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EDITORIAL

Primary Ear and Hearing Care : The Foreseable Solution for Prevention and Control of Deafness in Bangladesh

Normal hearing is an essential requirement for the development of speech and personality in children[1]. It is also important for an individual to perform his/her activities at an optimum level. Any alteration in this norm might lead to disability.

Bangladesh is a densely populated country having a total population of about 123m in a surface area of about 0.15m sq.km[2]. About 13m people are suffering from variable degrees of hearing loss of which 3m are suffering from severe to profound hearing loss leading to disability [3].

Though hearing loss is the second commonest disability in our country but unfortunately it could not yet draw proper attention[2,4]. Majority of the hearing impaired people are the children of deprived community in the developing countries like Bangladesh, where poverty, illiteracy, malnutrition, poor hygiene and infection proliferate and resources are scarce to non existent[5]. According to **World Health Organization** (**WHO**) 50% of the hearing impairment is due to otitis media, which is a complication of upper respiratory tract infection. If upper respiratory tract infection could be treated efficiently and in time hearing impairment can be prevented by primary, secondary or tertiary level measures[3,5]. To achieve such goal there should be comprehensive coordinated multidisciplinary approach from otolaryngologists and pediatricians, as most of the children are primarily treated by them[3]. 10% of world's population are suffering from various disabilities of which 10% are suffering from deafness[3,5]. Deafness is an invisible, ill recognized physical disability leading to health and social problem. Severe disability interfere with the disabled person's ability to provide his or her own self-support, welfare and happiness. They live in a silent, very uncertain world and unfortunately fail to draw attention or sympathy from their surroundings[3,5]. The frustrated parents sometimes find their only alternative as abandoning the child either at the doorstep of the nearest orphanage or foster home at another even more frightful location[5].

Lack of ENT services in rural community is a state reality and incorporation of **Primary Ear and Hearing Care** (**PEHC**) in the existing **Primary Health Care** (**PHC**) services is a necessity in all developing countries[4,5]. The theme of the second **SAARC** ENT congress held in Kathmandu, Nepal in May'2000 "Extending ENT Services to the community" was rightly selected by the organizers[4]. According to Priority for disease control in Bangladesh, **WHO** identified middle ear infection as first, congenital deafness as second, noise induced hearing loss as third and impacted wax as fourth common causes of hearing impairment[6]. Most of the hearing impairment and deafness cases are preventable and sometimes reversible provided it is detected early and managed properly through appropriate health and medical services[3,5]. There is an old saying that "An ounce of prevention is worth a pound of cure" and for hearing impairment it is also true.

Prevention of hearing impairment has been neglected by the **WHO** and its member countries for decades because they are invisible handicaps. Professional bodies ultimately could convince **WHO** for the

development of program for 'Prevention of deafness and hearing impairment' and then **WHO** medium term program (**PDH** program) was established in 1987[5].The otological center Bangkok unit was designated as the 'first **WHO** collaborating center for prevention of hearing impairment and deafness' in 1988[5]. The center then developed the '**Primary Ear and Hearing Care**' (**PEHC**) program with the concept of implementing through already existing 'Primary Health Care' system with community participation. The concept is well accepted by **WHO** and has now implemented in many countries worldwide[5]. **WHO** has designated a a centre as a **National Center for Hearing and Speech**, in Bangladesh with the approval of the Government to conduct different training program(WHO BAN,DPR-001) for developing skilled manpower for prevention of deafness and hearing impairment since August'94. Till today this program is in action[7].

Recently **WHO** has realized the need of further development of **PEHC** program in Bangladesh including some other SEA member countries. Accordingly some recommendations have been forwarded for action pointers (WHO, Governments, NGOs, Professional Societies, Professionals and Disabled Person's Organizations).

The recommendations for National Governments include[6]:

1. A national deafness prevention program should be formulated and implemented based on **WHO** guidelines, and needs assessment based on demographic information.
2. A focal person should be appointed to coordinate the program for prevention of deafness and hearing impairment in the Ministry of Health & Family Welfare.
3. A national working group should be setup for "Better Hearing" (prevention HI) to develop a national time bound plan based on **WHO** guideline and national need assessment. This committee should have representation from the Government, NGOs, professional societies and organizations of the deaf.
4. Training institutions should be set up for training of relevant medical and paramedical personnel.
5. Finance and other resources should be allocated for prevention of hearing impairment, and fund identified and allocated to support projects that lead to better hearing.
6. Existing laws related to better hearing including noise pollution, such laws where they do not exist should be enacted and enforced.
7. Research leading to better hearing should be supported. A national better hearing day should be supported and promoted for advocacy purposes.
8. The human rights of the hearing impaired must be respected.

Prevention of hearing impairment and deafness program at professional level has come across many difficulties as most of the target people live in the rural area in developing world where professional personnel are scarce to none, the resources and funding are lacking. Community understanding and participation are also poor. With the scarcity of resources and funding and lack of community participation sustaining the program is almost impossible. The detection of ear diseases and hearing impaired persons (the deaf) at the rural or at the community level, where resources are scarce or none is a nightmare for everyone involved. Detection itself needs some technology and know-how and is only the starting point for management. Overall work is difficult and even different in individual cases. It needs also a long term follow up and multidisciplinary approach of management. To ensure the sustainability, program should

be Implemented at the grass root level with community participation.

