Editorial

Skin Bank - Hope for the Patients of Major Burn

Skin is the largest human organ which protects us from heat, cold, UV rays, and bacteria and enables us to have our sense of touch. Our skin is capable of mending itself from regular wear and tear. But when it is badly burnt or damaged, it is unable to repair itself and in such cases, skin transplant is preferred, as a way to promote healing. A person can survive with more than 60% damage to other organs, such as liver and kidney, but loss of more than 40% of the skin by burn may be fatal, unless the lost skin is replaced. The unburnt skin in a major burn patient is not sufficient to cover the wound even after meshing of skin graft.[1] Available skin substitutes such as Integra may be not economical for burn patients, amniotic membrane is not available everywhere. In such situation, cadaveric skin graft may be the major source of the skin. In Bangladesh, burn injuries are increasing due to high density population, rapid urbanisations and industrialisation and most of them require skin cover. In case of massive burn, there is deficient donor skin and immediate early wound excision and cover can be done with skin allograft.

Skin Banking is a process in which skin is removed from a donor body, tested for suitability as a graft material, packaged, stored, and finally reused as a graft. In case of smaller percentage of burns, skin from the un-burnt area of the patient is taken out and put on the burn wound to cover it. But when burns percentage is more than 40% to 50%, then the patient's own skin is not available to cover the burn wound. In that scenario we need some skin substitutes. It is said that skin is the best substitute for skin.[2] The harvested skin from brain dead and dead donor is the best and cheapest substitute compared to artificial skin substitutes. Such skin is a temporary dressing and it tears off after 2 to 3 weeks. But, it is important as it helps in patient's own skin to regenerate. The advantages of skin allograft are- it reduces fluid, electrolyte, and protein loss, reduces potential infectious disease transmission, reduces hypermetabolic phases, prevents tissue desiccation, suppresses bacterial proliferation, reduces pain, reduces energy requirements, stimulates epithelialization, and prepares wounds for definitive cover. 80% of major burn patients can be saved if we have enough skin in skin bank.

One can donate one's skin above 18 years age within 6 hours after death to save someone else's life. Deceased person should not be suffering from any diseases like AIDS, HIV, Hepatitis B and C, Tuberculosis, Jaundice, Sexually Transmitted Diseases, skin cancer, active skin disease and septicemia. Before harvesting the skin, a blood sample is taken for necessary tests and after harvesting skin sample is sent to exclude skin diseases. Unlike other transplant, in skin transplant[3], there is no blood or tissue matching between donor and recipient required. Anyone's healthy skin can be put on any one. Skin allograft can be harvested, processed and preserved for upto five years in one of the following three methods- glycerol preservation, deep freezing, cryo preservation[3]. Realizing the importance of tissue banking and adequate reports on successful allografting, numerous tissue banks have been established around the world in past few decades. History of tissue banking is as old as use of skin grafting. Reverdin in 1869 described skin graft in clinical practice for the first time. In 1871, George Pollock used his own skin along with patient's skin for coverage of a burn wound. Girdner in 1881, first reported successful use of Cadaver allograft in burn wound. Wentscher in 1903, reported that skin graft stored in refrigerator after harvesting, retain their viability for 3-14 days. Following these successes, clinicians started using more allografts for wound coverage to save major burns patients. US navy established its first tissue bank in 1949. As development in field of skin grafting was going on, use of bone graft also progressed[4]. In India first skin bank was established at Mumbai in 2000 and it was only one skin bank before 2009. Now skin bank has been established in many states of India and in some states there are multiple skin banks.

In Bangladesh, tissue-banking research started in the '90s at Bangladesh Atomic Energy Commission (BAEC) with support from IAEA Research Programme. From 1997 to 2002. Bangladesh received required skills development training and research assistance under the IAEA-Gi Regional Cooperative Agreement. Later in 2003, BAEC launched an independent laboratory - Tissue Banking and Biomaterial Research Unit in Savar. It was renamed as Institute of Tissue Banking and Biomaterial Research (ITBBR) in 2017[5]. Since its establishment, this tissue banking institute follows the guidelines of the IAEA and European association of tissue banks. However, after a

long negotiation between scientist, physicians, politicians, tissue bankers, and social religious representatives, the Human Organ/Tissue Donation and Transplantation Act was adopted and the National Parliament of the People's Republic of Bangladesh approved it on 13 April 1999. Govt. of Bangladesh has approved the lawful, ethical and legal permission for procurement of tissues from living donors as well as from deceased onesrequiring consent from the donor or next of kins. The Act was amended by the Parliament on January 8, 2018, with the changes came into effect shortly afterwards on January 28. The Act was revised to extend a living donor pool from close relatives (e.g., parents, adult sons and daughters, adult brothers and sisters, uncles and aunts from both the paternal and maternal sides, and spouses) to include certain other relatives such as grandparents, grandchildren, and first cousins. The Act was also revised to allow individuals to prioritize family members in receiving their organs after their death[5].

The Institute of Tissue Banking and Biomaterial Research (ITBBR) controls microbiological quality of the grafts and stores them at minus 40 to 80 degree Celsius following guidelines from the International Atomic Energy Agency (IAEA). From 2009-2020, the bank has provided more than 1.39 lakh cubic metres of bones and 54,768 pieces of amniotic grafts to hospitals and clinics for use in various surgeries for a nominal price. Apart from collecting and supplying amniotic sacs and bone tissues, the bank has so far helped in transplanting 347 skulls[6]. Till now ITBBR has no skin bank.

The first skin Bank in Bangladesh has been successfully set up at Sheikh Hasina National Institute of Burn and Plastic Surgery (SHNIBPS) in 2021. But it is yet to start the procedure, as it needs proper campaigning[7]. As Bangladesh is a densely populated country, it is difficult for a single unit to cover the entire country's need. That's why, as a short term measure, ITBBR can take initiative to establish skin bank with its existing facilities. As a long term measure, seperate skin bank can be established at each divisional medical college hospital.

Nowadays, organ donation of the kidney, liver, and eye is becoming common, and skin donation should also be promoted. Awareness program for the public about skin donation should be emphasized along with other organ donation. Government and nongovernmental organizations, print media, electric media should be used to spread the knowledge about skin donation. People of Bangladesh have a religious fear for donating and taking deceased biomaterials. Cultural factors also play a major role in the disparities in access to cadaveric organ and tissue procurement in Bangladesh. Many people believe that skin is harvested from whole body causing disfigurement of the deceased and the deceased needs to take to skin bank which is hazardous. Theses are far from truth and there is lack of awareness on these issues. Skin is harvested from back of trunk, thigh and leg by a team who will reach to donor's place. Recently, the government has approved a Tk 173-crore project for the expansion of the ITBBR and establishment of a full-fledged Human Tissue Bank. We hope the institution will include skin bank in this project and expand the new project in each existing Atomic Energy Commission countrywide so that the patients across the country can avail these services at a nominal price. As SHNIBPS has set up first ever skin bank in Bangladesh, the model of this institution can be replicated in each divisional medical college hospital for establishment of new skin bank. We can also take supports from other countries who has full functioning skin bank.

Md. Tarikul Islam
Associate Professor, Department of Burn & Plastic Surgery, Khulna Medical College, Bangladesh. Email: tarikpsbd@gmail.com

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Original Article

Effect of Normal Third Trimester Pregnancy on Some Coagulation Parameters: A Cross-Sectional Study

Jolly SS[1], Sardar MMR[2], Pervin F[3], Rupa SN[4], Kabir F[5], Akter S[6]

Abstract

Background: Hemostatic abnormalities are associated with various complications of pregnancy. So hemostatic changes in pregnancy are significant and essential, and have the potential to cause adverse pregnancy outcome.

Objectives: The objectives of this study was to evaluate fibrinogen levels and platelet count among different age groups in apparently healthy pregnant women at 3rd trimester and to compare it non-pregnant healthy women.

Methods: A cross sectional analytical study was carried out in the Department of Physiology in collaboration with Department of Obstetrics and Gynecology of Rajshahi Medical College and Hospital, Rajshahi and Other clinics of Rajshahi City from July 2016 to June 2017. Study population was 60 healthy persons, out of them 30 were apparently healthy pregnant women, 30 were non-pregnant healthy women in the age group of 20-35 years. Study subjects were selected by simple random sampling technique. Plasma fibrinogen level and platelet count was measured using auto analyzer. The test of significance was calculated by using unpaired student-t test. P value at or less than 0.05 was considered as significant.

Results: Plasma fibrinogen level was significantly increased in the 3rd trimester of pregnancy, whereas platelet count was non-significantly decreased in comparison to non-pregnant healthy women.

Conclusion: Pregnancy is a physiological process. Coagulation parameters are altered as well as balanced during normal third trimester pregnancy. If this balance is disrupted, adverse outcome may occur.

Key words: Fibrinogen levels, platelet count, coagulation parameters, pregnancy

Introduction

Hemostatic complications often occur during pregnancy, delivery and puerperium leading to high maternal and fetal morbidity or mortality. Pregnancy and puerperium are well-established risk factors for venous thromboembolism (VTE), with an incidence 4-5 times higher compared to non-pregnant women especially in the third trimester of pregnancy and in the period of puerperium. Pregnancy is normally associated with significant changes in all aspects of the Virchow's classical triad: venous stasis, endothelial damage and a tendency to enhanced coagulation resulting in a shift of the hemostatic balance towards hypercoagulability.

This is one of the protective mechanisms involved in avoiding serious bleeding complications at delivery.[1]

Fibrinogen, a blood coagulation parameter and a positive acute phase protein. It is helpful in diagnosing DIC or hyper fibrinolysis. However, the conventional cut-off points and reference ranges for these parameter are mostly determined in non-pregnant women. So the estimation of plasma fibrinogen is helpful not only in the early diagnosis of hemostatic failure but also to guide replacement therapy during decrease fibrinogen.[2]

1. Sayeda Sultana Jolly, Assistant Professor, Department of Physiology, Khulna City Medical College, Bangladesh.

2. Md. Mijanur Rahman Sardar, Associate Professor (C.C), Department of Physiology. Khulna Medical College, Bangladesh.

3. Farhana Pervin, Associate Professor (C.C), Department of Pharmacology and Therapeutics, Sheikh Sayera Khatun Medical College, Gopalgonj, Bangladesh

4. Shamima Nazneen Rupa, Assistant Professor(C.C), Department of Physiology, Rajshahi Medical College, Bangladesh

5. Farjana Kabir, Assistant Professor(C.C), Department of Physiology, Rajshahi Medical College, Bangladesh

6. Shireen Akter, Assistant Professor, Department of Skin and VD, Khulna Medical College, Bangladesh

 Corresponding Author:

Dr. Sayeda Sultana Jolly, Assistant Professor, Department of Physiology, Khulna City Medical College, Bangladesh. Email: dr.jolle@gmail.com

Platelet plays an important role in hemostasis by forming primary (temporary) hemostatic plug when blood vessels are injured[3]. However thrombocytopenia affects 6-10% of all pregnancies. A decrease in platelet count is normal in pregnancy although most platelet counts remain within normal limits. A lower than physiological platelet count may occur in pregnancy for many reasons, ranging from the relatively benign, gestational thrombocytopenia to more sinister conditions, such as HELLP syndrome[4].

Reger et al (2013) observed that fibrinogen increased progressively throughout pregnancy.1 In contrast, Abass et al (2016) found no significant difference in fibrinogen level between pregnant and non-pregnant women[5]. Olorunshola et al (2011) showed lower platelet count during labor and one hour post-partum than non-pregnant control subjects[1]. On contrary, Durotoye et al (2012) observed no significant difference in platelet count between pregnant and non-pregnant women[6].

As a result, the reports about coagulation parameters during pregnancy are conflicting and not conclusive. Moreover most reference values established by laboratories about coagulation parameters are based on samples obtained from non-pregnant women. So the present study was aimed to measure fibrinogen and platelet count during normal third trimester pregnancy and compare the values with healthy non-pregnant women.

Methods

A cross sectional analytical study was carried out in the Department of Physiology in collaboration with Department of Obstetrics & Gynecology of Rajshahi Medical College and Hospital, Rajshahi and Other clinics of Rajshahi City from July 2016 to June 2017. Study population was 60 healthy persons, out of them 30 were apparently healthy pregnant women, 30 were non-pregnant healthy women in the age group of 20-35 years. The protocol of the study was approved by the Ethical Review Committee (ERC) of Rajshahi Medical College. Study subjects were selected by simple random sampling technique.

Criteria for sample selection: Inclusion criteria for case were all individuals who were apparently healthy pregnant women in 3rd trimester and age: 20-35 years. Inclusion criteria for control were non pregnant women assumed by menstrual history and age: 20-35 years. Absence of pregnancy was confirmed by urine for HCG and ultrasonography. Exclusion criteria for both case and control were known case of bleeding disorders, presence of hypertension, Diabetes mellitus, varicose veins, women who used anticoagulant and NSAID drugs, known case of pre-eclampsia and Eclampsia, known case of chronic kidney diseases and case of any chronic illness, known case of fibrinogen deficiency disorder and severe malnutrition.

Sample collection and estimation of Fibrinogen levels: The blood sample was collected by vene puncture after taking all aseptic precautions for estimation of fibrinogen. The blood was transferred into anti-coagulated tube without delaying the mixing of blood with anticoagulant. Exactly 9 parts of freshly collected blood was mixed with 1 part of trisodium citrate (0.11 mol/litre). The sample was centrifuged for 15 minutes at 3000 rpm and the plasma was separated. The separated plasma was transferred in a clean and dry test tube and was tested within 2-3 hours of blood collection. Sysmex Automated Blood Coagulation Analyzer CA-500 was used for the estimation of fibrinogen. This is a compact fully-automated instrument capable of analyzing of fibrinogen.

Sample collection and estimation of Platelet count: Venous blood without undue stasis was collected from peripheral vein by vene puncture under aseptic conditions. K2-EDTA was used as an anti-coagulant to prepare the anticoagulant blood sample (the dose of K2 EDTA is 1.5 mg/ml blood). Anticoagulant blood was mixed up. Auto-analyzer (cell counter) was used for the estimation of platelet count.

