MS subjects is an indicator of cardio metabolic disease. A cross sectional analytical study was carried out from July 2012 to May 2014 in the department of Biochemistry, Sir Salimullah Medical College & Mitford Hospital and National Health Care Institute (Branch of BIRDEM, 10/A Dhanmondi), Dhaka, with the objective to evaluate the association of serum Homocysteine level with components of Metabolic syndrome. A total of 100 subjects with age range 20-50 years were selected, 50 of them had MS and fifty were apparently healthy. Anthropometric measurements (BMI, WC, HC, WHC), blood pressure, biochemical parameters of the study subjects were evaluated. Fasting serum glucose, total cholesterol, triacylglycerol, LDL-C and homocysteine levels were significantly higher in metabolic syndrome subjects compared with the subjects without MS. In addition, serum HDL-C levels were significantly lower in subjects with metabolic syndrome. There is significantly positive correlation between serum homocystein level and total cholesterol and also with triacylglycerol levels.We concluded that the subjects with metabolic syndrome suffer from dyslipidaemia and hyper homocysteinaemia. These findings of our study will help the metabolic syndrome subjects to develop awareness for modification their lifestyle and dietary habit.

Keywords: *Metabolic syndrome, Serum Homocysteine level.*

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Introduction

Metabolic Syndrome is not only the problem for the affluent class and the western countries, but also a new hidden burden for developing countries and for the Bangladeshi population too. People with metabolic syndrome (MS) have greater risk of developing type-2 diabetes mellitus and atherosclerosis [1]. Homocysteine (Hcy) contributes to development of atherosclerosis and thereby cardiovascular disease[2]. Hyperhomocysteinaemia causes atherosclerosis by damaging the inner lining of arteries and promoting thrombosis through pathological collagen activation of the intrinsic pathway[3]. The elevation of Hcy occurs particularly in patients with type 2 diabeties, as well as in individuals in prediabetic states[2, 4].

Atif et al. (2008)[5] observed that among the hypertensive subjects 80% were hyper-homocysteinaemic. Obesity contributes to hypertension, high serum cholesterol, low HDL-C and hyperglycaemia, and is independently associated with higher cardiovascular disease risk[6]. Waist Circumference (WC) was found to be the best predictor of intra abdominal fat thickness and therefore of central obesity. Central obesity is a prerequisite risk factor for MS. Elevated Hcy levels are related mostly to abdominal obesity[7]. High serum TG levels and low serum HDL-C levels are independent risk factors for thrombosis and cardiovascular diseases, even in tightly controlled serum LDL-C levels[8]. Folic acid supplementation

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decreases fasting serum Hcy level in coronary artery disease patients [9].

This study was designed with the objective to evaluate serum homocysteine level in MS subjects. Serum Hcy level can be reduced through dietary measures, modification of sedentary life style and vitamin supplementation thereby decreasing the risk of MS induced health hazards.

Material and Methods

This cross sectional analytical study was carried out from July 2012 to May 2014 in the department of Biochemistry, Sir Salimullah Medical College & Mitford Hospital and National Health Care Institute (Branch of BIRDEM, 10/A Dhanmondi), Dhaka. Permission of the study was taken from the concern department and authorities. All participants were informed and explained about the nature of this study and gave written informed consent for the study.

All the participants were adult & middle aged male and female. One hundred subjects were selected**.** Out of them fifty were with metabolic syndrome (Group I) and fifty were without metabolic syndrome (Group II), between the ages of 20-50 yrs. Metabolic syndrome was diagnosed if any three or more of the following conditions were present according to National Cholesterol Education Program & Adult Treatment Panel III 2001(NCEP ATPIII 2001)[10]

I) Waist circumferencence ≥102cm for men and ≥88 cm for women,

II) Fasting plasma glucose ≥6.1mmol/L(110mg/dl

III) TG ≥ 150mg/dl,

IV) HDL-C ≤40mg/dl for male and ≤50mg/dl for women,

V) Systolic BP ≥130 mm of Hg & Diastolic BP≥85mm of Hg.

Subjects with coronary heart disease, significant valvular disease, life-threatening systemic disease, chronic obstructive pulmonary diseases, pregnant women, female taking oral contraceptive pill & also post menopausal women, subjects receiving steroid, antidepressants and anticonvulsants drugs were excluded. All the anthropometric measurements and sample for the measurements of fasting serum Hcy, blood glucose (FBG), total cholesterol (TC), triacylglycerol(TG) , HDL-C, LDL-C were taken after overnight fasting of at least 12-14 hrs . Height was measured (without shoes) by height and weight measuring digital instrument and taken to nearest centimeter. Body weight was measured in light clothing and without shoes. Weight was recorded to the nearest kg. Body mass index (BMI) was calculated as weight in kg divided by height in meter square. Waist circumference (in centimeter) was measured at midway between costal margin and iliac crest. Hip circumference (in centimeter) was taken as the maximum circumference at the posterior extension of the buttocks (Trans trochanteric). Waist hip ratio is then calculated by (WC/HC) Serum Hcy Assay is based on the Flurosence polarization immuno assay (FPIA) technology by Abbott Axsym system, USA was performed at the department of Biochemistry in BSMMU. Other biochemical parameters were done by enzymatic method, serum fasting HDL-C by Phosphotungstate / magnesium method and serum fasting LDL-C cholesterol was estimated by Friedewald formula by Semi auto analyzer. Data were collected, compiled and tabulated according to key variables. The analyses of different variables were done according to standard statistical analysis by using SPSS-17. The data presented on categorical scale were expressed as frequency and corresponding percentage, while the quantitative data were expressed as mean and standard deviation (±SD). For all analyses level of significance were set at 0.05 and p-value <0.05 were considered significant.

Result

Age distribution among the metabolic syndrome subjects and apparently healthy subjects without metabolic syndrome were depicted in table I. Female were predominated in both groups. 60% of total study population was female , 64% in group I and 56% in group II. Table II shows Anthropometric measurements and blood pressure of the study population. All the parameters showed significantly higher values in group I than that of group II ($p<0.001$). Table III shows Biochemical parameters of the study population. Serum FBG, TC, TG, LDL-C and Hcy were significantly higher in MS subjects than that of without metabolic syndrome subjects. On the other hand, HDL-C was significantly lower in group I than that of group II. In table IV Pearson correlation analysis showed that serum Hcy had significantly positive

correlation with serum TC (*r* 0.352, *p* 0.003) and TG (*r* 0.352, *p* 0.012) in MS, but not correlated significantly with BMI, WC, WHR, Systolic blood pressure (SBP), diastolic blood pressure(DBP), FBG, LDL-C and HDL-C in subjects without metabolic syndrome.