In this context, establishment of a full-fledged **Independent National ENT Institute** having all the **modern diagnostic** and **therapeutic facilities** with the **responsibility** and **accountability** of developing relevant skilled manpower and also provide **unique Tertiary Ear and Hearing Care** services has become essential for the implementation of the **WHO** recommendations. Under the guidance of the **National working group** if the **WHO** recommended program is implemented effectively, in near future, we will be able to salvage the nation from such a devastating silent disability.

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(J Bangladesh Coll Phys Surg 2003; 21 : 1-3)

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ORIGINAL ARTICLES

Presentation of the Patients with Cervical Spondylosis - A Study of 216 Cases

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MS AHMED, MBBS[d], AA KHAN, FCPS[e]

Summary :

A prospective study was conducted in the Department of Physical Medicine & Rehabilitation, Chittagong Medical College Hospital, Chittagong, during the period of June 2001 to August 2002, to find out the age, sex and occupational distribution of the patients with cervical spondylosis and their clinical presentation. A total of 216 patients attended in the department with cervical spondylosis. Male and female ratio was 1:0.80. Highest number of patients was in the 40-49 years age group (34%) and the mean age of the patients was 47.03 ± 03 years. In respect to occupation, housewives constituted the majority (39 %). Most of the patients presented with neck pain (98.6 %) and radiation of pain (61.6%) to the upper limb.. Maximum x-ray of the cervical spine showed osteophytic changes and narrowing of the space between c_5/c_6. By these findings we can conclude that the most common presentation of cervical spondylosis was pain in the neck found in the present study.

(J Bangladesh Coll Phys Surg 2003; 21 : 4-9)

Introduction :

Osteoarthritis is the most common rheumatological disease that affects more than 80% of the population aged 55 years and older [1]. Cervical spondylosis (c/s) is one kind of osteoarthritis, disc degeneration with associated osteophyte formation and osteoarthritis of the spinal apophyseal joints, collectively termed cervical spondylosis, is almost universal in elderly people [2]. Degenerative changes in the cervical spine may be associated with neck pain usually when the degenerative changes are severe. Pain referred to the arm may indicate irritation or entrapment of a nerve root. Common causes are a prolapsed cervical disc or degenerative changes, including apophyseal joint or ligamentous hypertrophy and osteophytes. Neurological examination will often reveal the level of entrapment [3].

Neck stiffness exists as a common disorder; the age group 25 to 29 years in our working population reports 25 to 30 percent frequency of one or more attacks of stiff neck. For working population over 45 years of age, this figure rises to 50 percent. Brachial neuralgia occurs later in life than stiff neck does with a frequency of 5 to 10 percent in the 25 to 29 years age group, rising to 25 to 40 percent after the age of 45 years and overall 45% of working men experience at least one attack of stiff neck, 23% report at least one attack of brachial neuralgia and 51% suffer from both symptoms [4]. Pain and stiffness in the neck can originate from many tissue sites and can result from a number of mechanisms. One of the most common causes of pain and disability in the neck and arm is cervical spondylosis[5]. Cervical spondylosis is a clinical syndrome in which cervical spine degenerates to such an extent

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that symptom arises [6]. It runs a prolonged course with intermittent periods of relief. It commonly affects people above the age of 40 years and is responsible for varying grades of disability [7]. A study was carried out by Alam et al. in 1995 in the Rheumatology clinic in the department of Physical Medicine, IPGMR Dhaka and they showed that cervical spondylosis was the commonest lesion (23.5%) amongst the various rheumatic disorders [8]. In the present study, we observed the clinical presentation of c/s in order to improve the present situation regarding proper diagnosis & treatment of the patients with c/s.

Materials and Methods:

Study population:

The study was conducted in the department of physical medicine, Chittagong Medical College Hospital (CMCH), Chittagong, Bangladesh. A total of 216 patients were included for the study. The patients having neck & neck related symptoms were selected from the department of Physical Medicine who were referred from out patient department of CMCH and also from general practitioners.

Clinical Examination: A thorough clinical examination including general examination & examination of the cervical spine and upper limbs with particular attention to neurological signs was carried out. The lower limbs were also examined for abnormal signs. All signs were recorded accordingly and a clinical diagnosis for c/s was made.

Investigations: Routin haematological examination, urine and stool examination and X-Ray of the cervical spine was done for all the patients. Radiological examination of the chest, blood sugar estimation and RA test were done in some cases, where indicated. Special radiological views of cervical spine specially oblique views and lateral views in full flexion and extension were taken in a few selective patients, to rule out the other causes of neck pain in some complicated cases. Then a confirm diagnosis was made.

Recording:

Before examination, verbal consent of the patients was taken and nature of the study was explained to them. History, clinical examination and relevant investigations were done. The findings were recorded properly in the data schedule.

Data analysis:

The numerical data was analysed statistically. The results were expressed as mean ± SD and percentage as applicable. Statistical analysis was done by using SPSS package for Windows.

Results :

In our observation a total of 216 patients with c/s attended the Physical Medicine department of CMCH. Among these patients there were 120 (55.6%) male and 96 (44.4%) female and the male female ratio was 1: 0.80 (Table No-I). The highest number of patients was in the 40-49 years age group (Table No-II), 75 patients (34 %) were in this group and

Table-I

Sex distribution of the subjects participated in the clinical survey.

Sex	Number (n)	Percent (%)
Male	120	55.6
Female	96	44.4
Total	216	100

n = Number of subjects

Table-II

Age distribution of the subjects participated in the clinical survey.