Data was analyzed by computer using SPSS software program. The test of significance was calculated by using unpaired student-t test. P value at or less than 0.05 was considered as significant.

Results

Comparison of general characteristics age (years), weight (kg), Height (cm), BMI (kg/m2), baseline pulse (beats/minute), systolic blood pressure (mm Hg) and diastolic blood pressure (mm Hg) in between third trimester pregnant and non-pregnant healthy women. (Table I)

Table-I: Demographic profile of study population (N=60

Parameters	Pregnant women (n=30) (mean±SD)	Non-pregnant women (n=30) (mean±SD)
Age (years)	27.27±3.72	27.13±4.01
Weight (kg)	58.23±4.26	54.77±3.30
Height (cm)	155.17±4.88	157.17±4.33
BMI (kg/m2)	24.20±1.21	22.37±1.61
Pulse (beats/min)	73.37±3.21	71.40±4.70
Systolic blood pressure (mm of Hg)	123.00±9.15	119.00±9.95
Diastolic blood pressure (mm of Hg)	78.67±8.60	75.30±13.92

Data were expressed as mean±SD. BMI= Body mass index. N=total number of population. n=number of study subjects in each group

Distribution of study population was showed according to their parity. Among the study population most of them were primipara followed by multiparous. (Table II)

Table-II: Distribution of study population according to their parity (N=60)

Parity distribution	Pregnant (n=30)	Non pregnant(n=30)	Total
Nulliparous	0(00%)	13(21.66%)	13(21.66%)
Primipara	22(36.66%)	0(00%)	22(36.66%)
Multipara	8(13.33%)	17(28.33%)	25(41.66%)
Total	30(50.0%)	30(50.0%)	60(100.0%)

Data were expressed as percentage.
N=total number of study population. n=number of study subjects in each group.

Fibrinogen level was significantly increased in healthy third trimester pregnant women in comparison to non-pregnant healthy women. However platelet count was non-significantly decreased in third trimester pregnancy in comparison to non-pregnant women. (Table III)

Table III: Fibrinogen and Platelet Count in apparently healthy third trimester pregnant women and non-pregnant women (N=60)

Parameters	Pregnant women (n=30) (mean±SD)	Non-pregnant women (n=30) (mean±SD)	p-value
Fibrinogen level (mg/dl)	328.07±79.76 (204-497.2)	265.70±56.71 (186-386)	<0.05
Platelet Count (lakh/mm3)	2.33±0.50 (1.00-3.00)	2.54±0.40 (1.90-3.60)	>0.085

Data were expressed as mean±SD. The significance of difference was calculated using unpaired'-test. P-value at or less than 0.05 was considered as significant.

N =total number of study population. n=number of study subjects in each group.

Discussion

Normal pregnancy is associated with some hemostatic changes; with features of increasing in several clotting proteins including fibrinogen, decreasing in the concentration of natural anticoagulants and less fibrinolytic activity. These changes result in a hypercoagulable state, which may increase the risk of thrombosis[5]. So the present study was aimed to measure fibrinogen and platelet count during normal third trimester pregnancy and compare the values with healthy non-pregnant women.

In the present study it was observed that fibrinogen level increased significantly during third trimester pregnancy in comparison to non-pregnant women. This finding is compatible with several authors[3, 7]. Moreover Amilo et al (2013) observed progressive rise of fibrinogen from first to third trimester pregnancy[8]. According to Hui et al (2012), during normal pregnancy, the hemostatic balance tilts in the direction of hypercoagulability which helps to reduce bleeding complications during delivery. Estrogen and progesterone increase several folds during pregnancy. Estrogen stimulates hepatocytes, thereby increase the production of virtually all coagulation factors. Progesterone has been found to increase decidual tissue factor and also increase the synthesis of plasminogen activator inhibitor type 1. Elevation of the levels of certain coagulation factors and the fibrinolytic inhibitors occur in practically all healthy pregnant women[9]. So the elevated fibrinogen concentration observed during pregnancy might be due to increased protein synthesis by liver hepatocytes. Moreover the increase might also be due to depressed fibrinolytic system during pregnancy[7]. Durotoye et al (2012) found that increased fibrinogen was an important factor in pregnancy as it assists in preventing postpartum hemorrhage with 5-10% of the total circulatory fibrinogen being deposited at the placental site[6].

In the present study, it was observed that the platelet count is non-significantly lower in third trimester pregnant women in comparison to non-pregnant women. This finding is in agreement with Durotoye et al (2012). They suggested that the occurrence of thrombocytopenia in labor or pre-partum might be related to the low grade "Physiologic DIC" that might accompany normal delivery. Although the various physiological changes, which occur in pregnancy, make pregnancy a hypercoagulable state, there is a balance between coagulation and fibrinolytic activities which limits the likelihood of actual thrombosis, Furthermore, changes in the hemostatic system during pregnancy may be more marked in the uteroplacental than in the systemic circulation and thus the pregnant women may be relatively well protected against the thrombotic effects of a hypercoagulable state[6]. In addition, decrease platelet count can be explained by haemo-dilution and increase consumption of platelet during pregnancy. Olorunshola et al (2011) found that gestational thrombocytopenia is more apparent during the 3rd trimester of pregnancy and normalizes within 2 to 12 days after delivery[3]. On the other hand, Yagmur et al (2019) observed that high prevalence of sticky platelet is responsible for pregnancy loss[10]. So decrease platelet count during pregnancy may be a protective mechanism.

One of the strength of our study was that we have included only healthy women who are relatively free from any disease. So, it was possible to detect any minute change of

hemostatic parameters due to pregnancy. However a cross-sectional study was done on small sample size of third trimester pregnant women and non-pregnant women. More-over only 3rd trimester pregnant women were included in this study. As a result, trimester variation regarding to the changes of hemostatic parameters could be studied. In addition, prothrombin time (PT), Activated partial thrombo-plastin time (APTT), Thrombin time, D-dimer should be measured in relation to pregnancy[1, 5, 8].

Conclusion

In the present study, normal third trimester pregnancy showed a physiological hypercoagulable state with an increased level of Fibrinogen and decreased platelet count. In other words, coagulation parameters are altered as well as balanced during normal pregnancy. If this balance is disrupt-ed, adverse outcome may occur. Pregnancy is a physiologi-cal process in women but it may be associated with certain risks to the health and life of both the mother and child. From this study, it was concluded that estimation of coagulation parameters play an important role in the diagnosis of some diseases and the evaluation of risk factors related to pregnancy.

Conflict of interest: None

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Original Article

Role of Pre-Operative Shower with Common Soap to Prevent Postoperative Wound Infection in Routine and Emergency Laparotomy

Ali MS[1], Newaz MM[2], Mazumder AK[3], Islam MS[4], Shahnewaz SM[5]

Abstract

Background: In different research studies and meta-analysis, it has been already established that preoperative shower with Chlorhexidine has protective role to prevent and reduce surgical site infections. However, in many guidelines, including the National Institute of Health and Care Excellence (NICE) guideline, UK, the role of showering is not recommended.

Aims & objectives: The aim of this research is to depict the role of preoperative showering to reduce surgical site infections.

Methods: This was a prospective study with a total 308 patients of Laparotomy in Khulna Medical College Hospital, Bangladesh, from January 2016 to December 2020. Convenient purposive sampling was the sampling method. Ethical clearance was taken individually from patient and from the ethical review committee of Khulna Medical College Hospital.

Results: Among the total 308 patients, 240 and 62 patients had emergency and routine Laparotomy respectively. 18.8% patients with emergency laparotomy (Group A) had surgical site infections, whereas 6.4% patients with routine laparotomy had surgical site infections. According to the Southampton wound grading system, in Group A, surgical site infections were either deep or organ space infections (Grade IV or V), whereas, in Group B, all infections were superficial (Grade II). In case of routine surgery, where the patients had a shower preoperatively at the day or before the day of operation, wound infection was nil. When the patients had no shower within 05 days prior to emergency surgery, the infection rate was 8.8%. And when the patients had a shower within 2-5 days prior to surgery, the infection rate was 7.1%. The patients who had a shower 01 day before surgery or at the day of surgery, the infection rates were 2.1% and nil respectively.

Conclusion: Taking shower with common soap before surgery reduces the rate of surgical site infections. Shower prior to or at the day of surgery greatly influences the overall infective outcome. Therefore, shower and it timing is an important factor in relation to both routine and emergency surgery.

Keywords: Surgical sites infection, Shower, Timing, Emergency, Routine, Laparotomy.

Introduction

According the United State Centre for Disease Control guideline, 1999, surgical site infections are infection is the infections which occur within 30 days of surgery at the site of operation, however, in case of implant surgery, the duration is one years following operation1, 2. Surgical wound infections continue to consume a considerable portion of health care finance. Even though the complete elimination of wound infections is not possible, a reduction of the observed wound infection rate to a minimum level could have marked benefits in terms of both patient comfort and resources used3. With the infection rate for clean wounds being inherently low, these indeterminate categories can comprise a significant proportion of wounds that are not clearly infected or uninfected and may skew data in any study of infection rates. Partly in order to address this problem of no uniform definitions, The Surgical Wound

1. Md. Showkat Ali, Assistant Professor, Dept. of Surgery, Khulna Medical College, Bangladesh.
2. Md. Mehedi Newaz, Associate Professor, Dept. of Orthopaedics, Khulna Medical College, Bangladesh.
3. Anup Kumar Majumder, Associate Professor, Dept. of Surgery, Sayera Khatun Medical College, Bangladesh.
4. Md. Shahidul Islam, Assistant Professor, Dept. of Surgery, Khulna Medical College, Bangladesh.
5. S. M. Shahnewaj, Senior Consultant, Orthopaedic Surgary, Sadar Hospital, Bagerhat, Bangladesh.

Corresponding Author:
Dr. Md. Showkat Ali, Assistant Professor, Dept. of Surgery, Khulna Medical College, Bangladesh. E-mail: drshowkathimel@gmail.com

Infection Task Force, including representatives from the Society for Hospital Epidemiology of America, the Association for Practitioners in Infection Control, the Centers for Disease Control, and the Surgical Infection Society, published in 1992 definitions of surgical site infections3, 4. In many recent studies, the role of preoperative showering has been linked up with the surgical site infections5-8. In a study it has be depicted that showering preoperatively with chlorhexidine gluconate is an issue that continues to promote debate; however, many studies demonstrate evidence of surgical site infection risk reduction. Methodological issues have been present in many of the studies used to compile guidelines and there has been a lack of standardization of processes for application of the active agents in papers pre-2009. This review and commentary paper highlights the potential for enhancing compliance with this low-risk and low-cost intervention and provides some guidance for enhancing implementation of preoperative showering with both chlorhexidine in solution and impregnated wipes5, 9, 10. In our current research our aim is to link up the surgical site infection with the timing of shower with common soap before operation in Khulna Medical College Hospital, Bangladesh.

Methods

This study was conducted as a prospective study with a total 308 patients of Laparotomy from January 2016 to December 2020 in Khulna Medical College Hospital, Bangladesh. Among the study population, 240 laparotomy were done as emergency procedure (Group A) and 62 laparotomy were done as routine procedure (Group B). Study population was selected by convenient purposive sampling based on inclusion and exclusion criteria. The survey data were usually be analyzed using both analytic as well as descriptive statistic. Such as; mean, SD, percentage etc. Ethical clearance was taken individually from patient and from the ethical review committee of Khulna Medical College Hospital. The Southampton wound grading2 system was applied to assess the surgical site infections in study population.

Results

The age and sex distribution of the Group A and B are shown in table 1 & 2 respectively. In group A, 59.6% patients were male. Majority of the patients were in 50-60 years age group in male, whereas in female the predominant group by age distribution was 40-49 years age group. Mean±SD age was 45±1.7 and 49±2.0 years respectively in both groups (Table-I).

Table I: Age and sex distribution of study population in Group A

Age group (Years)	*Male*			*Female*		
	N	%	Mean±SD	N	%	Mean±SD
<30	12	05		07	2.9	
30-39	25	10.4		18	7.5	
40-49	35	14.6	45±1.7	27	11.3	49±2.0
50-60	41	17.1		20	8.3	
>60	30	12.5		25	10.4	
Total	**143**	**59.6**		**97**	**40.4**	

In group B, 51.6% patients were female. Most of the patients were in >60 years and 40-49 years age groups respectively in male and female. Mean±SD age was 54±2.1 in male and 50±1.5 years in female (Table-II).

Table II: Age and sex distribution of study population in Group B

Age group (Years)	*Male*			*Female*		
	N	%	Mean±SD	N	%	Mean±SD
<30	02	3.2		00	00	
30-39	03	4.8		04	6.5	
40-49	08	12.9	54+21.1	12	19.4	50±1.5
50-60	07	11.3		06	9.7	
>60	10	16.1		10	16.1	
Total	**10**	**48.4**		**32**	**51.6**	

The overall wound infection rate in both groups is depicted in figure 1. Approximately 18.8% in group A and 6.5% patients in group B had surgical site infection (SSI) subsequently. The rate of SSI was significantly higher in group A in contrast to group B.
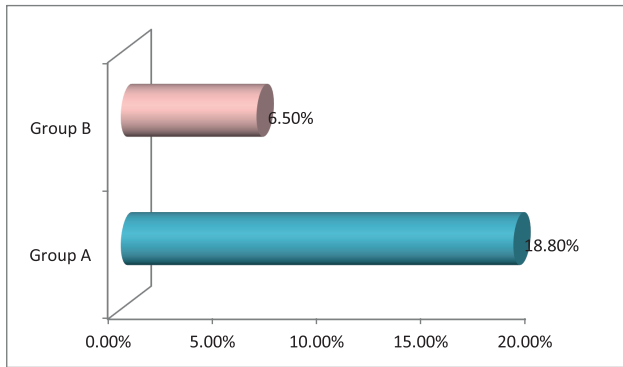

Figure 1: Wound infection rate in both study groups.