Table I
Age distribution of study subjects

	Group-I n=50	Group-II n=50	Total
21-30 years	01 (02%)	06 (12%)	07%
31-40 years	26(52%)	32 (64%)	58%
41-50 years	23(46%)	12 (24%)	35%
Mean(±SD)	41.10(±5.52)	38.48(±6.37)	26-50 years

Table II
Anthropometric measurement and blood pressure of the study groups.

	Metabolic syndrome subjects (Gr-I) n=50 Mean (±SD)	Without Metabolic syndrome subjects (Gr-II) n=50 Mean (±SD)	*P* value
BMI kg/m^2	32.05 ±2.89	25.40 ±1.71	< 0.001
WC in cm	106.65 ±10.61	74.91±7.26	< 0.001
HC in cm	99.86 ±9.11	82.61±6.93	<0.001
WHR	1.06 ±0.07	0.86 ±0.07	< 0.001
SBP (mm of Hg)	137.7 ±11.70	116.00 ±5.05	< 0.001
DBP (mm of Hg)	86.80 ±7.19	72.30 ±6.99	< 0.001

Table III
Biochemical parameters of the study population

	Metabolic syndrome subjects (Gr-I) n=50 Mean ±SD	Without Metabolic syndrome subjects (Gr-II) n=50 Mean ±SD	*P* value
Serum FBG (mmol/L)	9.59 ±02.15	4.87±0.58	<0.001
TC (mg/dl)	218.20 ±85.49	122.82 ±10.62	<0.001
TG(mg/dl)	223.16 ±83.03	124.82 ±12.57	<0.001
LDL-C (mg/dl)	141.98 ±28.07	97.24 ±11.26	<0.001
HDL-C (mg/dl)	35.34 ±04.10	45.64 ±01.56	<0.001
Serum Hcy (µmol/L)	5.78±6.70	13.48 ±3.42	<0.05
Range	15.59-35.28	7.17-20.55	

Table IV
Correlation of serum Hcy level with the components of MS

Variables	Metabolic syndrome		Non Metabolic syndrome	
	r	*P* value	*r*	*P* value
BMI kg/m^2	.161	0.264	-.172	.233
WC in cm	-.009	0.951	-.123	.396
WHR	-.014	0.922	.126	.382
SBP (mm of Hg)	.154	0.285	-.234	.101
DBP (mm of Hg)	.142	0.325	-.135	.349
Serum FBG (mmol/L)	-.130	0.369	-.051	.723
TC(mg/dl)	.352	0.003	.053	.713
TG(mg/dl)	.352	0.012	.053	.713
LDL-C(mg/dl)	.246	0.086	.131	.363
HDL-C(mg/dl)	-.175	0.225	-.040	.780

Discussion:

In this cross sectional study 100 subjects were included, 50 were with metabolic syndrome and 50 were without metabolic syndrome.

In this study mean age was 41.10(±5.52) years in group-I and 38.48(±6.37) years in group – II (range 26-50 yrs). Among both genders female were predominant comprising 60% of the study subjects. It is evident from the study that BMI was significantly higher in MS (32.05 ±2.89 kg/m^2) than without MS subjects (25.40 ±1.71 kg/m$^{2)}$. Similar observation was found in other studies [2,11,12]. This study shows that waist circumference of group I (106.65 ± 10.61 cm) differ significantly from that of group II (74.91 ± 7.26 cm). Present study is in agreement with other studies [2, 11]. In this study it was also found that WHR in MS subjects (1.06 ± 0.07) were higher than without MS subjects (0.86 ± 0.07). This finding is consistent with others [13]. Central obesity is a key feature of metabolic syndrome, reflecting the fact that the MS prevalence is driven by the strong relationship between waist circumference and increasing adiposity [14].

It was observed in our study that both SBP and DBP were significantly higher in MS subjects in comparison to group II. Similar findings were found in other studies [2,11]. The increase in adipose tissue also increases the number of immune cells present within, which play a role in inflammation. Chronic inflammation contributes to an increased risk of

hypertension, atherosclerosis and diabetes [15]. It becomes evident in our study that almost all the subjects of MS had been suffering from either diabetes mellitus or impaired fasting blood glucose. Similar results were found by others [2, 11]. Adipocytes of the visceral fat increase plasma levels of tumor necrosis factor-alpha (TNF-±) and alter levels of a number of the other substances (adiponectin, resistin and plasminogen activator inhibitor-1). TNF-± has been shown not only to cause the production of inflammatory cytokines, but also possibly to trigger cell signaling by interaction with a TNF-± receptor that may lead to insulin resistance[16]. Hypoadiponectinemia has been shown to increase insulin resistance[17] and is considered to be a risk factor for developing metabolic syndrome[18].

In this study it was observed that athrogenic components of lipid profile (TC, TG & LDL-C) were significantly higher in subjects with MS. However, serum HDL-C was found to be reduced significantly when compared with healthy subjects. These findings are in agreement with other studies [2,11,19]. The pathophysiology leading to the typical dyslipidemia of the MS is quite well understood, but whether dyslipidemia more commonly precedes follows or occurs simultaneously with the development of hypertension remain unclear. Incresed release of the free fatty acids from adipose tissue, particularly from visceral fat into portal vein, stimulates the production of triglyceride-rich lipoproteins in the liver with the release of more and larger VLDL particles. This intern has effects on other lipoprotein particles, resulting in reduced levels of HDL-C [5].

The present study shows that serum Hcy levels were significantly higher in MS than that of healthy individual. It was also found that serum Hcy were associated with TC and TG but not with LDL-C and HDL-C. Similar results were reported by other workers of different countries [2,11,,20,21]. But different results were found in studies of Others.[7,19]. They revealed no significant relationship between serum Hcy with the components of MS. However, it was also evident from their studies that Hcy levels are also related to serum creatinine, vitamin B_{12} & folic acid level.

Hcy may play a role in the pathogenesis of hypertension is based on the fact that Hcy induces arteriolar constriction, renal dysfunction and increased sodium reabsorption, increased arterial stiffness[22]. Hcy also increases oxidative stress, which causes oxidative injury to the vascular endothelium, diminishing vasodilation by nitric oxide, stimulating proliferation of vascular smooth muscle cells and altering the elastic properties of the vascular wall, leading to hypertension [22]. High WHR observed in this study suggests that that most MS subjects were of central obesity. This is in agreement with the study of others[24], who found that increased Hcy levels were related mostly with abdominal obesity. The elevation of Hcy occurs particularly in patients with type 2 diabetes, as well as in individuals in prediabetic states [2,4]. Hcy regulate glucose metabolism and insulin function[20].