Age in years	Number	Percent
30-39	54	25 %
40-49	75	34 %
50-59	49	22.7 %
60-69	24	11.1 %
70>	14	6.5 %
Total	216	100 %

n = Number of subjects

mean age of the patients was 47.03 ± 11.49 years (Table No-II). Regarding occupation of the patients, maximum patients of c/s were house wives (38.9 %), table workers were in the second (20.8%) and businessmen were in the third position (08.3 %, Table No-III). Regarding symptom of c/s, average duration of symptom was 2.60 ± 2.71 years at the time of first attendance and maximum patients presented with neck pain (98.6 %), with radiation of pain (61.6 %) and morning stiffness (37 %). But the morning stiffness lasts less than half an hour (Table No- V). Some of the patients presented with numbness of the upper limb (21.3 %) and weakness of the upper limb (09.3 %) in addition to other symptoms (Table No-V). The onset of pain was gradual in maximum patients (77.8 %), only 17.6 % presented with sudden onset and a few patients presented with pain after trauma (01.4 %). In our study, the site of pain in c/s was seen in the neck only in 96 patients (44.4 %), in the neck plus upper limb in 88 patients (40.7 %), in the neck plus upper back in 16 patients (07.4 %), in the neck plus shoulder in 13 patients (6 %) and only in the upper limb in 03 patients (1.4 %). Base line characteristics like pulse, BP and some routine investigations revels normal (Table No-IV). Regarding X-ray finding, there was space reduction in between $c_{5/6}$ in most of the patients (55.1 %), osteophyte formation only in several vertebral bodies in the cervical spine in 34.3 % patient, space reduction in between $c_{5/6}$ plus space reduction in between other vertebral bodies in 64 patients (29.5 %) and space reduction only in between $C_{5/6}$ in 55 patients (25.5 %, Table No-VIII).

Table-III

Distribution of occupation of the subjects participated in the clinical survey.

Occupation	Number (%)	Percent (%)
House wife	84	38.9
Table worker	45	20.8
Businessman	18	8.3
Retired serviceman	14	6.5
Teacher	11	5.1
Student	2	0.9
Others	42	19.5
Total	216	100

Table No-IV

Distribution of baseline characteristics of the subjects.

	Age in years	Duration in years	Pulse /m	SBP mm Hg	DBP mmHg	TC /cu mm	ESR in Ist hour	Hb %	2HPPBS (mg/dl)
Mean	47.03	2.60	82.07	120.94	78.05	9423.90	21.92	11.91	118.35
SD	11.49	2.71	7.02	13.39	8.39	1584.43	16.68	1.59	36.03

SD = Standard deviation
Duration = Duration of symptoms
SBP = Systolic blood pressure
DBP = Diastolic blood pressure
TC = Total count of WBC/ cu mm of blood
2HPPBS = Tow hours post prandial blood sugar

Table-V

Distribution of presenting complaints of the subjects.

Symptoms	Present (%)	Absent (%)	Constant (%)	Intermittent (%)
Neck pain	213 (98.6)	3 (1.4)	89 (41.2)	127 (58.8)
Radiation	133 (61.6)	83 (38.4)	N A	N A
Morning stiffness	80 (37)	136 (63)	N A	N A
Numbness of upper limb	46 (21.3)	170 (78.7)	N A	N A
Weakness of upper limb	20 (9.3)	196 (90.7)	N A	N A

N A = Not applicable

TableVI

Distribution of site of pain of the subjects

Site	Number (n)	Percent (%)
Only in the neck	96	44.4
Neck plus upper limb	88	40.7
Neck plus upper back	16	7.4
Neck plus shoulder	13	6
Only in the upper limb	3	1.4

n = Number of subjects

Table-VII

Distribution of onset of symptoms of the subjects

Character	Number (n)	Percent (%)
Gradual	168	77.8
Sudden	38	17.6
After trauma	10	4.6
Total	216	100

n = Number of subjects

Table-VIII

Distribution of X-Ray findings of the subjects.

Characteristics	Number (n)	Percent (%)
Osteophyte formation only	74	34.3
Space reduced in between $C_{5/6}$ & also in other spaces	64	29.6
Space reduced only in between $C_{5/6}$	55	25.5
Osteopanea plus other pathology	9	4.2
Osteophyte plus other pathology	6	2.8
Space reduced other than in between $C_{5/6}$	5	2.3
Cervical rib	3	1.4
Total	216	100

n = Number of subjects

Discussion :

We observed 216 patients of cervical spondylosis; most of them were in the 40- 49 years age group (34 %). The mean age of the patients in our study was found 47.o3 ± 11.49 years. Bhattecharjee B N et al. found, in their study on cervical spondylosis that maximum number of patients in the 40-49 years, which favours the same result found in our study [9]. On the other hand, the study of British Association of Physical Medicine showed most patients were in the 40 to 60 years age group, which is also favourable to our study [10]. In this series, there were 120 (55.6 %) male patients and 96 (44.6 %) female patients and the male: female ratio was 1:0.80. In a study in IPGM&R, Dhaka, it was found that the male and female ratio was 1: 0.50 [9]. This is nearer to our study. The more female in our study may be due to awareness and increasing female education.