Using the Southampton wound grading system, the overall grade of surgical site infections in Group A and B is shown in table-III. Severity and grade of SSI was much higher in group A in relation to group B. it is important to mention that severe form of SSI was only observed in group A, whereas in case of group B, it was mainly superficial infections.

Table III: Southampton wound grading system of surgical site infections in both study groups

Grade	Group A Frequency	%	Group B Frequency	%
Ia	00	00	00	00
Ib	02	0.8	00	00
Ic	02	0.8	00	00
IIa	01	0.4	02	3.2
IIb	00	00	02	3.2
IIc	05	2.1	00	00
IId	03	1.3	00	00
IIIa	08	3.3	00	00
IIIb	07	2.9	00	00
IIIc	07	2.9	00	00
IIId	02	0.8	00	00
IVa	04	1.7	00	00
IVb	04	1.7	00	00
V	10	4.2	00	00
Total	**45**	**18.8**	**04**	**6.5**

Among the 45 and 04 cases of wound infection, the timing of taking shower prior to surgery is shown in figure 2. Observation suggest that the frequency was less in group A, hence the rate of SSI was possibly much higher in group A in relation to group B. Moreover, the timing from last shower was prolonged in group A which was probably major contributing factor for the development of SSI.
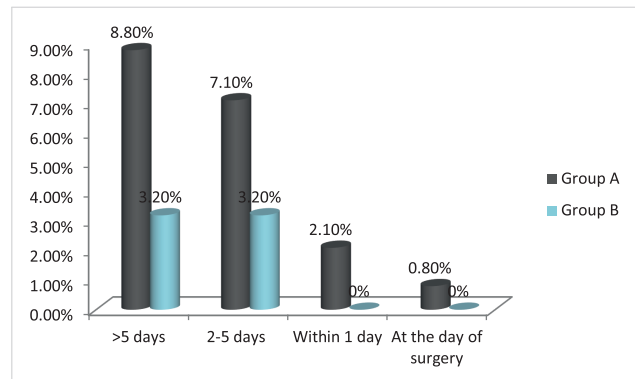

Figure 2: Approximate timing of shower among the patients with wound infection.

Discussion

Among the 240 patients of emergency laparotomy (Group A), 59.6% (143) and 40.4% (97) patients were male and female respectively. In case of male patients, 17.1% (41) were in 50-60 years of age group, followed by 14.6% (35) were in 40-49 years of age group. On the other hand, in the female patients, majority of the patients (11.3%, 25) were within 40-49 years of age group, followed by 10.4% (25) were in age >60 group. Mean±SD age was 45±1.7 and 49±2.0 years respectively in male and female group. During the study period, a total number of 62 patients of elective laparotomy were included (Group B), among which 48.4% (30) were male and 51.6% (32) were female patients. Majority of the male patients (16.1%, 10) were in >60 years of age group, whereas in case of female most of the patients (19.4, 12) were in 40-49 years of age group. Mean±SD age was 54±2.1 and 50±1.5 years respectively in male and female group.

In case of emergency laparotomy (Group A), 18.8% (45 out of 240) patients had surgical site infections, whereas among the patients with routine Laparotomy, 6.4% (04 out of 62) patients had surgical site infections. The Southampton wound grading system2 is a widely accepted tool to assess and categorize surgical site infections. Using this tool in case of both study groups, it was observed that in case of Group

A, in most patients, surgical site infections were either deep or organ space infections (Grade IV or V). On the contrary, in Group B, all infections were superficial (Grade II).

The most important finding of this research was that incidence of infection in relation to timing of shower with common soap in emergency and elective laparotomy. The results were suggestive that in case of routine surgery, where the patients had a shower preoperatively at the day or before the day of operation, wound infection was absolutely nil. On the contrary, a major portion of the patients were unable to have a shower before the operations due to their illness. As a result, when the patients had no shower within 05 days prior to emergency surgery, the overall infection rate was 8.8% (21 patients), whereas when the patients had at least one shower within 2-5 days prior to surgery, the infection rate was 7.1% (17 patients). But when the patients had a shower at least 01 day before operation, the infection rate was 2.1 % (05 patients). When the shower was possible on the day of operation even in case of emergency surgery, the infection rate was found nil. The observation suggests that surgical site infections have strong relationship with the timing of shower prior to surgery, which is major problem in case of emergency surgery as a result of severe illness.

The use of a pre-admission shower with 2% or 4% aqueous chlorhexidine gluconate (CHG), to reduce skin contamination prior to surgery, has been addressed in the 1999 US Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee (HICPAC) document, Guideline for the Prevention of Surgical Site Infection5. However, the National Institute of Health and Care Excellence (NICE) of the UK, in its guideline on prevention and treatment of SSI, have not strongly recommended bathing or showering with CHG. Moreover, some evidence-based analysis, including that presented in the NICE guideline, does not support the routine use of pre-admission whole-body cleansing or showering with CHG5, 6. But our study strongly supports the role of preoperative showering to reduce surgical site infections in surgical practice.

Conclusion

Surgical site infections are unavoidable but preventable scenario in many circumstances. The incidence is higher in emergency surgery, mostly are deep and organ space infections. Showering prior to surgery and the timing of shower greatly influence the incidence of surgical site infections, reflected in this research.

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Original Article

Serum Albumin, Uric Acid and Creatinine Levels in Early Pregnancy and Their Association with Preeclampsia

Das JK[1], Ray L[2] , Sardar MMR[3] Khaliduzzaman SM[4] , Biswas BK[5]

Abstract

Background: Preeclampsia is a common cause of both maternal and perinatal morbidity and mortality in both developed and developing countries. Currently there is no gold standard for prediction of preeclampsia during pregnancy. So a screening test for prediction of preeclampsia is a demand for general obstetric population.

Objectives: The objectives of this study was to evaluate serum albumin, uric acid and creatinine level at or before 20th weeks of pregnancy and its relation to subsequent development of preeclampsia.

Methods: It was a prospective study. A total of 138 pregnant women at or before 20th weeks of pregnancy and having no urinary protein from OPD of Gynecology and Obstetrics of institute of Child and Mother Health, Mutual Dhaka and Khulna Medical college hospital, during January 2013 to December 2018, were included in this study. Out of them, three were excluded from the study due to failure of follow up visit. Study subjects were selected by purposive sampling technique. The documentation include pregnant mother at or before 20th weeks of pregnancy, first follow up at or before 28th weeks and second follow up at or before 36th weeks who attended OPD. Urinary protein was assayed by dipstick reagent strip. Estimation of serum albumin, uric acid and creatinine was done by colorimeter. Receiver operator curve was constructed for prediction of preeclampsia. Data was analyzed by computer using SPSS software program. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was considered as significant.

Results: The study subjects who developed preeclampsia showed no significant difference in serum uric acid and serum creatinine level but had significantly higher serum albumin level in comparison to those who remained normal during pregnancy. Moreover serum albumin cut off value of >4.0 was the value with the best combination of sensitivity and specificity for prediction of preeclampsia.

Conclusion: Mean serum albumin level was significantly higher in those who developed preeclampsia in comparison to those who remained normal during pregnancy. As a result, a larger study is recommended to properly define the value of estimation of serum albumin levels and other parameters in early pregnancy in the prediction of preeclampsia.

Key words: Preeclampsia, Albumin, Uric acid, Creatinine, Pregnancy

Introduction

Preeclampsia (PE) is a pregnancy specific, multisystem disorder that is characterized by the development of hypertension and proteinuria after 20 weeks of gestation. Complication of hypertension are the third leading cause of pregnancy related deaths[1]. Women with preeclampsia are at increased risk for such complication like abruptio placentae, acute renal failure, cerebral hemorrhage, disseminatedintravascular coagulation, pulmonary edema, circulatory, collapse and eclampsia[2].

Second trimester mean arterial pressure has low sensitivity and low positive predictive value as an indicator of future development of preeclampsia. Angiotensin II infusion test

1.   Joyanta Kumar Das, Assistant Professor, Department of Gynecology and Obstetrics, Khulna Medical College, Bangladesh
2.   Lipika Ray, Assistant Professor, Department of Anesthesiology, Shaheed Sheikh Abu Naser specialzed hospital, Bangladesh
3.   Md. Mijanur Rahman Sardar, Associate Professor (C.C), Department of Physiology. Khulna Medical College, Bangladesh
4.   SM Khaliduzzaman, Assistant Professor, Department of Gynecology and Obstetrics, Khulna Medical College, Bangladesh
5.   Bipul Kumer Biswas, Department of Gynecology and Obstetrics, Kustia Medical College, Bangladesh

Corresponding Author:

Dr. Joyanta Kumar Das, Assistant Professor, Department of Gynecology and Obstetrics, Khulna Medical College, Bangladesh. Email: dasjoyanta43542@gmail.com

has high incidence of false negative and false positive results. Moreover it has been found to be unsuitable and impractical for the routine evaluation of pregnant women. Supine pressor rollover examination has poor sensitivity, poor specificity and limited clinical value[3].

Currently there is no gold standard for identifying the preeclampsia; therefore, this pregnancy specific disease continues to be defined by its clinical manifestation during the later stage of pregnancy. However to reduce the risks that are associated with the development of severe preeclampsia, early detection and timely assessment of the disease are essential. A screening test for preeclampsia is a demand for general obstetric population. It should be able to identify most women who ultimately develop the disease. In other words, it must have a high sensitivity and a high positive predictive value with an acceptable false positive rate. Most of the studies about estimation of serum uric acid, albumin and creatinine levels as biochemical markers of the subsequent development of preeclampsia, were performed late in the second and third trimester of pregnancy when the disease process usually manifest[4]. As a result, the aim of the study was to evaluate serum albumin, creatinine and uric acid levels at or before 20th weeks of pregnancy and its relation to subsequent development of preeclampsia.

Methods

It was a prospective study. A total of 135 pregnant women at or before 20th weeks of pregnancy and having no urinary protein from OPD of Gynecology and Obstetrics of institute of Child and Mother Health, Mutual Dhaka and Khulna Medical college hospital, during January 2013 to December 2018, were included in this study. Diabetic pregnant women, chronic renal disease, chronic hypertension, patient with any acute or chronic illness and patient with history of collagen vascular disease were excluded from the study. The protocol of the study was approved by the Ethical Review Committee (ERC) of ICMH. Study subjects were selected by consecutive sampling technique. Before recruitment, aim, benefit and procedure of the study was explained and informed written consent was taken from each study subject. Thorough physical examinations of all subjects were done. The documentation include pregnant mother at or before 20th weeks of pregnancy, first follow up at or before 28th

weeks and second follow up at or before 36th weeks who attended OPD. Urinary protein was assayed by dipstick reagent strip. Estimation of serum albumin, uric acid and creatinine was done by colorimeter. Receiver operator curve was constructed for prediction of preeclampsia. Data was analyzed by computer using SPSS software program. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was considered as significant.

Results

Distribution of the study population was shown by baseline parameters like age, BMI, gravida, and gestational age. (Table I)

During primary enrollment and first follow up, all study subjects had normal systolic, diastolic and mean arterial pressure. During second follow up, systolic, diastolic and mean arterial pressure were increased significantly in comparison to first follow up. (Table II)

Serum uric acid, serum creatinine and serum albumin levels in study subjects was shown with range (Table III)

The study subjects who developed preeclampsia showed no significant difference in serum uric acid and serum creatinine level in comparison to the study subjects who remained normal during pregnancy. But serum albumin level decreased significantly in study subjects who remained normal during pregnancy in comparison to preeclampsia. (Table IV)

Distribution of study subjects was shown by serum Albumin level during primary enrollment. The study subjects who developed preeclampsia had significantly higher serum Albumin level in comparison to those who remained normal during pregnancy. (Table V)

The area under the receiver-operator characteristic (ROC) curve was constructed for the prediction of preeclampsia. The curve was constructed using serum albumin value of the women, which gave a serum albumin cut off value of >4.0 as the value with the best combination of sensitivity and specificity for preeclampsia. Based on the curve, serum albumin had the best area under the curve in comparison to serum uric acid and serum creatinine level. (Table VI)

Table I: Distribution of study population by baseline parameters (n=135)

Variables	mean±SD	Range
Age in years	23.4± 3.4	18-33
Gravida	2.2± 0.7	1-4
BMI (kg/m2)	20.1± 1.6	15.8-22.9
Gestational age (wks.)	14.7.4± 2.5	10-20

n = number of study population, BMI= Body mass index

Table II: Distribution of the study subjects by blood pressure (n= 135)

Blood pressure	Primary enrollment (<20 weeks)	1st follow up (28 weeks)	2nd follow up (<36 weeks)	P value
Systolic BP(mm Hg) <140 >140 mean±SD Min-max	135 0 117.3±9.7 100-135	135 0 119.7±10.3 100-140	123 12 127±19.7 100-220	0.001S
Diastolic BP (mm Hg) <90 >90 mean±SD Min-Max	135 0 65±6.6 55-80	135 0 67.3±6.9 60-85	123 12 72.7±13.1 60-120	0.001S
MAP mean±SD min-max	82.7±6.3 70-100	83.7±6.8 78-105	91.1±15.0 76.6-153.3	0.001S

Data was expressed as mean±SD. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was considered as significant.

S=significant, n=number of study population, MAP= Mean arterial pressure.

Table III: Serum uric acid, Serum Creatinine and Serum Albumin levels in study subjects during primary enrollment (n=135)

Variables	mean±SD	Min-Max
Serum uric acid (mg/dl)	5.0±1.2	2.4-7.6
Serum Creatinine (mg/dl)	0.8±0.2	0.6-1.2
Serum Albumin (gm/dl)	2.8±0.8	2-4.8

Date was expressed as mean±SD. n=number of study population

Table IV: Serum uric acid, Serum Creatinine and Serum Albumin in subjects developing preeclampsia and remained normal during pregnancy (n= 135)

Variables	Preeclampsia n=12	Remained normal pregnancy n=123	P value
Serum uric acid (mg/dl) Range (Min-Max)	4.43±1.11 3.0-6.1	5.01±1.17 2.4-7.6	>0.05NS
Serum Creatinine (mg/dl) Range (Min-Max)	0.83±0.17 0.6-1.2	0.78±0.16 0.6-1.2	>0.05NS
Serum Albumin (gm/dl) Range (Min-Max)	4.4±0.44 3.8-4.8	2.74 ±0.47 2-3.2	0.001S

Data was expressed as mean±SD. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was considered as significant.