Endothelial dysfunction is an early manifestation of atherosclerosis in patients with diabetes and caused by hyper homocysteinaemia [23]. Thus it is evident from the study that Hcy is associated with MS.

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Review Article

Transfusion associated Graft Versus Host Disease : A Short Review

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Abstract:

Transfusion-associated graft-versus-host disease (TA-GvHD) is a rare, but almost universally fatal, iatrogenic complication of transfusion. All blood components like whole blood, red cells, platelets and granulocytes containing viable lymphocytes can potentially cause TA-GvHD. Frozen components and fractionated components have not been implicated in TA-GvHD. This disease was first reported in humans in 1959 after allogeneic bone marrow transplantation (BMT). Shared HLA types between the recipient and the donor is the main point of focus. The basis of pathogenesis is the transfusion of immunocompetent T lymphocytes which are not cleared by the recipient and subsequently engraft and proliferate in the recipient's bone marrow and give rise to disease state. A diagnosis of TA-GVHD is a clinicopathologic diagnosis requiring a high index of suspicion and should be considered in any patient with fever, erythema, neutropenia, diarrhea, and hepatitis within 30 days of a transfusion with non-irradiated cellular blood products . TA-GvHD is fulminant and rapidly fatal in the vast majority of cases. Death occurs on average 51 days following the transfusion. The case fatality rate approaches nearly 100%. The incidence of TA-GvHD is uncertain and may be underestimated due to a lack of recognition and under-reporting. In susceptible recipients the frequency may be 0.1-1% without appropriate preventative strategies. There is no effective treatment for TA-GvHD, management focuses almost entirely on prevention by irradiation of cellular blood components that are intended for susceptible recipients. As TA-GvHD is almost invariably fatal, the prime objective is prevention. Irradiation of blood products and leukoreduction by specialized filters can be considered sufficient for prevention of TA-GvHD. Case reporting systems should be more effective. Radiation of blood products is needed in indicated situations. The routine irradiation of blood products in Bangladesh is not justified at present.

Key Words: *TA-GvHD, Transfusion hazards, Irradiation of blood and blood products.*

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Introduction

Transfusion-associated graft-versus-host disease (TA-GvHD) is a rare, but almost universally fatal, iatrogenic complication of transfusion. The inherent risk associated with an individual transfusion depends on the interplay of several factors, including the number and viability of contaminating lymphocytes in the transfused cellular component, the susceptibility of the patient's immune system to the engraftment of donor lymphocytes, and the degree of immunological (human leucocyte antigen, HLA) homology between the donor and the recipient.[1] Although the graft-versus-host disease (GVHD) that occurs after allogeneic bone marrow transplantation and TA-GVHD share some clinical similarities, GVHD after bone marrow transplant is not uncommon and often responds positively to immunosuppression.[2]

This disease was reported in humans in 1959 after allogeneic bone marrow transplantation (BMT).[3] The much rarer TA-GVHD, however, in contradistinction to bone marrow GVHD, is associated with destruction of the recipient's bone marrow, does not respond to immunosuppressive therapy and is generally fatal.[4] Because there are no effective treatments for TAGVHD, management

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of this complication focuses almost entirely on prevention by irradiation of cellular blood components (whole blood, red blood cells , granulocytes, and platelets) that are intended for susceptible recipients. Over the past 10–15 years, the use of irradiation in high-risk situations has reduced the incidence of TA-GVHD in the Western world and Japan to almost undetectable levels.[5]

Pathogenesis

Billingham defined the three main requirements for the development of GVHD. These are:

1. The graft *must* contain immunologically competent cells.
2. The host must possess important transplantation alloantigens that are lacking in the donor graft, so that the host appears foreign to the graft and is therefore capable of stimulating it antigenically.
3. The host itself must be incapable of mounting an effective immunological reaction against the graft, at least for sufficient time for the latter to manifest its immunological capabilities; that is, *the graft must have the security of tenure*.[6]

TA-GvHD is a rare but serious complication of cellular blood component transfusion. Donor lymphocytes were first implicated in GVHD in the 1950s.[7] An inability of the host's immune system to recognize and/or eliminate foreign donor cells in allogeneic blood components was subsequently identified as a key mechanism.[8] Some of the first reported cases of GVHD attributed to transfusion occurred in immunocompromised infants and fetuses,and are likely to have inspired the historical attribution of TA GVHD to immune defects of the transfusion recipient; however, cases of a frequently fatal "postoperative erythroderma" syndrome concentrated in Japan were reported earlier, without initially identifying the significance of transfusions received by the subjects.[9] GVHD occured in subjects with immature immunological system eg. in neonates and infants.[10] HLA similarity between donor and recipient, and specifically, donor homozygosity for an HLA haplotype for which the recipient was heterozygous, was a likely explanation for the cases occurring within and beyond Japan in transfusions from related donors.[11,12]

The main requirement for the development of GVHD is that of shared HLA types between the recipient and the donor. In a normal recipient, immune cells will far outnumber donor-derived T cells, which are therefore eliminated by a host-vs-graft reaction. However, if a small number of functional T lymphocytes are transfused which derive from a donor who is homozygous for one of the recipient's HLA haplotypes, the recipient will not recognize these cells as foreign. The donor T cells will, however, recognize the host as foreign, undergo clonal expansion and establish TA-GVHD. This situation is referred to as a one-way HLA match.[13] The basis of pathogenesis in this condition is the transfusion of immunocompetent T lymphocytes which are not cleared (as normally occurs) by the recipient and subsequently engraft and proliferate in the recipient's bone marrow. Survival of these transfused lymphocytes may occur either as a result of shared human leucocyte antigen (HLA) epitopes and/or recipient immunosuppression. Engraftment and proliferation of CD4+ and CD8+ T cell lineages and subsequent immunologic responses culminate in GvHD. Recipient HLA class II antigens as well as minor histocompatibility antigens are presented to donor lymphocytes resulting in T lymphocyte activation, proliferation, cytolytic activity and cytokine liberation. The cytokine release and direct cytotoxic effect of the donor T cells produce the constellation of signs and symptoms associated with GvHD. (14) Donor B cells have also been observed to produce cytotoxic antibodies.[15]