Regarding occupation, housewife topped the list (38.90 %); table worker was in the second position (20.80 %). Highest number of patients seen in our study was housewife but Bhattecharjee B N et al. found that highest number of patients was table worker and housewife was the second [9]. This may be due to more activity in forward bending posture and frequent movement of the cervical spine. As most of the village house wives worked in poor developed kitchen and other house fittings such as low down burner, ancient utensils for cutting &chopping, low stool (Pira) for sitting, Indian commode, soil made burner, wooden fuel etc. There was a clear and significant linier trend of increasing likelihood neck pain according to the number of children [11]. This was also a cause of affecting the housewives with c/s as because most of the village women had multiple pregnancies.

In our study, maximum patients presented with neck pain. In a review it was found that the common presentation of c/s was mechanical neck pain [12]. Bhattecharjee B N et al. & Honet et al. also found the same presentation in their study [9,13]. We found many patients presented with radiation of pain, morning stiffness (less than one hour), and a few patients with numbness & weakness of the upper limb. Weakness and numbness of the upper limb was relatively less in our study than the study of Honet et al. as they studied the patients with cervical rediculities only [13]. The onset of symptoms in our study was gradual (77.8%). In a study, Warham T & Farrow R found that 90% of the patient's presentation was insidious and 10 % patient presented with a violent twist of the neck or a pull on the arm [14]. This was also in favour of our study. But we found

17.6% patient with sudden onset and 01.40 % patient with traumatic onset.

Site of pain was found in the neck only in most of the patients, in our study. Many patients presented with the complaints of pain in the neck plus upper limb, shoulder and upper back. Only a few patients presented with the complaints of pain in the upper limb only. Bhattecharjee B N et al, the British Association of Physical Medicine & Honet et al. also found more or less same results as found in our study [9, 10,13]. Regarding x-ray findings, there is degenerative changes e.g. osteophyte formation in the cervical spine was seen in most of the patients in the present study. There was narrowing of space in between c_5 / c_6 in maximum patients. Bhattecharjee B N et al also found this finding in their study [9]. We also found some x-ray of cervical spine with osteopanea and cervical rib but this was not found by Bhattecharjee B N et al [9]. This may not be included in their study. On the other hand, many of the patients in our study were elderly women (post menopausal women) and so osteopanea was seen in our study. Treatment by cervical traction may be harmful in presence of osteopanea in cervical spondylosis.

Conclusion :

In conclusion, it may be said that the common presentation of chronic cervical spondylosis was pain in the neck, upper limb & upper back and radiation of pain found amongst the patients attending the department of Physical Medicine, CMCH, Chittagong.

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Rectal use of Misoprostol in Controlling Postpartum Haemorrhage (PPH)

S NAHAR, FCPS, M.S

Summary :

Post-partum haemorrhage (PPH) is a nightmare for Obstetricians and a leading cause of maternal death around the world. During January to December 2002, we used tablet misoprostol 200 - 1000μgm rectally for controlling PPH refractory to oxytocin and ergometrine. Total patients were 31, within them 84% (25) patients developed PPH after normal vaginal delivery and 16% (5) after caesarean section. Age ranges of these patients were 19 – 40 years, parity 1 – 10 and gestational weeks in between 35 – 42. Use of misoprostol successfully controlled PPH in about 87% of cases from 40 seconds to 7 minutes. 67.74% patients responded with 200μgm of misoprostol per rectum, 12.9% with 400μgm and 6.45% with 600μgm. 12.90% not responded even after use of 1000μgm and they need hysterectomy. We have not found any complication on its use. So rectal use of misoprostol for controlling PPH is effective, safe, economic and easily administrable without significant side effect.

(J Bangladesh Coll Phys Surg 2003; 21 : 10-13)

Introduction :

Maternal mortality in Bangladesh is about 3 per 1000 live birth[1] but the postpartum haemorrhage (PPH) remains an important leading cause of maternal morbidity and mortality. In Global standpoint 12% of maternal death is related to antepartum haemorrhage and postpartum haemorrhage. In rural area the maximum causes of PPH are related to home delivery by untrained personnel's (87%) which include untrained TBA, relatives, neighbours and self. The post partum bleeding rate was 17.9%.[2] Majority of patients has no antenatal checkup; high risk group are not screened before delivery (no use or misuse of any uterotonic drugs before or after delivery). Pre-existing anaemia, lack of blood transfusion facilities worsens the out come in PPH. In the hospital we use traditional uterotonic drugs like oxyocin and methylergometrine for controlling PPH. Routine use of oxytocin will reduce PPH by 40%.[3] Misoprostol, a synthetic 15-deoxy-16 hydroxy-16 methyl analogue of naturally occurring prostaglandin E_1 (PGE_1) developed as a gastric cytoprotective agent has been used in first and second trimester abortion, ripening the cervix and induction of labour, and it has been shown in several randomized placebo controlled trials to significantly reduce the PPH and risk of PPH.[4, 5] It is stable, low cost, easily administrable, available in tablet form and definitely advantageous than the other PGs. Its absorption is rapid and effect on the post-partum uterus has been shown to be rapid.[6] Our aim is to show the effectivity of rectal use of misoprostol with appropriate dose in the treatment of severe atonic PPH not responding to oxytocin and methylergometrine in bolus doses.