NS=not significant, S=significant, n=number of study subjects.

Table V: Distribution of study subjects by serum Albumin level during pregnancy (n= 135)

Serum albumin (gm/dl)	Preeclampsia N=12	Remained normal pregnancy N=123	P value
< 4 gm/dl >4 gm/dl	2 (16.7%) 10 (83.3%)	121 (98.4%) 2 (1.6%)	0.001S

N = number of study subjects. The test of significance was calculated by using unpaired student-t test. P value less than 0.05 was considered as significant. S=significant.

Table VI: Receiver-operator characteristic (ROC) curve of serum uric acid, serum creatinine and serum albumin for prediction of preeclampsia

Variables	Cut off value	Sensitivity	Specificity	Area under the ROC curve	95% confidence interval (lower bound)	95% confidence interval (lower bound)
Serum uric acid	4.60	58.3	35.5	0.360	0.200	0.520
Serum creatinine	0.75	75.0	49.2	0.594	0.432	0.756
Serum albumin	4.0	99.2	87.2	0.913	0.787	1.00

Discussion

Pre-eclampsia is a multisystem disorder that complicates 3%-8% of pregnancies in Western countries and constitutes a major source of morbidity and mortality worldwide[5,6] Most of the studies about estimation of serum uric acid, albumin and creatinine levels as biochemical markers of the subsequent development of preeclampsia, were performed late in the second and third trimester of pregnancy when the disease process usually manifest[7, 8]. As a result, this prospective study was carried out with an aim to determine the serum levels of albumin, uric acid and creatinine at or before 20th week of pregnancy in normal pregnant women and to identify the relationship of serum level of albumin, uric and creatinine with the subsequent development of preeclampsia.

In this study, mean age was found 23±3.4 years with range 18 to 33 years. Findings of Gulati, (2005), Manjareeka and Nanda (2013) is consistent with this study[9, 10]. In the present study, the mean BMI was found 20.1±1.6 kg/m2 with range 15.79 to 22.9 kg/m2. Among them, 83.7% pregnant women had normal BMI and 16.3% were under weight. Benoit and Rey (2011) found the mean BMI higher than the present study during first trimester[11]. It may be due to their higher body surface area than the present study subjects.

In the present study, mean gravid was found 2.2±0.7 with range from 1 to 4. Benoit et al. (2011) found that more than two third of the subjects were primi-gravida which differs from the present study. In this study, it was observed that mean gestational age was 14.7±205 weeks varied from 10-20 weeks. Findings of Salako et al. (2003) closely resemble with the present study[12].

During primary enrollment and first follow up, all study subjects had normal systolic, diastolic and mean arterial pressure. However during second follow up, systolic, diastolic and mean arterial pressure were increased significantly in comparison to first follow up. Among the study subjects, twelve patients developed preeclampsia, out of them ten had moderate proteinuria (>l g/L), two had severe proteinuria (>3 g/L). Remaining of the study subjects had normal urinary albumin (Trace).

In the present study, all the study subjects had normal serum uric acid and serum creatinine level during primary enrollment. Moreover it was observed that the mean serum uric acid and serum creatinine levels had no significant difference between preeclampsia and the study subjects who remained normal during pregnancy. It proves that single estimation of serum uric acid and creatinine levels early in pregnancy are of little value in the prediction of pre-eclamp-sia. This finding is compatible with Hayashi et al. (1956) who demonstrated that abnormally high blood creatinine levels were seldom observed and those of uric acid often were normal even though the clearance was reduced in patients with preeclampsia[13]. On contrary, Manjareeka and Nanda (2013) found that the levels of serum uric acid and serum creatinine were significantly higher in pre-eclampsia patients in comparison to the study subjects who remained normal during pregnancy[10].

During primary enrollment, all the study subjects had normal serum albumin level. However it was observed that the serum Albumin level was significantly higher in preeclampsia patients in comparison to those who remained normal during pregnancy. This finding is compatible with Salako et al. (2003)[12]. In the present study it was observed that serum albumin level ≤4 gm/dl was found only 16.7% in preeclampsia patients and 98.4% in normal pregnancy. On the other hand, serum albumin level>4 gm/dl was found 83.3% in preeclampsia patients and only 1.6% in normal pregnancy. In other words, the study subjects who developed preeclampsia had significantly higher serum albumin level in comparison to those who remained normal during pregnancy. It indicates the importance of estimation of serum albumin level multiple times during pregnancy period for prediction of preeclampsia cases.

Based on the receiver-operator characteristic (ROC) curves, serum albumin had the best area under the curve compared to serum creatinine and uric acid level. Receiver-operator characteristic (ROC) were constructed using serum albumin value of the women, which gave a serum albumin cut off value of >4.0 as the value with the best combination of sensitivity and specificity for preeclampsia. The sensitivity, specificity and predictive values of the various parameters of the present study were compatible with Conde-Agudelo et al. (1994)[14].

One of the strength of the study was evaluation of study subjects during primary enrollment at or before 20th weeks, first follow up before 28th weeks and second follow up before 36th weeks for better decision Moreover strict exclusion criteria was used to select each study subjects. However strict exclusion criteria affected the number eligible for the study because our patients in this part of the world rarely book early in pregnancy unless they develop complications. In addition, the study was conducted at a very short period of time with small sample size which was limitations of the present study. Therefore, in future, further study should be under taken with larger sample size and longer duration.

Conclusion

This study was undertaken to detect the biochemical changes in term of serum albumin, creatinine and uric acid in pregnant women and their relation to subsequent development of preeclampsia. The findings of this study showed that single estimations of serum uric and creatinine concentrations early in pregnancy are of little value in the prediction of subsequent development of preeclampsia, either alone or in combination. However, mean serum albumin level was significantly higher in those who developed preeclampsia in comparison to those who remained normal during pregnancy. As a result, a larger study is recommended to properly define the value of estimation of serum albumin levels and other parameters in early pregnancy in the prediction of preeclampsia.

Conflict of interest: None.

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Original Article

Study of Acute Meningo-Encephalitis Syndrome-50 Cases

Tarafder P[1], Tarafder P[2], Hossain SM[3], Chanda UK[4]

Abstract

Background: Acute meningo-encephalitis syndrome (AMES) is not an uncommon illness in adult age group. It is a global health problem as mortality is high and a large proportion of survivors suffered from significant sequelae. The physicians are facing this challenge of emergency identification of the clinical syndrome, establishing its etiology and its prompt treatment not only to ensure survival but also to prevent long term sequelae of these patients.

Objective: The study was conducted to find out the clinical profile of AMES, etiological identification of pyogenic or viral AMES and treatment outcome.

Methods: It is a prospective observational study, conducted in Khulna Medical College Hospital including 50 cases of acute meningo-encephalitis syndrome those fulfilled the inclusion criteria. A preformed questionnaire was filled up for every case which comprises history, examination, investigation, management and outcome information.

Result: Maximum patients were presented with fever (100%), headache (88%) and altered mental status (88%). 33 (66%) cases were diagnosed as pyogenic AMES and 17 (34%) were viral AMES. Convulsion was more common in viral AMES. Unconsciousness was more common in viral AMES. Total 7 (14%) patients expired. 4 (25%) out of 16 comatose patients expired and 3 (12%) out of 25 lethargic patients died. So death was high in unconscious patients. Mortality rate was high in viral AMES (23.53%) compared to pyogenic AMES (9.09%). Total 7 (14%) patients developed sequelae of which 5 patients had motor disability and 2 patients had cognitive impairment and later was more in viral AMES.

Conclusion: A patient presented with acute onset of fever and altered consciousness should be screened for AMES. The morbidity and mortality rates are quite high in this hospital. In all cases of AMES early diagnosis and appropriate treatment can reduce the rate of mortality and morbidity. Long term follow up of survived AMES cases will help in identifying sequelae and early rehabilitation.

Key words: Acute Meningo-encephalitis (AMES), Fever, Convulsion, Mortality.

Introduction

Bacterial or viral meningitis or meningo-encephalitis are serious infections that can kill affected patients and cause permanent neurological sequelae among survivors.

Encephalitis is an inflammation of the brain parenchyma. Meningitis refers to the inflammation of the meninges overlying the brain and the spinal cord. Because these anatomic boundaries are often not distinct, many patients have evidence of both meningeal and parenchymal involvement and should be considered to have meningoencephalitis.

It is postulated that alteration in sensorium in a patient with CNS infection indicates an element of parenchymal involvement. This can explain the altered mentation in meningo-encephalitis patients. Raised intracranial pressure may contribute to altered mentation to some extent. The reason for altered sensorium in meningitis is postulated to be the spillage of inflammatory cells to the adjacent brain parenchyma and the resultant parenchymal involvement?

1. Pritish Tarafder, Assistant Professor, Department of Medicine, Khulna Medical College, Bangladesh.

2. Palash Tarafder, Assistant Professor, Department of Nephrology, Khulna Medical College, Bangladesh.

3. Sk Moazzem Hossain, Assistant Professor, Department of Medicine, Khulna Medical College, Bangladesh.

4. Utpal Kumar Chanda, Assistant Professor, Department of Medicine, Khulna Medical College, Bangladesh

Corresponding Author:
Dr. Pritish Tarafder, Assistant Professor, Department of Medicine, Khulna Medical College, Bangladesh. Email: pritishtarafder@gmail.com

Acute meningo-encephalitis syndrome[1] is a term, used to identify the patients who develop acute onset of fever with one or more of the following:

1. Change in mental status (confusion, lethargy, agitation, irritability, inability to talk and coma)
2. New onset seizures
3. Signs of meningeal irritation like neck stiffness.

It is the surveillance case definition for acute meningo-encephalitis syndrome.

Acute meningo-encephalitis syndrome cases are not uncommon and a serious condition leading to hospital admission in both adult and children in Bangladesh. It is associated with high mortality globally. The burden of disease from Bacterial meningitis is higher in low resources settings with poor health infrastructure because of higher rates of malnutrition, generally poor living conditions and inadequate access to preventive and curative services which may predispose individuals to infection and limit opportunities for optimal treatments.

Importantly all three leading bacterial causes of meningitis and the leading cause of viral encephalitis are preventable with vaccines. Indeed, new vaccines are becoming available for each of these agents that appear to be safe and highly effective. However each of these vaccines is expensive.

In many resource poor settings, higher diagnostic facilities are scarce, unreliable, unaffordable and patients presenting with meningoencephalitis are treated empirically rather than on the basis of definitive laboratory diagnosis[2]. In such settings data on the local causes of meningo-encephalitis can assist clinicians in determining empiric treatment guidelines and assist policy makers and public health officials when establishing priorities for health spending, especially if vaccine preventable etiologies are identified.

In cases of meningitis (bacterial) antibiotics have a good role in outcome. On the other hand in case of viral encephalitis antiviral have doubtful effect. If we can find out some clinical or laboratory parameters which correlate with good or bad outcome of AMES cases then antiviral therapy can be given empirically to those patients who have bad prognostic features with the hope to help the patient by any means. So it is important to find out the clinical profile of AMES, laboratory findings of pyogenic or viral AMES and treatment outcome that will be helpful in the diagnosis and prompt management of the same.

Methods

It is a prospective observational study, conducted in Khulna Medical College Hospital over 6 months period from July 2017 to December 2017 including 50 cases of acute meningo-encephalitis. Patients both male and female above 12 years of age admitted in medicine units full filing the inclusion criteria were enrolled. An informed consent was sought from the patient or eligible attendants to take part in this study. Patients were selected on the basis of case definition of acute meningo encephalitis syndrome created by the Institute of Epidemiology, disease control and Research (IEDCR) Bangladesh.

A preformed questionnaire was filled up for every patient which comprises careful history, clinical examination, investigation, management and outcome information. Important variables of history included age, sex, region, occupation, socio-economic status, immunization history, travel history and treatment history. After doing thorough physical examination some important points were noted such as appearance, level of consciousness, signs of meningeal irritation and ophthalmoscopic examination of fundus of eyes.

Important investigations were done in all cases. In CSF study cytological. biochemical, Gram and AFB staining were done. We tried to isolate bacterial organisms by latex agglutination test for H. influenza-b, strept. pneumoniae, N. meningitides and group-B streptococcus.

Results

A total of 50 patients were included in the study. The age distribution of study population showed that within 13-20 years of age 22(44%) patients, 21-30 years of age 8 (16%), 31-40 years 3 (6%), 41-50 years 3 (6%) 51-60 years 6 (12%) and beyond 60 years of age 8 (16%) patients were found. So in this study maximum number of AMES cases were in 13-20 years age group. (Table-I).

Almost all the patients presented with acute onset fever, altered mental status and headache. Out of 50 AMES cases 36 (72%) patients developed new onset seizure and 60% patients developed signs of meningeal irritation. Among the 50 cases of AMES 33 (66%) cases were diagnosed as pyogenic AMES. Out of 31 male patient 19 (61.29%) had pyogenic AMES and 12(38.71%) had viral AMES. In case of female 14 patients (73.68%) had pyogenic AMES and 5 (26.32%) had viral AMES. The difference was statistically

not significant (P>0.05). 7 viral AMES cases were comatose out of 17 (41%) and 9 Pyogenic AMES cases were comatose out of 33 (27.27%). That is unconsciousness was more common in viral AMES group. The difference was statistically not significant (P>0.05). Convulsion were more common in viral AMES 82% compared to pyogenic AMES which was 66%. The difference was statistically not significant (P>0.05).