Transfusion-associated microchimerism (TA-MC) is a condition that occurs after transfusion of cellular blood components, in which a small number of donor allogeneic lymphocytes proliferate within a host and remain detectable for years. TA-MC is associated with perhaps 10% of patients transfused after sustaining traumatic injury, but is not known to have any clinical sequelae.[16] Recently cases of long-lived lymphocyte survival and "engraftment" have been demonstrated in the setting of massive transfusion following trauma as well as in post-partum women. Such lymphocyte engraftment results in microchimerism without causing TA-GvHD. Why microchimerism can persist without evolving into overt disease remains to be elucidated, however, in some studies, the presence of such microchimerism has been linked to development of autoimmune disease.[17]

Clinical features of TA-GvHD

TA-GvHD presents clinically like GvHD associated with allogeneic haematopoietic stem cell transplantation (HSCT), with multisystem and cutaneous involvement. However, when compared with transplant-associated GvHD, the transfusion-associated syndrome typically manifests earlier. Fever is most commonly the first presenting symptom, occurring as early as day 4 post-transfusion, with a median onset of 10 days, with most patients developing signs and symptoms 2-30 days after transfusion.[18] The diagnosis of TA-GVHD requires a high degree of clinical suspicion, particularly given the relatively long latency period between transfusion and the development of symptoms (up to 30 days). In addition, if patients are critically ill at the time of their transfusion, it may be difficult to differentiate the clinical signs of TA-GVHD from their underlying illness. For these reasons, TA-GVHD may be underdiagnosed.[19]

According to criteria devised by the National Health and Safety Network (NHSN), the diagnosis of TA-GVHD is based upon a combination of characteristic clinical findings and a tissue biopsy consistent with GVHD, with imputability established via the demonstration of leukocyte chimerism, specifically donor lymphocytes in recipient tissue (Table 1)[20]

Table-I

National Health and Safety Network TA-GVHD case definitions and determination of imputability

Transfusion-associated graft vs. host disease (TAGVHD)

Case Definition	Severity	Imputability
Definitive: A c inicai syndrome occurring from 2 days to 6 weeks after cessation of transfusion characterized by; • Characteristic rash: erythematous, maculopapular eruption centrally that spreads to extremities and may, in severe cases, progress to generalized erythroderma and hemorrhagic bullous formation • Diarrhea • Fever • Hepatomegaly • Liver dysfunction (i.e., elevated ALT, AST, Alkaline phosphatase, and bilirubin) • Marrow aplasia • Pancytopenia AND Characteristic histological appearance of skin or liver biopsy. **Probable:** Meets definitive criteria EXCEPT Biopsy negative or not done. Non.se vers: N/A **Possible:** N/A	**Severe:** N/A **Severe:** Patient had marked symptoms and responded to treatment. **Life-threatening:** Patient had severe symptoms and required life-saving treatment (e.g.. immunosuppression). **Death:** The recipient died as a result of the adverse transfusion reaction. Death should be used if death is possibly, probably or definitely related to transfusion, If the patient died of a cause other than the transfusion, the severity of the reaction should be graded as appropriate given the clinical circumstances related to the reaction. **Not Determined:** The severity of me adverse reaction is unknown or not stated.	**Definite:** WBC chimerism present in the absence of alternative diagnoses. **Probable:** WBC chimerism present BUT Other potential causes are present (e.g. stem cell transplantation). **Possible:** WBC chimerism not present or not done OR Alternative explanations are more likely (e.g.. solid organ transplantation). **OPTIONAL** **Doubtful:** Evidence is clearly in favor of a cause other than the transfusion, but transfusion cannot be excluded. **Ruled Out:** There is conclusive evidence beyond reasonable doubt of a cause other than the transfusion. **Not Determined:** The relationship between the adverse reaction and the transfusion is unknown or not stated.

The case fatality rate for TA-GVHD approaches 100%.[4,21] Nonetheless, a diagnosis of TA-GVHD should be considered in any patient with fever, erythema, neutropenia, diarrhea, and hepatitis within 30 days of a transfusion with non-irradiated cellular blood products (whole blood, RBCs, granulocytes, or platelets). It is notable that reports of TA-GVHD have never been attributed to transfusions with plasma, cryoprecipitate, factor concentrates, albumin, intravenous immunoglobulin, or previously frozen, deglycerolized RBCs. This is presumably due to the absence of sufficient viable donor lymphocytes in these products.[1] An erythematous maculopapular rash indistinguishable from that complicating HSCT subsequently develops.

Gastrointestinal complications may range from abdominal pain to profuse bloody diarrhoea. Liver dysfunction manifests predominantly as a cholestatic hepatitis due to lymphoplasmacytic infiltration of portal tracts and damage to bile duct epithelium with consequent destruction of bile ducts. Bone marrow failure, presenting as progressive pancytopenia with neutropenic infections, occurs at a median of day 16. The bone marrow aplasia is the most significant contributor to the dismal prognosis in TA-GvHD. TA-GvHD is fulminant and rapidly fatal in the vast majority of cases. Death occurs on average 51 days following the transfusion.[22]

Immunosuppressive regimens including corticosteroids, antithymocyte globulin and OKT3 have yielded poor results with only a few documented survivors.[18] The clinical presentation in infants and neonates is similar to that seen in adults, however, the interval between transfusion and symptom evolution may be delayed compared with that seen in adults.[23] If TA-GVHD is suspected clinically, donor lymphocytes can be differentiated from host lymphocytes by measuring differences in restriction fragment length polymorphisms or numbers of short tandem repeats between the donor and the host. These tests can be performed using molecular assays that are routinely utilized to detect donor–recipient chimerism in patients who have undergone allogeneic stem cell transplantation.[19] One strategy is to biopsy both affected and unaffected patient tissues and to compare the results to samples obtained from the blood donor (if available).[1]

Blood components associated with TA-GvHD

All blood components containing viable lymphocytes potentially can cause TA-GVHD. Whole blood, red cells, platelets and granulocytes have been implicated as causes of TA-GVHD. Frozen components and fractionated components have not been implicated in TA-GvHD.[2]

Incidence

The incidence of TA-GvHD is uncertain and may be underestimated in the world literature due to a lack of recognition and under-reporting. In susceptible recipients the frequency may be 0.1-1% without appropriate preventative strategies. As the clinical signs and symptoms are non-specific and may mimic drug reactions, viral infections and autoimmune conditions, the diagnosis is often delayed and may be missed. Therefore, TA-GvHD should be suspected in any patient presenting with rash, fever, liver dysfunction and gastrointestinal symptoms with a recent history of transfusion.[24] One study showed 61.6% of those diagnosed with TA-GVHD were male with median age at diagnosis was 58 years. The most frequent underlying diagnoses or indications for transfusion on those cases were non-cardiac surgery cardiac surgery, hematologic malignancy and congenital immunodeficiency.[9]

Histological diagnosis of TA-GvHD can be made from any affected tissue, although skin biopsies are usually the most easily accessible. While the histological findings are characteristic, they are not pathognomonic. Bone marrow biopsy frequently reveals a variably hypocellular marrow with a lymphocytic infiltrate. Haemophagocytosis may be prominent. HLA typing plays a central role in the diagnosis. DNA-based analysis demonstrating foreign cells or DNA in the recipient's circulation or in tissue infiltrates is more sensitive than serological methods.