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Methodology :

Randomized trial of rectal use of misoprostol tablet has done to all types of patients after vaginal or caesarean delivery with atonic uterus and PPH. This study was done in Khulna Medical College Hospital from January to December 2002, which is a tertiary care centre handling approximately around 2500 delivery per year. The data sheet was completed by the doctor supervising the delivery and collected and checked by the consultant. The data form contained information on maternal characteristics such as age, parity, gestational age at delivery, obstetrical history, and labour

procedure as it is spontaneous, augmented or induced. Variables concerning delivery included mode of delivery. After delivery linen soiled with amniotic fluid was removed and a fresh plastic rubber sheet was replaced. Blood loss assessed by collecting blood within a plastic bowl measured by using a calibrated plastic water Jag. Before application of the misoprostol tablet rectally, hospital protocol for management of PPH is maintained. This included resuscitation of the patient, massage of the uterus, bimanual compression (exclusion of traumatic bleeding) simultaneously intravenous oxytocin in bolus dose of 10-20 units directly and infusion of 20 units in 500ml normal saline or 5% dextose in normal saline and methylergometrine 0.5mg (2 amp) intravenously as a first aid measure in all cases.

When all primary or first aid measures failed we used misoprostol tablet rectally before going for surgery as ligation of internal iliac artery or uterine artery or sub-total hysterectomy as a last resource.

Tablet misoprostol placed in small pot, wet by drinking water, blended by finger adding 10ml drinking water for dilution, collected by syringe, pushed rectally through intravenous cannula. The patient followed up for five minutes for uterine contraction and amount of blood loss. The dose is repeated at five minutes interval upto 3-4 doses. When the result was satisfactory following points were observed and recorded;

a) Total dose of oxytocin and ergometrine.

b) Total dose of misoprostol.

c) Time needed for uterine contraction and control of PPH.

d) Total amount of blood loss.

e) Need for blood transfusion.

f) Side effect of PGs like nausea, vomiting, and hyperpyrexia.

Patients were followed up for 24 hours.

Results :

Total 31 patients of PPH due to atonic uterus were included in the study. We used misoprostol rectally initially 200μgm and repeated 200μgm subsequently at five minutes interval in 2 to 5 doses.

Table-I shows maternal demographic data including maternal age; ranges from 19-40 years, parity ranges from 1-10 and gestational age 35-42 weeks.

Table-I

Maternal demographic features.

Characteristic	Mean ± SD
	n - 31
Age	24.61 ± 04.66
Parity	02.39 ± 01.95
Gestational weeks	37.65 ± 01.77

Table-II presented the misoprostol dose responses for uterine contraction and 67.74% patient responded only with 200μgm misoprostol.

Table-II

Misoprostol dose respons

200μgm		400μgm		600μgm		Failed	
No	%	No	%	No	%	No	%
21	67.74%	4	12.90%	2	6.45%	4	12.90%

Fig.-I presented the high risk group patients. 74.19% of the patients were grand multipara with toxemia in pregnancy, antepartum haemorrhage and twin pregnancy.

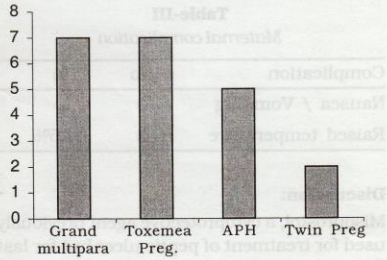

Fig.-1 : *Shows high risk patients*

Labour induction and augmentation were done in 55% patients by cerviprim gel and misoprostol tablet or by oxytocin, and presented in Fig.-2. Fig.-3. Table-III presented the mode of delivery and maternal complications.

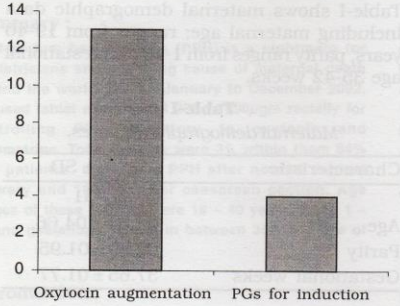

Fig.-2 : *Use of oxytocins and PGs for augmentation of pregnancy.*

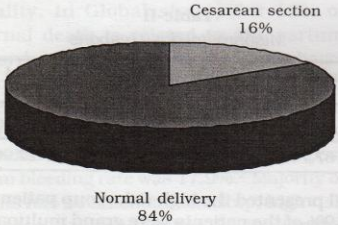

Fig.-3 : *Mode of delivery.*

Table-III

Maternal complication

Complication	No	%
Nausea / Vomiting	0	0
Raised temperature	2	6.45%

Discussion:

Misoprostol, a cytoprotective agent previously used for treatment of peptic ulcer but for last few years it is used for cervical ripening and induction of labour because it is more stable, low cost and effective than other prostaglandins specially PGE_2 gel or tablet[7,8,9]. PPH is defined as a measured blood loss of more then 500ml and severe PPH as blood loss more then 1000ml. In case of atonic PPH when primary uterotonics (oxytocin, ergometrine) with massage, bimanual compression are failed, we used misoprostol tablet rectally. We could not try intravenous or intramyometrial PGE_2 (enzaprost) due to non availablity. Our results shows successful control of PPH in 27(87%) patients which coincide with O' Brein et al.[10] who studied 14 women with atonic PPH and H. Abdel - Aleen et all [11] who studied 18 cases of severe atonic PPH not responding to oxytocin , methyl ergometrine and enzaprost but successfully controlled PPH in 88.2% cases with misoprostol. Time required controlling PPH from 30 seconds to 3 minutes in Abdel-Aleen et al study, but our recorded time to control PPH about 40 seconds to 7 minutes. In 12.90% (4) cases misoprostol failed to control PPH. After laparotomy of these cases, high-up lateral cervical tear were found in two cases and the rest two cases not responding even after 1000 μmg misoprostol. All four patients undergone subtotal hysterectomy. Transfusion of 3 to 6 units of fresh whole blood was necessary for this high risk group. In our study 74.19% (23) patients were high risk group and include grand multipara, APH, toxemia in pregnancy and twin pregnancy 67.74% patients responded to minimum dose of misoprostol i.e. 200μmg. In previous 2 studies they used to higher doses of misoprostol about 1000 μmg. Rectal use is preferable because it is easy to use, no need for sterilization and can be applied safely by midwifes. In our study group we did not find out any major complication except 2 cases where shivering and transient pyrexia developed and it is related to high doses of misoprostol. In Bangladesh where 90% deliveries are conducted at home, any attending midwife can use the low cost

medicine rectally when attending delivery at home or confronted with a case of PPH before referral to a hospital.