Average CSF glucose was less in Pyogenic AMES (36 mg/dl) patients and average protein was high in Pyogenic AMES (196.7 mg/dl) patients. High cell count were found in Pyogenic AMES cases above 4200/mm3 of which most were neutrophil (80%) but in viral AMES most were lymphocytes (90%).

7 patients (14%) were developed sequelae out of 50 AMES cases. Motor and cognitive impairment both were more in viral AMES patients. High mortality in viral AMES 23.53% group compared to that in Pyogenic AMES which was 9.09%16 patients were comatose and 4 of them (25%) died. On the other hand normal and confused patient were 9 in number without any death. Out of 25 lethargic patients three (12%) of them expired. So death was high in unconscious patients.

Table I: Age distribution

Age in years	Number	Percentage (%)	Mean±SD
13-20	22	44	
21-30	8	16	
31-40	3	6	33.04 ± 18.08
41-50	3	6	
51-60	6	12	
>60	8	16	

Figure 1: Gender distribution

Table II: Signs and symptoms of the patients with AMES

Presentation	Number	percentage
Acute onset Fever	50	100%
Altered mental status	44	88%
Headache	49	98%
New onset seizure	36	72%
Signs of meningeal irritation	30	60%

Table III: Mental status and diagnosis

Mental status	Pyogenic AMES	Viral AMES	P value
Normal	3	0	
Confused/Agitated	5	1	
Lethargic	16	9	0.381
Coma/unconsciousness	9	7	
Total (50)	33	17	

Table IV: Result of samples tested in IEDCR

Organism	Percentage
Bacteria	4 (8%)
Strept. Pneumoniae	2 (4%)
Neiss. Meningitidis	2 (4%)
Virus	1 (2%)
JE positive	1 (2%)

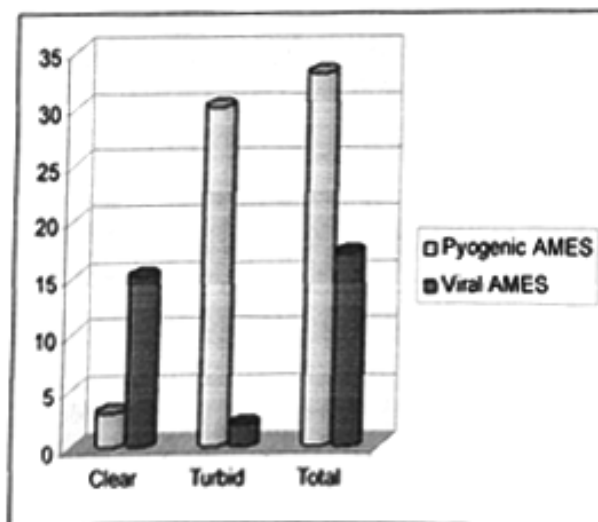**Figure 2:** CSF study: Physical findings (N=50)

Table V: Diagnosis and disability

Disability	Pyogenic AMES	Viral AMES	Total
Normal	30	13	43
Hearing	0	0	0
Auditory	0	0	0
Visual	0	0	0
Cognitive	0	2	2
Motor	3	2	5
Total	33	17	50

Table VI: Mental status and outcome

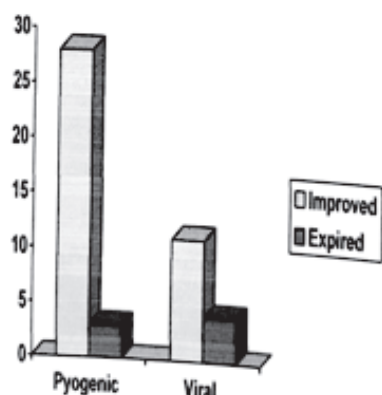| Mental status	Improved	Death	Not known
Normal (3)	2	0	1
Confuse (6)	5	0	1
Lethargic (25)	20	3	2
Coma (16)	12	4	0
Total (50)	39	7	4

Figure 3: Outcome of AMES.

Discussion

Infection of the central nervous system is a medical emergency. Acute meningo-encephalitis syndrome is usually caused by viruses or bacteria. Symptoms and signs of AMES include acute onset of fever, headache, neck stiffness, altered mental status (confusion, lethargy, agitation, irritability, inability to talk and coma) and new onset seizure.

Fifty consecutive cases (age above 12 years) were recruited. The mostly affected group were betow 40 years of age comprising 66%. 22 cases (44%) were in 13-20 years age group and also there was a small rise in elderly patients (8 cases, 16% above 60 years of age). Mean age was 33.04 (±18.08 SD) years which correlates with another study done in India where mean age was 32.54 ± 13.32 years (range from 15-70 years) of which 56% were male and 44% were female[4]. In a hospital based prospective study[3] done in Bangladesh (2003-2005) for etiology of bacterial meningitis. 66% adult patients were in 15-36 years age group. In AMES surveillance[5] study in Bangladesh from 2007 to 2009 mean age of Japanese encephalitis patients was 31 years ranging from 1 month to 85 years and mean age of total AMES patients was 18 years.

There was an overall male preponderance with a male to female ratio 1.63:1 (N=31 vs N=19). This finding has similarity with a prospective clinical study published in Arch Neurol Journal in 1993[6].

In this series maximum patients were presented with fever (100%), headache (98%) and altered mental status (88%). Out of 50 cases 36 (72%) patients developed new onset seizure and 30 (60%) developed signs of meningeal irritation. 25 patients (50%) were lethargic and 16 (32%) cases were comatose. Female were more comatose (36.84%) compared to male (29%). It correlates with hospital based prospective study of Bangladesh. In a nationwide study done in Netherlands to determine clinical features and prognostic factors in adult with community acquired acute meningitis from October 1998 to April 2002, 95% patients had at least two of four symptoms of headache, fever, neck stiffness and altered mental status[7].

Out of 33 pyogenic AMES cases 22 (66%) developed convulsion and 14 (82%) out of 17 viral AMES cases had convulsion, that is convulsion was more common in viral AMES cases.

A study on JE encephalitis in India showed that altered sensorium in (96%), convulsion (86%) and headache (85%) were the main symptoms for hospitalization[8].

Among all 50 cases of AMES 33 (66%) were diagnosed as pyogenic AMES and 17 (34%) were found viral AMES. 19 male patients (61.29%). and 14 female patients (73.68%) had pyogenic AMES. On the other hand, 12 (38.71%) male and 5 (26.32%) female had viral AMES. P value was 0.369, so the male and female difference was not statistically significant. Diagnosis was made on the basis of clinical findings and CSF study (Cytology, biochemistry, Latex agglutination test). Pyogenic were more common than viral AMES cases.

7 (41%) viral AMES cases were comatose out of 17 and 9 (27.27%) pyogenic AMES cases out of 33 were comatose. So unconsciousness was more common in viral AMES group. This finding correlates with another study[9].

Color of CSF was turbid in maximum (90.9%) pyogenic AMES patients and clear nearly in all viral AMES cases.

In this series CSF glucose concentration was very low 36mg/dl and protein concentration was high 196.7 mg/dl in case of pyogenic AMES cases. In viral AMES cases glucose and protein were normal. This findings correlates with hospital based study of Bangladesh.3 In a study of CSF analysis- acute bacterial versus viral meningitis done in Dubai, United Arab Emirates from 2005-07, CSF Glucose was found to be very low in bacterial than viral meningitis where mean CSF glucose concentration was 26.50 mg/dl (+21.56) Vs 67.00 (18.96) mg/dl[10].

CSF cell counts were very high (average >4200/mm^3) in case of pyogenic AMES of which most were neutrophils (80%) but in cases of viral AMES cell counts were increased mildy (average 70/mm^3) of which most were lymphocytes (90%). This finding correlates with the findings of maximum authorities[11-14]. In another hospital based epidemiological study of Taiwan from 1981-1998, mean CSF cell counts were 3159 (±838/mm3)[15].

In maximum pyogenic AMES cases, there was neutrophilic leucocytosis and average total blood leucocytes count was about 14500/mm^3 which doesn't differ but correlates with the study done by G.E Thwaites et al (>15,000/mm3)[16].

Among 50 cases latex agglutinition test of CSF revealed two positive cases of Neiss. meningitidis and two positive cases of strep. Pneumoniae. As most patients were admitted after receiving antibiotics from primary health care centers, there might be CSF sterilization. CSF sterilization following antibiotic use occurs rapidly. Sterilization of meningoncoccus may occur within two hours, whereas pneumococci four hours of antibiotic therapy is needed. It has also shown in several other studies[17, 18, 19]. Only one JE positive AMES case was detected by IgM ELISA on CSF and serum.

Total 7 (14%) patients expired out of 50. Total 16 patients were comatose and 4 (25%) of them died. On the other hand normal and confused patients were 9 without any death. Out of 25 lethargic patients 3 (12%) expired. So death was high in unconscious patients. Mortality was high in viral AMES cases 23.53% compared to pyogenic AMES (9.09%) cases. These findings correlate with other studies[20, 21, 22].

In another study mortality rate in untreated HSE is around 70%, 40% to 70% in Nipah virus encephalitis[23].

Total 7 (14%) patients developed sequelae out of 50. Motor disability was most common (5 patients out of 7). Only 2

patients developed cognitive impairment but both of them were viral AMES. So cognitive impairment was more in viral AMES. This finding correlates with the reports of Meningitis and Encephalitis Fact Sheet of National Institute of Neurological Disorder and stroke of USA[24]. In another study neurological sequelae occurred in 28 out of 238 (12%) patients, particularly hearing loss[25]. In a prospective longitudinal study from 1997 to 2006 among 279 adult patients of acute meningitis, Mortality rate was found 20% and neurological sequelae developed in 23% patients published in scand J infect Dis journal.[26]

Limitation of the study was that most patients were referred from primary and secondary care hospital after receiving some treatment. So clinical signs and symptoms were partially changed. Laboratory facilities were limited. So that isolation of virus or bacteria was not possible. Long term follow up could not be done as study time was short and most patients and their attendants were reluctant to come for follow up due to transport cost, as most patients came from low socio-economic status.

Conclusion

A patient presented with acute onset of fever and altered consciousness should be screened for AMES. Delayed hospitalization, inadequate treatment, altered consciousness at admission were high risk factors for mortality. The morbidity and mortality rates are quite high in this hospital. In our country laboratory facilities are limited. PCR for virus is not readily available. MRI and EEG facilities for viral AMES are also inadequate. Even CSF culture and other serological tests are not available in maximum district towns. So available vaccines (H. influenza, pneumococcal, measles, mumps, rubella, rabies) should be given in early childhood which can reduce the incidence of meningo-encephalitis. Meticulous history, clinical examination and CSF study are the main factors for the diagnosis of AMES in the context of our country. At the same time in all cases of AMES early diagnosis and appropriate treatment can reduce the rate of mortality and morbidity. Long term follow up of survived AMES cases will help in identifying sequelae and early rehabilitation.

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Original Article

Cervical Cancer Screening and Vaccine- Dissemination of New Opportunity of Cervical Cancer Prevention Among Women – A Hospital- Based Study.

Jesmin ZF[1], Saha E[2], Akhter MD[3], Afroz NM[4], Fatema M K[5], Rahman T[6]

Abstract

Background: Cervical cancer is one of the most common causes of cancer death in women of low income countries. Most of cervical cancer caused by Human Papillomavirus (HPV) infection .Cervical cancer could be eliminated by HPV vaccine ,screening , early treatment of preinvasive lesions . Government of Bangladesh has adopted only cancer screening program by Visual inspection of cervix with Acetic acid (VIA) . To be effective vaccination for adolescent girls is highly recommended.

Objective: Aims of this study to investigate awareness of women for cervical cancer screening and inform them about new HPV DNA based cervical cancer screening and HPV vaccine.

Methods: This prospective cross sectional study was conducted in Gynae and obs outpatient department of Khulna medical college hospital from January to December 2019. A total 665 women were included for study by interview with a questionnaires relevant to study and clinical history.

Results: Most of the women were multipara, common age were in between 30 to 40 years. Women simply heard about cervical cancer screening but unaware about its importance 281(42.25%), screened by VIA 169(25.41%), do not know about screening 215 (32.33%). Heard about HPV test 26(3.90%), only 02 (.3%) had knowledge about the existence of HPV vaccines. Knowledge of HPV vaccine was significantly corelated with higher education (p value .01).

Conclusion: One fourth of women were screened currently and adherent to cancer screening guideline. Knowledge for HPV screening and HPV vaccine are low. More educational program is needed both at community and facility level before introduction of newer screening by HPV assay and HPV vaccine.

Keywords : VIA, HPV vaccine, HPV testing, Bangladesh.

Introduction

GLOBOCAN 2020 estimated about 604127 new cases and 431831 deaths from cervical cancer. Unfortunately 90% of the new cases and global deaths occur in countries without population based screening and also no HPV vaccination program. Cervical cancer is second most common cancer in women of Bangladesh and there were 8268 new cases and 4971 deaths from cervical cancer in the year 20201.

Depending on country and resource screening test for cervical cancer are cervical smear for Papanicolaou test (Pap test), Human Papillomavirus (HPV) DNA test ,Visual inspection of cervix with Acetic acid (VIA) and colposcopy for detection of cervical intraepithelial neoplasia (CIN) or combination of them. Pap test were practiced over last three decades in developed countries has resulted dramatic decrease in

1. Zannatul Ferdous Jesmin, Assistant Professor, Department of Gyne & Obs, Khulna Medical College, Bangladesh

2. Eti Saha, Associate Professor, Department of, Gyne & Obs, Khulna Medical College, Bangladesh

3. Most. Dalia Akhter, Associate Professor, Department of Gyne & Obs, Khulna Medical College, Bangladesh

4. Nargis Monjura Afroz, Junior Consultant, Department of Gyne & Obs, Khulna Medical College, Bangladesh

5. Muckti Kaniz Fatema , Junior consultant, Department of Gyne & Obs, Khulna Medical College, Bangladesh

6. Tahmid Rahman, Medical officer, Khulna City Medical College, Bangladesh

Corresponding Author:
Dr. Zannatul Ferdous Jesmin, Assistant professor, Department of Gyne & Obs, Khulna Medical College, Bangladesh. E mail zannatd7@gmail.com

cervical cancer mortality. Diagnosis and treatment of CIN is the core of any type of screening program[2].