Diagnosis

TA-GvHD is a clinicopathologic diagnosis requiring a high index of suspicion. As the clinical signs and

symptoms are non-specific and may mimic drug reactions, viral infections and autoimmune conditions, the diagnosis is often delayed and may be missed. Therefore, TA-GvHD should be suspected in any patient presenting with rash, fever, liver dysfunction and gastrointestinal symptoms with a recent history of transfusion.[24] Histological diagnosis of TA-GvHD can be made from any affected tissue, although skin biopsies are usually the most easily accessible. While the histological findings are characteristic, they are not pathognomonic. Bone marrow biopsy frequently reveals a variably hypocellular marrow with a lymphocytic infiltrate. Haemophagocytosis may be prominent. HLA typing plays a central role in the diagnosis. DNA-based analysis demonstrating foreign cells or DNA in the recipient s circulation or in tissue infiltrates is more sensitive than serological methods.[2]

Risk factors and clinical scenarios associated with TA-GvHD

1) **Recipient-related factors**: Transfusion recipients most vulnerable to TA-GvHD are those with congenital or acquired immunodeficiencies. These render the recipient at risk of engraftment by donor lymphocytes, due to an inability to recognise these cells as foreign and consequent failure to destroy them. Foetuses, low birth weight and premature babies are at particular risk, and some authors suggest all newborns should also be considered as at risk. Acquired cellular immunodeficiency may result either from disease states (such as haematologic malignancy) or be therapy-related (such as purine-based chemotherapeutic agents and in organ transplantation). Older age has also been implicated as a putative risk factor, with over 80% of patients with TA-GvHD being older than 65. However, it is not clear whether these reports simply reflect the typical age of transfusion recipients rather than any inherent susceptibility. Case series from the UK Serious Hazards of Transfusion (SHOT) data and other reports have highlighted coronary artery bypass grafting as a potential predisposing factor. (12) (25) Among immunosuppressed patients, those considered at highest risk for the development of TA-GVHD include patients with severe T-cell immunodeficiency syndromes (e.g., severe combined immunodeficiency or DiGeorge syndrome), patients undergoing allogeneic or autologous bone marrow transplant, patients diagnosed with Hodgkin's lymphoma or aplastic anemia on immunosuppressive therapy, neonates, a fetus receiving intrauterine transfusions, and patients being treated with purine analogs (fludarabine, cladribine,or deoxycoformicin) or alemtuzumab (anti-CD52). dared to be lower compared to the first groups listed above. No cases of TAGVHD attributed only to immunodeficiency caused by HIV/AIDS (in the absence of other conditions listed above) have been reported in the medical literature to date.[1,2,26] Cardiopulmonary bypass and extracorporeal circuits have been shown to have an immunomodulatory effect, causing a transient reduction in lymphocyte function in immunocompetent patients.[27] However, it is unclear whether cardiac surgery produces the immunosuppression required for TA-GvHD or whether the increased incidence merely reflects the high number of donations used in this setting.[25]

2) **Donor-related factors**: Presence of a one-way HLA match between donor and recipient (the donor is homozygous for an HLA haplotype for which the recipient is heterozygous) is associated with a significantly increased risk of TA-GvHD. Owing to HLA similarities between donor and recipient, donor lymphocytes are not rejected as foreign. This is the likely mechanism of underlying TA-GvHD in immunocompetent transfusion recipients. In a heterogeneous Caucasian population, the calculated risk of a patient with a particular HLA haplotype receiving a transfusion from a donor homozygous for the same HLA haplotype was reported as 1 in 7174, which translates to an actuarial risk of TAGvHD due to homozygous HLA-haplotypes at 1 in 17,700-39,000. A significantly higher risk in populations such as the Japanese, who

have higher degrees of HLA-homology, translates into the Japanese population risk being estimated at 1 in 1160 to 7900. The highest proportion of cases in the literature have been reported from Japan.[28] In a case of intrauterine transfusion of non-leukoreduced non-irradiated maternal blood to a anaemic fetus due to maternal parvovirus infection, the fetus was delivered as pancytopenic. HLA typing showed mother to be HLA homozygous with unidirectional tolerance to her baby. The neonate was diagnosed as TA-GVHD and died later on.[29] Cases have been reported in this subcontinent among unrelated HLA homozygous donor[30], following blood transfusion from a first-degree relative[31], whole blood transfusion from an unrelated donor in an immunocompetent patient[32], immunocompromised patient by acute myeloid leukemia by unrelated donor.[33]

3) **Blood component-related factors**: The principal risk factor here is the number of viable lymphocytes in the component. The minimum number of viable T cells required for TA-GvHD is unknown. As few as 104 per kg may be lethal in immunocompromised hosts.[34] Further, reports have suggested that TA-GvHD may occur with transfusion of as few as $8x10^4$ lymphocytes. The viability of lymphocytes is not constant throughout storage life and decreases as a function of component age, with the greatest risk being during the first 3 days, after which lymphocyte viability decreases exponentially. Further studies using flow-based assays detected essentially no viable T cells surviving in cold storage in red cells beyond 3 weeks.[35]

Thus, three significant factors appear to directly relate to increased risk of TA-GvHD including:

1. Susceptibility of the recipient's immune system to engraftment by donor lymphocytes
2. HLA homology between recipient and donor
3. Number of viable lymphocytes transfused.

Principles of prevention of TA-GvHD

Although the introduction of universal leukoreduction is associated temporally with a reduction in the reported incidence of TAGVHD, cases of TA-GVHD have been reported in patients receiving leukoreduced (but nonirradiated) cellular blood transfusions.[36] In addition, the minimum dose of lymphocytes required to cause TA-GVHD in humans is not precisely known, and it may be influenced by factors that are not likely to be fully known prior to transfusion. These factors include the degree of HLA match between donor and recipient, the viability of the remaining transfused lymphocytes, and the degree of immuno-suppression of the recipient. Consequently, leukoreduction alone is not considered to be sufficient prophylaxis against TA-GVHD; irradiation of cellular blood components is the only widely recognized method to prevent TA-GVHD in all cellular blood components.[1]

As TA-GvHD is almost invariably fatal, the prime objective is prevention. The principles central to prevention of TA-GvHD include the following:

(1) Appropriate clinical use of blood transfusions: Transfusion of blood components should be in accordance with relevant guidelines to ensure clinical appropriateness of indication, component and dose; to avoid unnecessary transfusions; and to thereby minimise transfusion-associated risks.