Conclusion :

In this study it is difficult to establish that misoprostol itself is enough to control PPH or its action was potentiated by oxytocin and ergometine. Further study is needed with a large sample to find out the effect of rectal use of misoprostol alone for control of severe atonic PPH and also identify the adequate dose for controlling PPH.

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Relation of High TG (Triglyceride) and Low HDL (High Density Lipoprotein) with Coronary Artery Disease – An Analysis

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Summary :

In a prospective study we analyzed the lipid profile of 499 patients with documented coronary artery disease (CAD). Patients with diabetes mellitus were not included in this study. Out of these 499 patients 311 (62. 3%) had various forms of dyslipidemia. High LDL (Low density lipoprotein) with normal triglyceride (TG) was noted in 142 patients (28. 4%), combined dyslipidemia (high LDL and high TG) was noted in 27 patients (5. 4%), high TG and low HDL (high density cholesterol) with normal LDL level was detected in 106 (21.2%) patients, isolated high TG was found in 25 patients (5.0%) and isolated low HDL in 11 patients (2. 2%). In a sub group analysis the average TG level was documented to be higher in patients with CAD compared to matched control, 206±51 mg% versus 121±37 mg%.

This study demonstrates that subjects with high TG and low HDL have a substantial increased risk of developing subsequent CAD.

(J Bangladesh Coll Phys Surg 2003; 21 : 14-19)

Introduction :

Previous studies indicated that people of South Asian origin have higher rates of CAD than people of European origin,a finding that can not be explained by differences in conventional cardiovascular risk factors,such as smoking,raised blood pressure,diabetes or high cholesterol level[1-3].There is increasing evidence that rate of CAD vary between different ethnic groups[4-6]. The consistency of the high risk of CAD in South Asian populations around the world affecting both sexes and with early onset,suggests a common underlying explanation but the conventional risk factors,however,do not fully account for the excess of CAD among Bangladeshis. Indians and Pakistanis suggesting that other risk factor may be more important[7-9]. A pattern of metabolic disturbances related to insulin resistance might underlie the high rates of CAD in South Asian people.These physiological disturbances include hypertriglyceridemia (TG),low concentration of high density lipoprotein cholesterol (HDL) and hyperinsulinaemia.The mechanisms underlying these associations even in non diabetic patients are poorly understood[10-15]. Association of high TG and low HDL as an independent predictor of CAD in non diabetic patients have been reported. This form of dyslipidemia is associated with a three fold higher risk of CAD irrespective of the level of LDL[13,14].

High TG and low HDL has already been identified as a risk factor for CAD among the immigrants of our country in the western nations. But this hypothesis has never been tested on our own population.We sought to evaluate whether high TG and low HDL is related to CAD in our population in a prospective case control study.

Methodology :

This prospective case control study was carried out in the Department of Cardiology,Bangladesh Medical College, Dhaka and in a private out patient clinic with Cardiological bias from June 2001 to June 2002. Dyslipidemia (high TG and low HDL) in patients with documented CAD were included in this study and the results were compared with the matched controls without CAD.Dyslipidemia was defined on the basis of National Cholesterol Education

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Program,Adult Treatment Panel II recommendation[16]. Patients with myocardial infarction,unstable angina and stable angina during their initial presentation and diagnosis was included in the project as study subjects.ECG,Echo-Doppler study,cardiac scan and coronary angiogram reports were evaluated for establishing the diagnosis of CAD.The patients with CAD and diabetes mellitus were not included in the study.The lipid profile of the control subject without any CAD were compared with the study group. The guidelines published by the Adult Treatment Panel II of National Cholesterol Education Program: second report of the Expert Panel on Detection,Evaluation and Treatment of High Blood Cholesterol in Adults was followed in this study. Serum triglyceride level more than 200 mg/dl was considered to be high and HDL level less than 40 mg/dl was considered to be low[16,17].

During the study period, 722 patients were documented to have various forms of CAD (myocardial infarction,unstable angina,stable angina with stress test positive or stable angina with perfusion scan defect,suspected CAD with abnormal coronary angiogram or silent ischaemia with regional wall motion abnormality detected in Echo-Doppler study).Out of these 722 patients 223 patients (30.9%) were diabetic and these patients were excluded from the study.The remaining 499 patients (69.1%) were non diabetic and found eligible for the study.Out of these 499 patients 311 (62.3%) patients had various forms of dyslipidemia. 100 controls were prospectively selected either from individuals attending the hospital outpatient clinic for consultation regarding non cardiac ailments and other persons admitted in the hospital for non cardiac causes that were unlikely to confound a comparative analysis.Individuals with any previous diagnosis of heart disease,history of exertional chest pain,clinical evidence of heart disesae or a 12 lead ECG showing pathological Q waves,ST segment deviation,T wave inversion,bundle branch block or atrioventricular block or chamber hypertrophy were excluded.Controls were matched to case for age, sex and other parameters. Appropriate steps were taken to control confounders if any.