Bangladesh implementing population based screening in phased manner from 2005 by a cheaper cost effective screening by VIA test. Screen-positive women are referred for colposcopy and treatment[3]. At present there are more than 500 facility for screening in Bangladesh with in Government health infrastructure[4, 5]. Problem is most of women have not yet been screened. There are many determinants of cancer control. Coverage of target population, adherence for periodic screening linkage with treatment, low socioeconomic condition, provision for using new promising screening tests and HPV vaccine, budgetary allocation for health care, womens education and screening awareness ,all are relevant for cervical cancer control in Bangladesh perspective[6, 7].

Over the last 15 years, cervical cancer prevention guidelines have changed dramatically following introduction of HPV DNA assay and HPV vaccine. Role of high risk types HPV infection in etiopathogenesis of CIN and cervical cancer is well understood[8]. From 2018 new strategy of global call of action by WHO is to eliminate cervical cancer by next century with access of women to more effective HPV based primary screening and HPV vaccination for girls[9, 10]. HPV infection common in young women with onset of sexual activity, though 90% of this infection cleared with natural immunity[11, 12]. Infection with one or more of 15 oncogenic HPV sub types (HR-HPV) may persist in susceptible host causing cellular changes to CIN over 4-70 months and invasive cancer over years to decades if not treated . HPV 16,18 prevalence in invasive cervical cancer is 99.7%[13, 14].

Why new strategies are more effective ?HPV DNA test for cervical smear offer high negative predictive value and long screening interval. A woman with negative HPV test has low probability of developing cervical cancer. It is also important to follow up of post treatment of CIN cases preventing recurrences. HPV DNA assay by Commercial Kit are more sensitive as a primary screening and many advantages in low resource settings with problems of inadequate screening ,including cost effectiveness[15, 16].

Human Papillomavirus (HPV) vaccine are more effective for adolescent girl aged 9-14 years. Bar of age limit of vaccine are also decreasing .Vaccines stimulate the body to produce antibodies and reduces development of high grade lesion .Vaccine safety was excellent in surveillance[17]. Successful implementation of WHO Global elimination

strategy would reduce cervical cancer death by 99% and save 62 million women's life by 2120, until switchover is possible we should continue on going national cervical cancer control program[18].

Like other Southeast Asian country, Bangladesh, has burden of disease still lacking target coverage of screening and provision for HPV DNA assay. Strategy plan for HPV vaccination through GAVI was interrupted in midst of COVID pandemic. More than 50% of all new cervical cancers are in women who have never been screened or have not been screened in last five years. Perceived benefits of cancer screening and education on HPV are most important approach to overcome these obstacles. The outpatient department is a place that has an opportunity for dissemination of update of health information to population and also counsel them for screening[19].

Aims of this study to investigate awareness of women for cervical cancer screening, HPV testing and HPV vaccine and sharing of knowledge to inform them.

Objective of this study to know screening status of women and assessment of their knowledge about new cervical cancer preventive measures as well as refer them for screening.

We hypothesized that females who are aware of cervical cancer screening are most likely to support upcoming programs at schools . It is unclear woman has how much knowledge about HPV facts in cervical cancer. Ultimate aim of study therefore women should learn the benefits of screening and vaccine that we wanted to examine in detail. As no data were available about knowledge and awareness activity for these preventive tools based on HPV in Khulna, the results of this study may help to design improve intervention as well as sensitize the women for cancer prevention care.

Methods

A cross sectional type of study was conducted from the month of January to December 2019 among gynecological patients, Khulna medical college hospital, Khulna. Women consulting in Gynae out door selected by purposive sampling and invited to participate in study. A semi -structured questionnaire used as an instrument based on national guideline and updated literature of information and education of cervical cancer prevention tools. Reproductive history, sociodemographic history were obtained from the respondent by face to face interview. Questions were asked to assess knowledge about cervical cancer and cancer screening by VIA test,

HPV vaccine and HPV based test .They were also asked whether ever had been screened for cervical cancer by VIA with in last 5 years. Individual answers were noted, who responded "yes" to questions were regarded to have knowledge or know the facts .At the end of interview information given as availability of VIA test in outpatient clinic and also about newer tools of HPV vaccine and HPV test facts. Women were counselled for benefits of screening and feedback was taken. Screening centers nearby available to them were mentioned. Patients willing to participate in local center and referred for VIA test with National identity card (NID). Interview and questionnaire were conducted in Bangla, complied in English during data interpretation. Womens were informed and educated for screening and requested to share with family and friends. Inclusion criteria were women in between 30 to 60 years. Exclusion criteria were acutely ill patient, known case of cervical cancer, pregnancy, women without cervix, unwilling to participate following verbal consent. Knowledge of cervical cancer screening in Bangladesh based on different study was found about 41.5%. We calculated study population of 665 with 95 % confidence level and margin of error 3.74%. Data analysis was done by IBM SPSS version 23. Results were in frequency and percentage. Pearson coefficient analysis was done. P value <.05 was considered to be significant.

Results

Age of study population were in between 30-60 years with mean age 39.20± 7.55 years, majority 500 (76.21%) were in age group 30 –40years .Mean duration of marriage 20.33±8.468 years ,most were para 1-3, grand multi para 42 (6.31%), urban 301 (45. 27%), periphery to city 364(54.73%).

Education level were illiterate 102 (15.54%) , primary 174 (26.1 6%), secondary (SSC) 250 (37.59%) , Higher secondary 60 (9.02%) ,graduation and Post graduation 79 (11.87 %), Most of them were house wives 645 (97.00%) and employed were 20 (3.00%). Demographic information of participants were presented in Table I.

Women simply heard VIA but they were unaware about screening and about cervical cancer 281(42.25%), 215 (32.33%) donot know about the same, here 169(25.41%) of participant were screened by VIA. Employed women and those had primary education had better understanding on screening.

26(3.90%) participant heard about HPV test, no knowledge about HPV test in 639(96.09%), while only 02 (.3%) had knowledge about the existence of HPV vaccines. Knowledge of HPV vaccine was related with higher education and Pearson coefficient was significant. (p .01) Table II.

Table I- Socio -demographic characteristics of respondents

Variable	N (%)
Age range (years)	
30-40	500 (76.21)
41- 50	145 (21.8)
51- 60	20(3.00)
Education and employment	
Illiterate	102(15.54%)
Primary	174(26.16)
SSC	250(37.59)
Higher Secondary	60(9.02)
Graduation and PG	79(11.87)
Service holder	20(3.00)
Living place	
Urban	301(45.27)
Peri-urban	364(54.7 3)
Reproductive status	
Years of Productivity	20.33+8.468
Para (mean)	2.16+.971

Table II- VIA Screening and HPV knowledge among respondents.

Variable	N (%)
VIA testing	
Unaware	281(42.25%)
Screened	169(25.41%)
Don't know	215 (32.33%)
HPV testing	
Not heard	639(96.09%),
Heard	26(3.90%),
HPV vaccine	
Know	02 (.3%)
Don't know	663(99.6%)

Discussion

This study explore awareness women for cervical cancer prevention by screening and HPV vaccine. The fundamental goal of cervical cancer screening is to prevent morbidity and mortality from cervical cancer[20]. Demographic characteristics of study population were comparable with other study, majority of women were 30 to 40 years, mean 39.20 +7.55

years ,venerable age for cancer screening. Most of the cervical cancer diagnosed in 35 - 55 age group.   WHO recommends screening at least once in a life time between 30 and 49 years of age and effective treatment.Screening of older woman leads to substantial reduction and mortality of cervical cancer[21].

In this study most common co factors are early age at marriage ,mean duration 20.33±8.468 and multiparity (Table-I)[22]. Only 24.4% % of respondents had screening, though 42.8% of women heard of cervical cancer and VIA, the results that are similar to study in chattagram medical college[23].   Level of awareness and interest are also low for screening an issue that was observed with other study in Bangladesh[24]. Study results identified several factors affecting their   knowledge. Those have at least primary education underwent more screening by VIA, older women in rural area less informed about screening[25, 26].

About 55.4 million of Women more than 15 years of age are at risk of cervical cancer in Bangladesh, till now only 18.54% of population underwent screening (BSMMU). Like this study in one study in Addis Ababa among 2140 women only 215 (10%) screened by VIA[27] .Though VIA is a effective and promising alternative intervention reducing burden of Cervical cancer revealed in many Indian study, achievement are different in low -and middle income country[28].

Target woman should be informed that diagnosis in precancer stage is highly curable creating interest for screening.

 Knowledge and information about role of HPV test in cervical cancer is lower than other study (Table-II). Campaign for HPV role in cervical cancer are sporadic in Bangladesh, only 2.4 % of respondents had heard of HPV and .3% heard of HPV vaccine. These results are very much lower than reported in survey in developed country .Discrepancy from other results may reflect lower rate of higher education in study population.   A study results of girls and women in Spain showed they knew better about HPV facts[29].

Our results suggest the urgent the need to disseminate knowledge about HPV and its association with cervical cancer, and such activity are likely to be effective for increasing the awareness for vaccine for their girls .New technologies like HPV testing identified more women subsequently diagnosed with cancer and pre-cancer than Pap test and VIA. More ever primary vaccination will reduce reduces incidence of infection and periodic screening . HPV -negative cervical cancer is extremely rare[30].

WHO now recommend new technology approaches HPV testing from 30 years, with a interval of 5 to 10 years, with screen, triage and treat approach[31].

The study results showing low level of awareness and knowledge of cervical cancer screening to a great extent reflect the work load that needs to overcome for introducing HPV based screening. Though Bangladesh developed National cancer control strategy paper for 2017 -2022, community participation and non-compliance are major obstacles for successful reduction of cancer in country[32]. Regarding vaccine experience in Bangladesh bivalent HPV vaccine 16,18 program implemented among 50 adolescent students in Dhaka in 2008 – 2009 , and in another demonstration piloting among girls in a school of Gazipur under GAVI in 2016. Our Hope is that GAVI will provide support for national introduction of HPV vaccine at school[33, 34].

Issues that promote screening are behavioral changes at the community, social media networks, social empowerment and counselling by health care providers. Without understanding and addressing these obstacles, these promising new tools for cervical cancer prevention may not be effective. So discussion about vaccine in this study will heard of it to mother considering immunization for their girls. Cervical cancer is now considered as a vaccine preventable disease.

Screening for cervical cancer may also generate anxiety related to the screening procedure itself, negative perception for test results, and for any subsequent diagnostic and treatment and follow up, explanation and offering by gynecologist could be more reassuring ,the strength that was observed in this study and an important art to practice. An specialist as a facilitator has strong impact as her relationship with woman build good rapport for screening and treatment[35]. Our study results may be more reliable conducted by direct interview by a group of gynecologists .Study could also emphasize about some of things that a gynecologist could do in every day practice that is talk on cervical cancer during consultancy, a missed opportunity! Discussion and understanding of women in cancer prevention opportunity would led to enhancement in health literacy. A concerted efforts need for HPV vaccine and HPV screening, a policy point suggested for stake holders[36].

Limitations of this study are questionarie based study may had some bias. Strength of the study researchers are colposcopists directly communicating with patient. Prolonged engagement that is sufficient time in data collection might offer in -depth understanding of phenomena to learn culture

of the group under study .This activity not only increases awareness but also will increase the frequency of early detection at best opportunity. Results of this study serve as a valuable data on HPV infection and awareness which has impact on future planning .Finally results of this this study can provide input for further studies on the subject under study. The dynamics of cervical cancer prevention guideline continually change and updating by scientific development. Study recommend that there is urgent need to incorporate new global strategy of HPV vaccination and HPV DNA based screening in cervical cancer in upcoming national cancer control programe, for that we need more assessment of knowledge in different region of Bangladesh documented in this this study .

Conclusion

Most of women at risk of cervical cancer did not screened. VIA is an essential test for resource limited country is still underutilized. Majority has poor knowledge about HPV DNA testing and HPV vaccine. Our results point to urgent intervention to disseminate these new tools at each contact of women with health facility.

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Review Article

Oxidative Stress: A Silent Killer

Sardar MMR[1], Pervin F[2]

Abstract

Oxidative stress occurs due to excess production of free radicals (oxidants) and failure of the body's anti-oxidant defense mechanism to prevent its injurious effect. In other words, increase oxidant-anti-oxidant ratio is the reason of increase oxidative stress. Free radicals are produced inside the cell during normal metabolic process, metabolism of drugs or chemicals, phagocytosis by the leukocytes, absorption of radiant energy like Ultraviolet ray or X-ray and Fenton reaction. Free radicals are noxious for the cells. It causes lipid peroxidation of the cell membrane, oxidative modification of the proteins and D.N.A lesion. Body has numerous enzymatic and nonenzymatic anti-oxidant defense mechanism which can reduce free radicals mediated cellular injury and remove free radicals. Enzymatic anti-oxidants are Catalase, Superoxide dismutase and Glutathione peroxidase. Nonenzymatic antioxidants are vitamin A, C and E. Moreover, certain plasma proteins like Ferritin which binds with Iron and Ceruloplasmin which binds with Copper also reduces free radical generation, thereby reduces oxidative stress. Successive accumulation of free radicals mediated cellular injury affect healthy living. It is associated with pathogenesis of many noncommunicable diseases like Atherosclerosis, Hypertension, Diabetes mellitus, Ischemic Heart disease, Ischemic Stroke, Malignancy etc. Moreover, increased oxidative stress is related to ageing process. As a result, increased antioxidant capacity may reduce the morbidity and mortality which are related to oxidative stress. Healthy life style may reduce oxidative stress and improve body's antioxidant defense capacity like regular exercise, avoiding smoking and excess alcohol consumption, calorie restriction, night shift work etc. The objective of this review is to focus on researches about oxidative stress which is related to pathogenesis of noncommunicable disease and healthy ageing. Furthermore, to increase awareness about healthy lifestyle which reduces oxidative stress. Future researches should address on improving antioxidant defense capacity by diet, drug and lifestyle modification.