(2) Irradiation of blood components: Irradiation of cellular blood components is the mainstay of TA-GvHD prevention. Ionising radiation doses are employed that inhibit the proliferative ability of lymphocytes, while preserving the integrity of the component to be transfused. Dosing of radiation: Initial work based on abolition of MLC reactions suggested that a dose of 15 Gy was sufficient to inactivate lymphocyte responses. TA-GVHD has, however, since been reported following components irradiated with 20 Gy. Techniques of residual T lymphocyte growth detection have led to the recommendation of 25 Gy as the appropriate dose.[29]

A current list of indications from hospitals of USA and Canada showing indication for irradiation of blood components for prevention of TA-GVHD is shown in Table 2.[9]

Table-II
Irradiation of Blood components for prevention of TA-GVHD

Indication	Institution		
	MGH	SBK/UHN	HSC
Stem cell transplant recipients	√	√	√
Congenital immuno deficiencies or infants with features suggestive of an undiagnosed immunodeficiency	√	√	√
Intrauterine transfusion	√	√	√
Premature, low birth weight	√	√	√
Term infants (<6m old)	√	√	√
Acute lymphoplastic leukemia	√	√	√
Other lymphoid malignancies	√	√	√
Acute myeloid leukemia	√		√
Chronic leukemias	√		√
Stem cell donors during harvest	√		
Fludarabine, Alemtuzumab, and ATG recipients	√	√	√
Children on intensive myeloablative chemotherapy regimens	√		√
Children with solid tumours or malignant hematologic disease			√
Children with solid organ transplants			√

MGH= Massachusetts General Hospital, Boston, United States; SBK= Sunnybrook Health Sciences Centre, Toronto, Canada; UHN= University Health Network, Toronto, Canada; HSC= Hospital for Sick Children, Toronto, Canada

(3) Directed transfusions and donations from HLA-selected/matched donors: Directed transfusions from family members significantly increase a recipient's susceptibility to TA-GvHD, as blood relatives share HLA haplotypes, thus increasing the risk of a one-way matched transfusion. Therefore, directed transfusion from relatives should not be encouraged outside specific medical indications. These are rare, and include patients who have rare blood groups or antibodies to high incidence antigens. Directed family donations and HLA-matched or otherwise selected donations should always be irradiated before being transfused.[2]

A more precise list of indications for radiation is as follows who are at particular risk of TA-GvHD. These include:[37]

- Patients receiving transfusions from family members, tissue type matched donors or granulocyte (a type of white blood cell) donors
- Patients with an inherited immune system disorder
- Patients who have developed an immune system disorder, such as Hodgkin's disease; or due totreatment with certain drugs; or because of a bone marrow/stem cell transplant
- Unborn babies and babies needing exchange transfusions.

Important topics regarding prevention of TA-GvHD :-

a) Avoidance of transfusion of fresh blood

There is some evidence that the fresher the blood the higher the risk of TA-GvHD. Case series have identified use of "fresh blood", evidenced by the fact that in about 90% of cases of TA-GvHD in the United States transfused blood was less than 4 days old.[23,28] Further studies examining the influence of storage on T-cell function and survival have demonstrated that, after 2 weeks of storage, leucocytes progressively undergo apoptosis and lose their in vitro proliferative ability.[29] Consideration could be given to using red cells that have been stored for greater than 1 week in at risk patients and cardiac surgery patients, as fresh blood (7

days).[18] Outside of large volume transfusions to neonates, there are no other established specific medical indications for blood less than 5 days old.[25] However, there is little evidence to guide practice in this area and the potential adverse effects related to duration of storage, including potassium leakage and cytokine generation, must also be considered. Other potential adverse effects of the blood storage lesion are the subject of active research but are as yet unresolved.

b) Universal leucocyte depletion of cellular blood components

With the implementation of universal pre-storage leucodepletion for cellular components such as red cells and platelets in many centres around the world, there are emerging data to suggest that leucodepletion may reduce the incidence of TA-GvHD. For example, according to the UK SHOT data (SHOT report 2007), thirteen cases of TA-GvHD were reported between 1996 and 2001. Only two of these thirteen cases occurred in patients who received leucodepleted units. Of these 2 cases, one was a patient with myeloma and the other a child with relapsed acute leukaemia. No cases have been reported in immunocompetent recipients since the implementation of routine leucodepletion in the UK in 2001. While this may reduce the incidence of TA-GvHD, especially in immunocompetent recipients, by reducing the number of viable lymphocytes in a transfused component, it does not obviate the need for irradiation of blood components in at risk patients.[21]

Conclusions and Recommendations

Graft-versus-host disease after transfusion continues to be reported both in recipients known to be at risk for this complication and in those who are not thought to be immunodeficient. The incidence of the disease among the former may reflect a lack of awareness of this complication on the part of those caring for the patients, and that among the latter highlights our inability to define all the risk factors for transfusion-associated graft-versus-host disease. More generalized recognition of this syndrome, prompt reporting of all cases, and studies of the recipients' immune status may allow more precise categorization of patients at risk. It is well accepted that patients who have congenital immunodeficiencies or those who undergo bone marrow transplantation should routinely receive only irradiated blood components. Blood products for intrauterine transfusion should also be irradiated. The other indications for irradiation are less well delineated.[40]

Irradiation of blood products in Bangladesh is still not established so far. TA-GVHD cases are under reported along with low reporting of transfusion associated reactions due to absence of a strict reporting system and protocols. Documented cases are very few in comparison to proper figure. Preventive radiation should be carried out in necessary cases. In hemolytic disease of the newborn, and in premature or newborn infants, the necessity of prevention remains controversial. Patients with cancer may be immunocompromised as a result of their underlying disease, chemoradiotherapy, or both. Within this group, however, patients receiving high-dose chemoradiotherapy (e.g., in preparation for autologous marrow transplantation) and those with Hodgkin's disease appear to be at the highest risk for the disease.

Finally, immunocompetent patients who share an HLA haplotype with HLA-homozygous blood donors appear to be at risk for transfusion-associated graft-versus-host disease. On this basis, it has been recommended that donations of cellular blood components from the recipient's first-degree relatives also be irradiated. In view of the millions of patients who receive transfusions annually and the rarity of transfusion-associated graft-versus-host disease, the routine irradiation of blood products in Bangladesh is not justified at present.