Statistical analysis was performed with a commercially available software package. Difference between the mean values of measurements between groups was analyzed by paired or unpaired,two sample "t" test and a two tailed "p" value <0.05 was considered significant.Correlation between various measurement was assessed by linear regression method. Univariate analysis was performed but multivariate analysis was done.

Results :

Out of these 499 patients 311 (62.3%) patients had various forms of dyslipidemia.High LDL with normal TG was noted in 142 patients (28. 4%),combined dyslipidemia (high LDL and high TG) was noted in 27 patients (5.4%),High TG and low HDL with normal LDL level was detected in 106 (21. 2%) patients,isolated high TG was found in 25 patients (5.0%) and isolated low HDL in 11 patients (2.2%) (Table-1).

In a sub group analysis majority of the patients with high TG and low HDL group (n-106) had TG level in the range of 200-300 mg%. 51 patients (48. 1%) had TG level in this range. TG level in the range of 301-400 mg was noted in 38 patients (35. 8%) and in the range of 401-500 mg% in 12 patients (11. 3%).Very high TG > 501 mg% was documented in 5 patients (4. 7%) in series .High TG (> 200mg%) was documented in only 5 subjects (5%) in control group. 31% of the subjects in the control group had TG level <100 mg%, 44% in the range of 101 to 150 mg% and 20% had TG level in the range 151 to 199 mg%.

Considering all CAD patients as one group the mean TG level among the CAD patients (n-499) was higher compared to control, 206±51 mg% (range 91 - 1124 mg%) versus 121±38 mg% (range 51- 306 mg%) (Table-2).Mean HDL level was 27±6 mg% (range 24 to 37 mg) in the patients with CAD whereas mean HDL was 40±12 mg% (range 34 to 57 mg) in the control group.

Table-I

Pattern of dyslipidemia in CAD patients (n-499)

Type of Dyslipidemia	Total number	Percentage
High LDL and Normal TG	142	28. 4%
High LDL and High TG	27	5. 4%
High TG,Low HDL and Normal LD	106	21. 2%
Isolated High TG	25	5. 0%
Isolated Low HDL	11	2. 2%

Table-II

Level of TG in study group vs control group

Group	n	Range in mg%	mean
Study group	499	91 mg% to 1124 mg%	206±51 mg%
Control group	100	51 mg% to 306 mg%	121±38 mg%

P value- <0.05

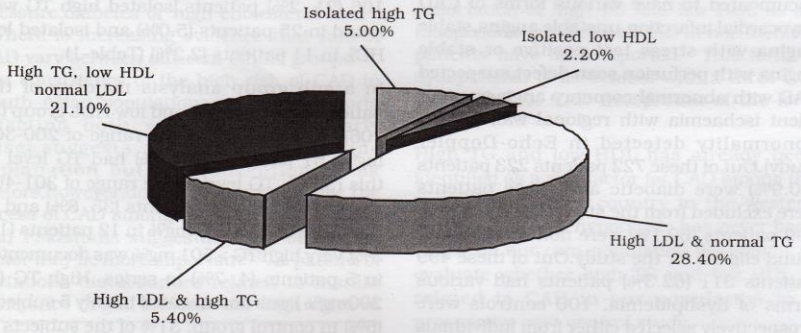

Fig.-1 : *Pattern of dyslipidemia in CAD patients*

Discussion :

Despite a large body of research conducted in the last 40 years, the significance of elevated TG and low HDL as a major CAD risk factor remains controversial. This is in contrast to the well accepted role of low density lipoprotein cholesterol as a contributing cause of CAD and of high density lipoprotein cholesterol in having an apparent protective effect. Plasma triglyceride concentration predicts major ischaemic events after allowance is made for total and HDL cholesterol concentrations and other risk factors in the recent past[18-21].High TG and low HDL has been documented to be associated with high rates of CAD in different

ethnic groups . Recent studies showed that high TG and low HDL may be an atherosclerotic determinant[22-24].

Based on combined data from prospective studies,triglyceride is a risk factor for CAD,particularly so if it is associated with low HDL[19-22,25,26]. Our present study results are in agreement with other prospective study results published in recent past. It has been documented that CAD risk factors for the western population and South Asian population may not be same.There are ethnic disparities among the CAD risk factors[7-10]. In our study 21.2% patients with documented CAD had high TG and low HDL but this pattern of dyslipidaemia was documented only in 5% in the matched control subjects which is statistically significant.

The Regional Heart Study found that TG concentration did not predict incidence of CAD once other risk factors had been taken into account[27].This accords with other published views[27-29] but the evidence is not consistent.For example,Carlson et al found in the Stockholm Study that after allowing for age,blood pressure,and smoking, plasma triglyceride concentrations were more strongly predictive than was cholesterol[30].In our study 21.2% patients with documented CAD had high TG and low HDL.

Some studies including ours were based on fasting TG concentrations whereas others,such as the Regional Heart Study,measured non-fasting concentrations.Non fasting samples contain higher and more variable concentrations of TG than do fasting samples because of the presence of chylomicrons when not fasting.It is debatable whether fasting or non-fasting samples are more appropriate.One advantage of fasting samples is that all subjects are in the same metabolic state.