Key words: Oxidative stress, Oxidants, Free radicals, Antioxidants.

Introduction

Free radicals were first regarded as the cause of oxygen toxicity in 1954 and soon afterward Denham Harman integrated the " rate of living theory " with the " free radical theory of oxygen toxicity", proposing that aging is due to the harmful activities of free radicals endogenously formed during normal metabolism.1

Free radical (FR) can be defined as a chemical species, an atom or a molecule that has one or more unpaired electrons in its valance shell and is capable of existing independently. Free radical contains an odd number of electrons which makes it unstable, short lived and highly reactive, therefore it reacts quickly with other compounds in order to capture the needed electron to gain stability. Generally, free radical attacks the nearest stable molecule by stealing its electron. When the attacked molecule loses its electron, it becomes a free radical itself, beginning a chain reaction cascade resulting in disruption of a living cell.2

Oxygen free radical mediated cell damages are implicated in the aging process. Oxidative damage to DNA, proteins and lipids induced by the overproduction of reactive oxygen

1. Md. Mijanur Rahman Sardar, Associate Professor (C.C), Department of Physiology, Khulna Medical College, Bangladesh
2. Farhana Pervin, Associate Professor (C.C), Department of Pharmacology, Sheikh Sayera Khatun Medical College, Gopalgonj, Bangladesh

Corresponding Author:
1. Dr. Md. Mijanur Rahman Sardar, Associate Professor (C.C), Department of Physiology, Khulna Medical College, Bangladesh. Email: mijanrmc@hotmail.com.

species (ROS) accumulate with age and contributes to degenerative diseases and the aging phenomenon by disrupting cellular homeostasis. On the other hand, the human body generally has anti-oxidant system which plays an important role in the suppression of ROS over production and protects cells from oxidative stress. Anti-oxidant system is comprised of endogenous compounds (billirubin, uric acid, super oxide dismutases, catalase, glutathione peroxidase etc.) and exogenous compounds (carotenoids, tocopherols, ascorbate, bioflavonoids etc.).

Oxidative stress results from the imbalance between oxidative and anti-oxidative mechanisms with increased levels pro-oxidants and depletion of anti-oxidants leading to tissue damage. 3 An increase in oxidative stress by free radicals or imbalance in antioxidant status may be one of the causes of aging. With age and increasing oxidative stress, endogenous antioxidant systems may be challenged beyond their ability to maintain the pro-oxidant to anti-oxidant equilibrium.4

Biomarkers of oxidative stress:

Antioxidant capacity of plasma: Since imbalance between antioxidant and oxidants generates the condition of oxidative stress, estimation of the reducing power/ antioxidant capacity plasma is the first step in the prediction of oxidative stress. The FRAP (ferric reducing ability of plasma) assay developed by Benzie and Strain gets superiority because it is not dependent on the enzymatic/non-enzymatic methods to generate free radical prior to evaluation of the anti-radical activity of plasma.

Lipid peroxidation: Lipid peroxidation was first studied in relation to the deterioration of foods in 1930s, when the study on the chemistry of free radical reactions made remarkable advancements. One of the most often used biomarker to investigate the oxidative damage on lipids is the measurement of MDA, Since the measurement of Malondialdehyde (MDA) is easy and fast to perform and the results are very reproducible, it is one of the most important biomarkers for the evaluation of the status of lipid peroxidation and is a biomarker of aging.

Protein oxidation: Reactive oxygen species can lead to oxidation of amino acid residue side chains, formation of protein-protein cross-linkages, and oxidation of the protein backbone resulting in protein fragmentation. Use of protein carbonyls as index of oxidative stress has some advantages in comparison with the measurement of other oxidation products because of the relative early formation and the relative stability of carbonylated proteins.

Reduced Glutathione: Reduced glutathione (GSH) is a major intracellular non-protein –SH compound and is accepted as the most important intracellular hydrophilic antioxidant. GSH plays a key role in protecting cells against electrophiles and free radicals. The reduced glutathione and membrane –SH group are important markers of oxidative stress 5

Determination of plasma levels of vitamins A, C and E: Plasma alpha-tocopherol (vitamin E) and retinol (vitamoin A) can be determined by reverse phase HPLC and can be detected by an UV detector at 292 nm for vitamin E and 325 nm for vitamin A. Vitamin C levels can be detected by using the method of Roe and Kuether.6

Determinations of erythrocyte antioxidant enzyme activities: Catalase activity can be measured by spectrophotometric analysis of the rate of hydrogen peroxide decomposition at 240 nm.7 Glutathione peroxidase can be assessed by Paglia and Valentine method.8 Glutathione reductase activity can be determined by the measuring of the rate of NADPH oxidation in the presence of oxidized glutathione.9 Superoxide dismutase activity can be measured by the NADPH oxidation procedure.10

Generation of Free Radicals:

Free radicals may be generated within cells in several ways.

- The reduction-oxidation reactions that occur during normal metabolic processes. During normal respiration, molecular oxygen is reduced by the transfer of four electrons to H_2 to generate two water molecules. This conversion is catalyzed by oxidative enzymes in the ER, cytosol, mitochondria, peroxisomes, and lysosomes. During this process small amounts of partially reduced intermediates are produced in which different numbers of electrons have been transferred from oxygen, these include superoxide anion (one electron), hydrogen peroxide (two electrons), and hydroxyl ions (three electrons).

- Absorption of radiant energy (e.g., ultraviolet light, x-rays). For example, ionizing radiation can hydrolyze water into hydroxyl ion and hydrogen free radicals.

- Rapid bursts of ROS are produced in activated leukocytes during inflammation. This occurs by precisely controlled reaction in a plasma membrane multi-protein complex that uses NADPH oxidase for the redox reaction. In addition, some intracellular oxidases (such as xanthine oxidase) generate super oxide.

- Enzymatic metabolism of exogenous chemicals or drugs. It can generate free radicals

that are not ROS but have similar effects (e.g., CCL 4 can generate CCL3)

- Transition metals such as iron and copper donate or accept free electrons during

intracellular reactions and catalyze free radical formation, as in the Fenton reaction.

- Nitric oxide (NO). An important chemical mediator generated by endothelial cells, macrophages, neurons, and other cell types, can act as a free radical and can also be converted to highly reactive peroxynitrite anion as well as NO2 and NO3-.

Removal of Free Radicals

Free radicals are inherently unstable and generally decay spontaneously. Super oxide ion, for example, is unstable and decays (dismutates) spontaneously into oxygen and hydrogen per oxide in the presence of water. In addition, cells have developed multiple non-enzymatic and enzymatic mechanisms to remove free radicals and thereby minimize injury. These include the following:

- Antioxidants either block the initiation of free radical formation or inactivate (e.g., scavenge) free radicals. Examples are the lipid soluble vitamins E and A as well as ascorbic acid glutathione in the cytosol.

- As we have seen, iron and copper can catalyze the formation of ROS. The levels of these reactive metals are minimized by binding of the ions to storage and transport proteins (e.g., transferrin, ferritin, lactoferrin, and ceruloplasmin), thereby minimizing the formation of ROS.

- A series of enzymes acts as free radical-scavenging systems and breaks down hydrogen peroxide and super oxide ions. These enzymes are located near the sites of generation of the oxidants and include the following:

1. Catalase, present in peroxisomes, decomposes hydrogen peroxide into water and oxygen.

2. Superoxide dismutases (SOD) are found in many cell types and convert superoxide ion to hydrogen peroxide. This group includes both manganese-SOD, which is localized in mitochondria, and copper-zinc-SOD, which is found in the cytosol.

3. Glutathione peroxidase also protects against injury by catalyzing free radical breakdown. The intracellular ratio of oxidized glutathione (GSSG) to reduced glutathione (GSH) is a reflection of the oxidative state of the cell and is an important indicator of the cell's ability to detoxify ROS.

Pathologic Effects of Free Radicals

- Lipid peroxidation in membranes. Oxidative damage is initiated when the double bonds in unsaturated fatty acids of membrane lipids are attacked by oxygen derived free radicals, particularly by hydroxyl ion. The lipid-free radical interactions yield peroxides, which are themselves unstable and reactive, and an autocatalytic chain reaction ensues (called propagation), which can result in extensive membrane damage.

- Oxidative modification of proteins. Free radicals promote oxidation of amino acid chains, formation of protein-protein cross-linkages (e.g., disulfide bonds), and oxidation of the protein backbone. Oxidative modification of proteins may damage the active sites of enzymes, disrupt the conformation of structural proteins, and enhance proteasomal degradation of unfolded or misfolded proteins.

- Lesions in DNA. Free radicals are capable of causing single- and double-strand breaks in DNA, cross-linking of DNA strands, and formation of adducts. Oxidative DNA damage results in cell aging and in malignant transformation of cells.[11]

Researches about factors affecting oxidative stress status in healthy adults

Age: Ozbay and Dulger (2002) state that serum MDA level was higher in elderly than in children and in adults. Superoxide dismutase and Glutathione peroxidase levels of children and adults were significantly higher than those of elderly group.

Gender: Ozbay and Dulger(2002) state that no significant change was apparent between MDA, SOD, GSH-Px levels determined in the male subjects and those in the females in blood.[12]

Kharb and Ghalaut (2003) state that the women had significantly higher MDA values for plasma. Cause of increased levels of MDA in women is not known. It might be due to the fact that women have more adipose tissue reserve as compared to males.[13]

Casado et al. (2008) state that no significant variations with respect to sex were detected in MDA levels.[14]

Kasapoglu and Ozben(2001) state that they found no evidence that gender, weight, blood pressure influenced significantly the parameters measured in the same and different age groups.[15]

Mendoza-Nunez et al. (2007) state that LPO serum levels were significantly higher in older subjects than in the younger ones of the same sex, however, significant differences were not observed between sex by age group. Moreover, significant differences were not found in oxidative stress markers between pre-menopausal versus post-menopausal women.16

Pregnancy: Amirkhizi et al. (2007) state that those in the highest quartiles of number of pregnancies also had the highest mean values of plasma MDA.4

Exercise: Ozbay and Dulger(2002) state that adult volunteers in the sedentary groups run 20 minutes sub-maximally. MDA, SOD and GSH-Px levels were measured after 20 minutes run. There were a significant reduction in blood SOD and GSH-Px activities and an increase in MDA level.12

Dittmar et al. (2008) state that exhaustive exercise causes oxidative stress, whereas moderate exercise may act as an antioxidant.17

Smoking: Ozbay and Dulger(2002) state that serum MDA level of smokers was higher whereas SOD activity was lower than those of nonsmokers and GSH-Px did not change significantly.12

Nielson et al. (1997) state that we found a significant correlation between plasma MDA and the number of hours of exposure to cigarette smoke, but we found no correlation between plasma MDA and the number of cigarettes smoked by the individual. It states that cigarette smoking is known to increase production of oxygen free radicals by poly morpho nuclear leukocytes and to decrease activities of some free radical scavengers.18

Marriage: Casado et al. (2008) state that with regard to marital status, significant variations in MDA levels were detected between single and married workers but not with respect to divorces. No significant differences in SOD and CAT activities and MDA levels were observed between having children or not, or the number of children they had.14

Calorie restriction: Sohal and Weindruch (1996) state that a reduction in calorie intake per se, rather than of a particular nutrient, is required to increase maximum life span.19

Specimen variation: Knight et al. (1987) state that in comparison with EDTA, samples treated with lithium, heparin, sodium citrate or CPDA-1 give significantly higher results, as also does serum. In addition, there is less variation in the EDTA anti-coagulated specimens. For these reasons,

use of EDTA is to be preferred. Hemolysis significantly increases the MDA in plasma. Therefore, plasma should be separated as soon as reasonably possible.20

Nielsen et al. (1997) state that the consistently lower MDA concentrations observed in EDTA treated plasma are probably related to EDTA chelation of iron in the TBA assay as well as its weak activity as an antioxidant. The higher content of MDA in serum versus plasma could be explained by lipo-peroxides being formed during coagulation. Thus, MDA measured in EDTA treated plasma seems to generate the least interfered indication of the degree of lipid per-oxidation at the time of blood sampling.