Conflict of interest

The author has not communicated any conflict of interest.

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Case Report

OHVIRA Syndrome - An Unusual Presentation

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Abstract

OHVIRA (Obstructed Hemi-Vagina and Ipsilateral Renal Anomaly) syndrome also known as Herlyn-Werner-Wunderlich (HWW) syndrome, is a rare Mullerian duct anomaly with uterus didelphys, unilateral obstructed hemivagina and ipsilateral renal agenesis. Patients with this anomaly usually present after menarche with pelvic pain and/or a mass and rarely in late ages with primary infertility.

An 18 years old married girl presented with lower abdominal pain, dysmenorrhoea, foul smelling vaginal discharge and was admitted in Obs and Gynae department of Sir Salimullah Medical College and Mitford Hospital. According to clinical presentation, physical examination and investigations she was diagnosed as a case of OHVIRA syndrome. The patient was treated surgically by creating an opening in the septum between the two hemivagina and drainage of haematocolpos. The outcome was satisfactory and patient was relieved of symptoms.

OHVIRA syndrome should be considered among the differential diagnosis in young females with renal anomalies presenting with pelvic mass, symptoms of acute abdomen, and acute urinary retention.

Key Words: *OHVIRA Syndrome, Renal agenesis, Herlyn-Werner-Wunderlich (HWW) syndrome, Mullerian anomaly, Mesonephric anomaly.*

(Sir Salimullah Med Coll J 2015; 23: 95-98)

Introduction

OHVIRA syndrome is a mesonephric duct induced Mullerian agenesis. This rare entity consists of a triad of uterine didelphys, obstructed hemivagina and ipsilateral renal agenesis[1,2]. Patients with these anomalies may remain symptomless till their menarche, after which they usually present with pelvic pain, dysmenorrhoea and /or a mass, and in later years, with primary infertility or poor pregnancy outcome[3]

By the end of the 20th century embryology of female urogenital system was accepted to be a truly- settled issue. But some complex uterine anomalies like OHVIRA syndrome still defied conventional theory of urogenital development until recently when theory of development of entire vagina from mesonephric duct was postulated by Acien[4]. Here we are presenting an 18 year old married girl who reported to hospital with the features of OHVIRA syndrome.

Case Report

An 18 years old married girl presented with history of lower abdominal pain and dysmenorrhoea since her menarche, which became severe in recent days. She also complained of foul smelling vaginal discharge. She had menarche at 11 years and a normal menstrual cycle of 7/30 days. She was married for 3yrs but had no issue.

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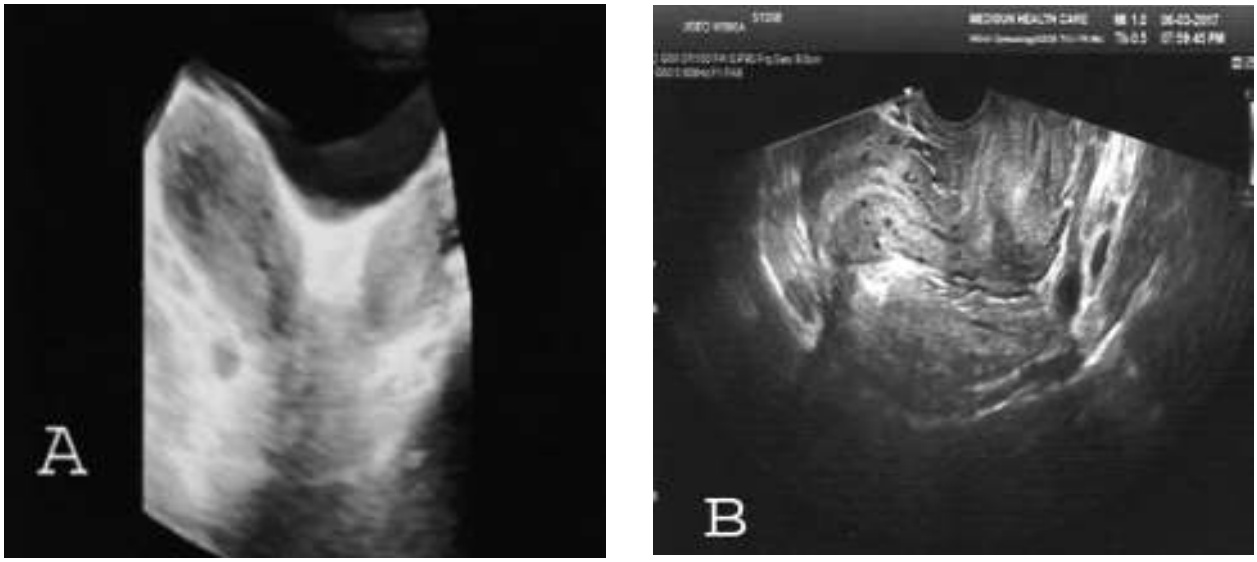

Fig.1.(A,B): *TVS shows uterine didelphys with right sided hematocolpos due to partial septum in the lower vagina.*

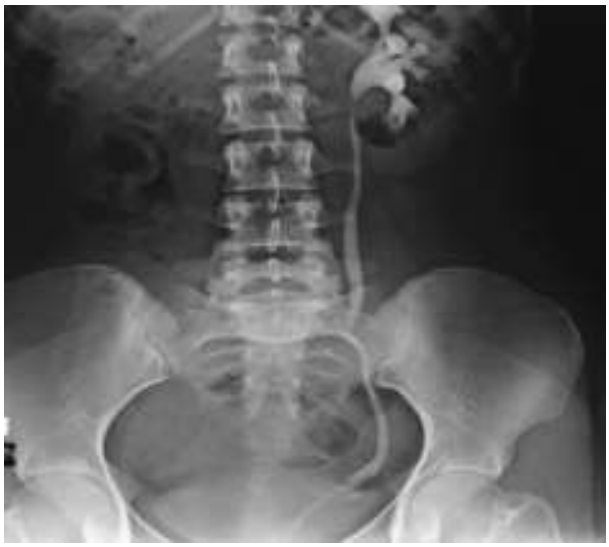

Fig.2. *IVU shows Non-visualized right kidney (probably agenesis).*

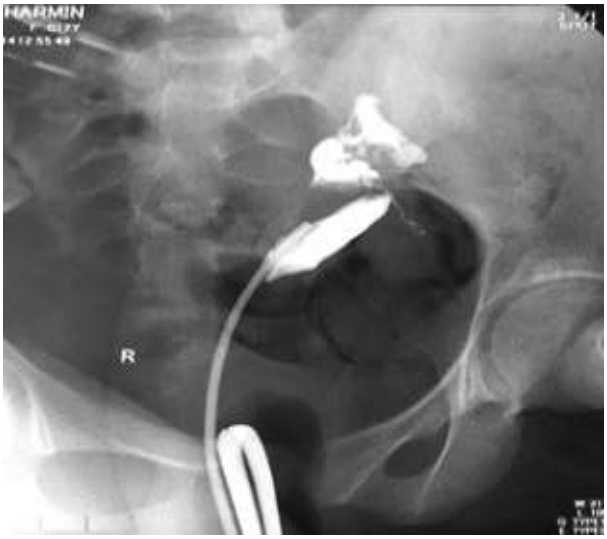

Fig.-3: *Hysterosalpingography shows unicornuate uterus with single patent dilated tube, as right sided vagina obstructed, dye could not be passed through right cervix.*

Physical examination revealed the followings: Findings of per abdominal examination were unremarkable. Per vaginal findings: on inspection, external genitalia were found normal. Per speculum examination showed apparently healthy cervix. Bimanual examination revealed a bulge on the right side of vagina, other fornices were normal, uterus was also normal in appearance and size.

Laboratory findings were within normal ranges USG of whole abdomen and TVS suggested uterine didelphys with right sided hematocolpos due to partial septum in the lower vagina and non-visualized right kidney. IVU showed non-visualized right kidney (probably agenesis). DTPA renogram revealed normal functioning left kidney, and non-visualized right kidney.

Hysterosalpingogram showed unicornuate uterus with single, patent dilated tube. (As right sided vagina obstructed dye from passing through right cervix).

The patient was treated surgically by creating an opening in the septum between two hemivagina and draining the collection into patent left hemivagina. Patient was relieved of symptoms. The surgical outcome was satisfactory with expectation of near normal fertility and normal sexual abilities.

Follow up: As advised at the time of discharge, the patient reported to our department during her next menstrual cycle. Now patient is free of symptoms and on examination, menstrual blood was found to come through surgically created right cervical opening as well as left cervical opening.

Discussion

OHVIRA syndrome is a rare congenital anomaly of paramesonephric (Mullerian) and mesonephric (Wolffian) ducts. The triad of uterine didelphys, obstructed hemivagina and ipsilateral renal anomaly was initially reported in 1955[5]. Incidence of these anomalies is believed to be between 0.5 to 5[6]. Approximately 75% of patients with dydelphys uterus have a complete or partial vaginal septum which is most commonly longitudinal in HWW syndrome and is thought to reflect a disorder of lateral fusion between the interior of the two mullerian ducts[7]. A strong association of renal agenesis with uterus didelphys (81%) has also been reported[8].

To understand the pathogenesis of Mullerian anomalies with renal abnormalities, the embryology of uterovaginal development needs to be reviewed. The classic theory of vaginal development says that upper part of vagina develops from Mullerian (paramesonephric) duct and the lower part from sinovaginal bulbs, derived from urogenital sinus. The fusion of two sinovaginal bulbs forms the vaginal plate, which canalizes later to form vaginal lumen.

The classic theory was found inadequate in explaining complex Mullerian malformations like OHVIRA syndrome. Acien proposed that, while uterus and cervix were derived from fused paired paramesonephric ducts (2nd part) and divergent distal paramesonephric ducts (3rd part), the vagina was completely mesonephric origin, although its lining reveals Mullerian cells derived from Mullerian tubercle.

An early failure of metanephric diverticulum to develop from mesonephric duct results in agenesis of ureteric bud, which leads to agenesis of ipsilateral ureter and kidney. Due to failed positioning of paired paramesonephric ducts, the two hemiuteri & hemicervices fail to unite, resulting in uterus didelphys. In OHVIRA syndrome, developmental arrest of ipsilateral mesonephric duct results in failure to distal hemivagina to develop, thereby resulting in obstructed hemivagina[9]. Renal agenesis predicts an ipsilateral obstructive Mullerian duct abnormality in 50% cases. The right side is affected nearly twice more frequently than the left one[10,11].

Typically, the most common findings of a patient with OHVIRA syndrome are- pelvic pain shortly following menarche, in association with vaginal or pelvic mass and normal menstrual cycles. Pelvic examination may show a bulging vaginal mass. However, a vaginal mass may be small and difficult to determine[9,12].

OHVIRA (HWW) syndrome is commonly diagnosed at the time of menarche. Rarely, the clotted blood may become infected, leading to a condition termed as pyocolpos[13], which can lead to pelvic inflammatory disease and tubo-ovarian mass / abscess. Patients start to experience abdominal and less commonly perineal discomfort, secondary to enlarging haematocolpos. In case of infected haematocolpos-fever, chills, nausea, vomiting and foul smelling vaginal discharge may also be present.

Delay in diagnosis is common due to a number of factors, especially in incomplete hemivaginal obstruction; as there is normal menstruation from non obstructed side and outflow obstruction is not suspected[14,15,16].

Although, now-a-days, MRI is considered as the gold standard tool for diagnosis and preoperative planning for treatment, transvaginal ultrasound has traditionally been the preferred initial imaging modality due to low cost[7]. Hysterosalpingography may also help in diagnosing the condition. Laparoscopy is not needed for the diagnosis of most of the cases[17].

Most patients with OHVIRA syndrome can be treated solely with single-stage vaginoplasty. Vaginal stenosis is a postoperative possibility, and may be associated with vaginal adenosis.

Conclusion

OHVIRA (HWW) syndrome is a rare anomaly with potential short and long term complications. The diagnosis is likely to be missed because of normal menstruation and nonspecific abdominal pain. So, seeing patients diagnosed with renal agenesis, all health care providers should be aware of the possibility of associated uterine and vaginal abnormalities. Conversely, in patients with uterine and vaginal abnormalities, work up for associated abnormalities, especially renal developmental defects should be performed. Initial work up should include vaginal examinations as well as transvaginal ultrasound and/or pelvic MRI.

An early correct diagnosis is the key to relieving the symptoms and preventing the complications, and also to preservation of sexual and conception abilities.

Reporting such cases will increase awareness among the health care providers about the syndrome and will help to achieve early diagnosis followed by appropriate treatment and thus, to avoid potential complications. Further research is needed to find out a precise embryological explanation of these developmental defects and to characterize risk factors for such defects in order to minimize morbidity from the conditions.

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