Life style factors: Nielsen et al. (1997) states that a positive correlation was demonstrated between plasma MDA and weekly alcohol consumption.18 Casado et al. (2008) state that significant differences were detected in SOD and CAT activities and MDA levels between smokers and non-smokers, but not for alcohol consumption, or coffee, tea and cola consumption. Significant differences were obtained in MDA levels between those who frequently practice some kind of sport and those who never practice sport. Moreover, higher SOD activity and MDA levels were detected in nurses working night and evening shifts. 14

Researches about oxidative stress status in healthy aging

Researches in India

Akila et al. (2007) observed that there was increase in free radical generation and decrease in antioxidant defense mechanism in elderly people when compared to normal young subjects. Highly significant increase in MDA and decrease in antioxidants was observed in elderly people when complicated with diabetes and hypertension. They state that high blood levels of G-SH predict good health, whereas, low levels predict early disease.21 Jawalekar et al. (2013) measured total antioxidant capacity (TAC) in the plasma. The majority of the TAC is composed of uric acid. Uric acid tends to increase with age, which may cover part of the antioxidant deficiency in old age. They state that the total antioxidant capacity is not a simple sum of the activities of the various antioxidant substances but the cooperation of the antioxidants in human serum that provides a greater protection against attacks by free radicals. It is the dynamic equilibrium between various antioxidants. A non-equilibrium or poor cooperation between the antioxidants may possibly result in low TAC.22 Singh et al. (2009) stated that the activity of GPx, a selenium containing enzyme was found to be decreased from 6.64% to 20.79% in plasma with increasing

age groups in both sexes upon increase in lipid peroxide level. Moreover, they observed highest GPx concentrations in younger female group.[23]

Researches in Iran

Amirkhizi et al. (2007) stated that plasma MDA levels were positively related to age, number of pregnancies, fat intake and vitamin E intake. They state that double bonds in the fatty acid molecules are vulnerable to oxidation reactions and consequently may cause lipid peroxidation.[4] Marjani et al. (2007) observed among different ethnic groups of Gorgan that the balance between antioxidant and pro-oxidant factors in free radical metabolism shifts towards increased lipid peroxidation with advancing age.[24]

Researches in Turky

Ozbay and Dulger (2002) observed that serum MDA level was higher in the elderly than in the children and in the adults. MDA levels were higher in the smokers, acute exercise than their counterparts in the control groups.[12] Kasapoglu and Ozben (2001) observed that there was an age-related increase in the concentration of lipid peroxides. The mean MDA values were significantly higher in the age group (50-59) years as compared with that of (30-39) years age group. Moreover, they state that vitamin C and E levels did not change with age and there was also no gender difference. [15] Saraymen et al. (2003) showed the activities of antioxidant enzymes and the correlations of these enzymes' activities with each other in healthy human PMNLs were age and sex dependent.[25]

Research in Spain

Casado et al. (2008) did research about relationship between oxidative and occupational stress and aging in nurses of an intensive care unit. It shows that MDA levels increase with age, supporting the premise that MDA levels are a valid marker for oxidative stress and aging, as it is known that cell membrane structures are subjected to increased oxidative stress as a consequence of age and occupational stress.[14]

Research in France

Winklhofer-roob et al. (2004) studied about effects of vitamin E depletion / repletion on biomarkers of oxidative stress in healthy aging. It shows that supplementation with vitamin E to above average levels in healthy, male non-smoking volunteers significantly enhances antioxidant

protection, as evidenced by decreased LDL susceptibility to oxidation and decreased biomarkers of lipid per-oxidation and oxidative DNA modification.[26]

Research in Germany

Dittmar et al. (2008) gave evidence for a tendency towards increased DNA damage (single strand breaks) in older males. They found the highest oxidative status in young females. They assume that female sex hormones, which are highest in young women, interact with the analytical test system. They opine that the test system for oxidative status might be one limitation of the study.[17]

Research in Italy

Andriollo-sanchez et al. (2005) observed that plasma TBAR's were significantly higher in middle aged group (61 years) than in the older group (71 years), with the highest values in females. They opine that TBAR's production is dependent on polyunsaturated fatty acid intake, and it cannot be ruled out that a possible lowered consumption of polyun-saturated fatty acids by older elderly resulted in a lesser extent of lipid peroxidation.[27]

Research in Mexico

Mendoza-Nunez et al. (2007) showed a significant increase of lipid peroxide in subjects more than 60 years in comparison with 25-29 years group, and at the same time an age-related decrease of total antioxidant status.[16]

Research in USA

Knight et al. (1987) studied about reference intervals for plasma lipo-peroxides to observe age, sex and specimen related variations. Liquid chromatographic profiles for plasma lipoperoxides, expressed as MDA (Malondialdehyde). The men were divided, by age, into four age groups: 18-25, 26-35, 36-45, and 46-65 years. Means and SD for the first three groups were very similar, those for the last group were significantly higher.[20]

Research in Japan

Suzuki et al. (2010) studied about oxidative stress and longevity in Okinawa. They state that both lipid peroxide and vitamin E tocopherols were lower in centenarians. They opine that since tocopherols are lipid soluble, it is possible that very old persons, who generally have low blood lipids, display artificially low blood tocopherol levels since it is mainly lipid bound.[2]

Researches about oxidative stress status in different diseases

Hypertension: Ceriello, A. (2008) states that oxidative stress favors the development of hypertension.29

Acute myocardial infarction: Aznar et al. (1983) state that MDA levels are within normal range in Angina Pectoris patients but MDA levels significantly increases in Acute Myocardial Infarction patients following acute event.30

Ischemic Stroke: L.S. Bir et al. (2006) state that serum MDA levels increases in chronic stroke patients with small or large vessel diseases.31

Atherosclerosis: Yang et al. (2008) state that positive correlation is present between MDA and atherogenic index.32

Alzheimer disease: Ozcankaya and Delibas (2002) state that MDA level increases in Alzheimer disease.33

Diabetes Mellitus: Marjani, A. (2010) States that lipid peroxidation increases in type two Diabetes Mellitus.24

Rheumatoid Arthritis: Mahajan and Tandon (2004) state that free radicals is a cause of tissue damage in Rheumatoid arthritis.2

Pre-eclampsia: Dave et al. (2012) state that marker of oxidative stress MDA increases and anti-oxidant enzyme decreases in pre-eclampsia.34

Arsenicosis: Pi et al. (2002) state that oxidative stress increases due to chronic exposure of Chinese residents to arsenic contained in drinking water.35

Cancer: Klaunig et al. (1998) state that oxidant induced injury has a role in the cancer process specially during the promotion stage.36

Age related macular degeneration: Totan et al. (2001) state that MDA level increases significantly in age related macular degeneration in comparison to controls.37

Conclusion

Oxidative stress represents increased oxidant to antioxidant ratio which facilitates free radical mediated cell injury. Free radicals are highly reactive and unstable chemicals which react with lipid, protein and nucleic acids, thereby alters their normal function. As a result, increased oxidative stress is related to pathogenesis of numerous noncommunicable diseases and ageing related morbidity and mortality. Future studies are needed to find out better biomarkers to identify unknown oxidants and antioxidants to assess oxidative stress status of the individual. Moreover, research is required to find out the compensatory responses against the increased oxidative stress and the measures to improve the defense mechanism. In addition, research should put emphasis on pathogenesis of different noncommunicable diseases related to increased oxidative stress and to develop new drugs, dietary and lifestyle modification to reduce oxidative stress.

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A Lady with Hematidrosis: An Exceedingly Rare Clinical Situation

Faruquzzaman[1], Ahmed QM[2], Rob A[3] , Sarkar HS[4]

Abstract

Hematidrosis, also known as bloody sweat is an extremely rare condition and is characterized by blood mixed with sweat oozing out skin and mucosa. Most often, this rare condition is idiopathic. Hematidrosis also known as hemidrosis or hematohidrosis, is a situation in which capillary blood vessels that feed the sweat glands rupture, causing them to exude blood, and more commonly occurs under conditions of extreme physical or emotional stress. It is proposed the term "hematofolliculohidrosis" because it appeared along with sweat-like fluid and blood exudes via the follicular canals. Though its etiopathogenesis remains unclear, is precipitated during conditions of extreme stress, which can be physical, emotional, or psychological. It is hypothesised that capillary blood vessels feeding the sweat glands rupture, causing exudation of blood on the surface mixed with sweat like material. It is a physician challenge as the patient is often subjected to multiple investigations and seldom has to face social stigma associated with it. This condition is usually self resolving once the stressor is controlled. Here in this case report, the history of a 41 years aged lady having recurrent episodes of blood stained sweat is going to be discussed.

Key words: Hematidrosis, hemidrosis, hematohidrosis, hematofolliculohidrosis.

Introduction

Hematohidrosis is a rare clinical condition of sweating blood. It may occur when a person is suffering from extreme stress, for example, facing his or her own death[1]. Very few cases of hematohidrosis have been reported in literature. Hematohidrosis is also known as hematidrosis and hemidrosis. Exceedingly rarely, it may be associated with Haemolacria (blood tear). The exact etiology of hematohidrosis is unknown. It is believed to be a systemic disease, e.g., it has been associated with vicarious menstruation, a condition in which bleeding occurs from a surface other than the mucous membrane of the uterine cavity at a time when normal menstruation should take place. Hematohidrosis has been reported with primary thrombocytopenic purpura[2].

In another study, a case of hematidrohosis, accompanied with otorrhea and otoerythrosis, has been reported[3]. Hematohidrosis can also occur in the settings of excessive exertion, psychogenic and other unknown factors. It has also been reported in an 8-year-old child just as in this case without any specific pathology[4].

1. Faruquzzaman, Junior Consultant (Surgery), 250 Beds Razia Naser Zila Hospital, Bagerhat, Bangladesh.
2. Quazi Mehranuddin Ahmed, Assistant registrar, Dept of Casualty, Dhaka Medical College Hospital, Bangladesh.
3. Abdur Rob, Assistant registrar Dept. of Surgery, Khulna Medical College Hospital, Bangladesh.
4. Himadry Shakhar Sarkar, Assistant registrar Dept. of Surgery, Khulna Medical College Hospital, Bangladesh.

Corresponding Author:

Dr. Faruquzzaman, Junior Consultant (Surgery), 250 Beds Razia Naser Zila Hospital, Bagerhat, Bangladesh. Email: drfaruquzzaman@yahoo.com

Few theories have been proposed regarding the etiopatho-genesis of hematohidrosis. One such school of thought says that there are multiple blood vessels around the sweat glands arranged in a net like form. It is believed that under the pressure of great stress the vessels contract. Subsequently as the anxiety passes the blood vessels dilate to the point of rupture. The blood at this point goes into the sweat glands which push the blood to the surface and manifests as droplets of blood mixed with sweat[5]. The term "hematofolliculohi-drosis" was proposed because it appeared along with sweat-like fluid and the blood exuded via the follicular canals[6].

Historical Background

Jesus Christ experienced hematohidrosis while praying in the garden of Gethsemane before his crucification as it is quoted from American King James version Bible "Being in an agony he prayed more earnestly: and his sweat was as it were great drops of blood falling down to the ground"-Luke22:44. Leonardo Da Vinci reported a soldier who sweated blood before one of the battles and there have been several other observations seen in individuals before execution since ancient times[7].

Case Description

A 41 years Muslim housewife has got presented to Depart-ment of Surgery, Khulna Medical College Hospital, with the complaints of spontaneous bleeding underneath the sole of her both feet (Fig-1&2) for the last few days. It was not associated with any history of trauma or burn. The consisten-cy of blood was however thinner and it appeared as blood stained fluid. According to the patient, she was familiar with the situation, as she had similar episodic attacks for the last few years, most often during the attack, her palms were also affected along with the feet. And according to her statement, she was relatively and reasonably alright about 12 years back. Then in a summer, she noticed for the first time that her garments were gradually stained with blood stained sweat. The episode lasted for a couple of weeks and then subsided spontaneously without any medication. After that, she had a history of similar episodic several attacks of blood stained sweaty discharge for the last 12 years. There was no seasonal variation and about 7 years ago, she noticed for the first time that her palms and soles also got affected. Each episode started and stopped spontaneously, and then after infrequent interval, it recurred in an unpredictable manner. She had no clinical evidence of vasculitis.

Figure 1: Oozing from right foot.

Figure 2: Oozing from left foot.

Clinical Details

Regarding the associated history of the patient, there was no history of previous jaundice or prolonged bleeding from other injuries. No history of any associated drug intake or blood transfusion in recent past. There was no significant past history or any family history of bleeding disorders. There was no consanguinity in the family and birth history was normal. Her general and systemic examinations were completely normal. It had no relation with menstruation. The finding of the local examination was essentially normal.

Complete blood count and routine blood biochemistry was within normal limits. His Bleeding time, Prothrombin time (PT), Activated Partial Thromboplastin time (APTT), Thrombin time were normal. Fibrinogen and Factor XIII levels were normal. Platelets function tests were normal. Anti Nuclear Antibody (ANA) levels was normal. Blood stained sweat analysis was not done.

Diagnosis

The lady was very anxious and desperate this time to know, "What is happening with her? Why she was oozing bloody sweet at infrequent interval? as her disease was under-diagnosed for a very long period (last 12 years). At first we were in dark regarding her case. We took the lady as a case of academic interest and consulted with our colleagues, made panel discussion and discussed her issue with different expert surgical panels on internet. We also reviewed previous case reports and evidence based medicine. Later on, we were able to establish a possible clinical diagnosis of "hematohidrosis". To have a confirmation, we made an arrangement of full thickness skin biopsy (incisional wedge biopsy) from the affected skin during the active episode of oozing (Foot or palm). Our histopathologist colleagues were informed regarding the issue of academic interest. Months later, we were able to perform the biopsy during the episode of re-bleed. 2 samples were taken from both feet and sent for histopathology and confirmation of diagnosis. Histopathology report was strongly suggestive of "Hematohidrosis".

Treatment

Careful counseling of the patient and her husband was done, regarding her condition. Assurance and elimination of her anxiety was found as the best part of her management. Anxiolytic and sedative medication were given initially to relieve stress. Beta blocker was given for a short period after performing ECG and consultation with our colleague of Cardiology Department. Evidence based medicine suggests that in particular situation and selective patients, Aluminium Hexahydrate, Aluminium Chloride, Atropine etc. medication may be helpful[5, 7].

Discussion

Regarding hematidrosis, there are several theories for pathogenesis of hematidrosis but none of them is conclusive[8]. Immediate skin biopsy, during the episode of bleeding is important for definitive diagnosis. Zhang et al[9]. observed some intradermal bleeding and obstructed capillaries but the sweat glands, hair follicles and sebaceous glands showed no abnormalities. They concluded that distinctive vasculitis can account as a pathological basis for this condition[9]. Benzidine test can confirm the presence of hemoglobin. In this case study, Benzidine test was not done. Usually blood investigations reveal no abnormality. No definitive management has been identified so far. It is important to identify the stress, which can be physical, or psychological. Counseling along with pharmacotherapy can yield better results[10]. Drugs like Propranolol have been tried for this condition. It has been suggested that sympathetic nerve activation might be contributory for these events and β-adrenoceptor antagonists might be an effective treatment for this disorder[11]. This phenomenon is usually intermittent and self-resolving.

Conclusion

Hematidrosis is an extreme rare haematological scenario. Physicians, Surgeons as we as Histopathologist are very much unfamiliar with the clinical situation, reflected in different previous case studies. Even a high index of suspicion is not always good enough to overcome the diagnostic challenges. Thus, this condition is very difficult to diagnose, even more difficult to manage. Treatment is mainly conservative for an active episode, but recurrence and flare up is inevitable. Therefore, counseling and reassurance with patient and patient's party play crucial role.

Conflict of interest: The author declares no conflict of interest.

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