Early reports from the Framingham Study suggested that TG is not an independent risk factor for men[31].A more recent report found that it is risk factor in men with low concentration of HDL cholesterol[32].We found similar evidence for such interaction in our series.Incidence of CAD increases with increasing TG concentration particularly if it is associated with low HDL concentration. Initially,the Regional Heart Study reported that HDL was not a major risk factor for CAD[33]. A later report revised that view and concluded that it was important but less so than cholesterol,which is the most important single blood lipid risk factor in men. But high TG along with low HDL level may be a very important predictor of CAD in men[32].

The changing trend in lipid levels in South Asian population has been reported in recent past[34].

One study showed that in both males and females there is a significant increase in the levels of total and LDL-cholesterol and triglycerides.The level of HDL-cholesterol has decreased significantly. In the series reported by Gupta et al, the average TG level in Indian population was 126±55 mg/dl[34]. We also noticed a high average TG level even in the control population. In our series the average TG level was 206±51 mg/dl in the study population and 121±37 mg/dl in the control population. Prevalence of CAD varies among different ethnicities[7,35-37]. This variability may be due in part to ethnic differences in the prevalence of atherosclerosis and it's risk factors. Changing trends of lipid level among the South Asians may be one of the important cause of very high prevalence of CAD in this part of the world.

An unresolved issue in preventive cardiology is whether the high serum triglyceride level along with low HDL level is an independent risk factor for CAD and as a direct practical consequence,whether it has value as a diagnostic test. Evidence published in the past few years has contributed substantially to clarifying this issues. The risk of developing CAD has repeatedly been shown to be associated with this form of

dyslipidaemia[1-4]. The present series documents that high TG and low HDL may be an important predictor of CAD. 21.2% of patients with documented CAD had this form of dyslipidaemia in our present series.This form of dyslipidaemia is associated with higher risk of CAD irrespective of the level of LDL[38, 39]. On the basis of a study comparing Bangladeshi migrants to United Kingdom with native Europeans,it was suggested that a pattern of metabolic disturbances related to insulin resistance might underlie the high rates of CAD in South Asian people[11,40].These physiological disturbances include hypertriglyceridemia,Low HDL and hyperinsulinaemia .This pattern of dyslipidaemia is more prevalent among the patients with non insulin diabetes mellitus. The mechanisms underlying these associations of high TG and low HDL even in non diabetic subjects of our population is poorly understood.

Conclusion :

CAD is a major cause of mortality and morbidity in all ethnic and racial subsets.Often,the first indication of CAD is acute myocardial infarction or sudden cardiac death. Identification of those subjects with a very high probability of suffering from CAD and myocardial infarction, therefore, it is of great interest, particularly because primary prevention may reduce CAD mortality and morbidity significantly. From the data of the present series we conclude that high TG and low HDL may be an important predictor of CAD. 21.2% of patients with documented CAD had this form of dyslipidaemia in our present series.This form of dyslipidaemia is associated with higher risk of CAD irrespective of the level of LDL. A reduction in the risk of CAD in South Asians is likely to require different strategies from those recommended for the western population. Treatment of high TG and low HDL may have a real positive impact in prevention of CAD among Bangladeshis. Large prospective study is warranted to evaluate whether treatment of this form of dyslipidaemia among the asymptomatic subjects can prevents incidence of premature CAD events.

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Iatrogenic Femoral Artery Pseudoaneurysm : Incidence and Management at NICVD, Dhaka

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Summary :

Femoral artery pseudoaneurysm is one of the commonest complications of angiographic procedures. 5310 angiographic procedures were done during 1997-2001 in NICVD Dhaka. Amongst 5310 patients 56 developed iatrogenic pseudoaneurysm. Out of these 56, 29 had diagnostic procedure and 27 theraputic. (PTCA with or without stenting). Pseudoaneurysm developed in 0.59% of diagnostic angiograms and 6.5% of interventional procedures. Diagnosis was confirmed by duplex ultrasonographic evaluation of the affected artery and pulsatile mass. Out of total 56 patients, 38 showed spontaneous thrombosis of the aneurysm. Eighteen patients underwent surgical reconstruction in the form of closure of rents, venous patch angioplasty or end to end anastomosis of the affected artery.

Associated A-V fistula of 06 patients were also taken care. Post operative period in 17 patients were uneventful. Only one patient had longer hospital stay due to secondary wound infection. Longer angiographic procedures, large bore catheters, anticoagulation and technical faults are associated with higher incidence of pseudoaneurysm formation. Identification of high risk patients and meticulous care during angiography can reduce the incidence of this vascular complication.

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Introduction :

It is difficult to imagine what our concepts of heart disease might be like today if we had to construct them without the enormous reservoir of physiologic and anatomic knowledge derived during the past 70 years in the cardiac catheterization laboratory[1].

Dramatic advances have been achieved in the practice of interventional cardiology since the Seldinger technique of percutaneous arterial catheterization was used by Judkins to examine the coronary circulation. Although this percutaneous procedure is safe and effective, it carries with it the risk of potentially serious peripheral vascular complications.

As the interventional techniques increase in sophistication and frequency of practice, the incidence of peripheral vascular problems complicating these procedures has also increased, specially with the use of larger devices and aggressive anticoagulation. These complications, in turn have a significant impact on the morbidity and hospital cost of the procedure as a whole[2].

With regard to the diagnostic and the therapeutic interventional procedures, common and potential local complications include arterial or venous thrombosis, distal embolization, pseudoaneurysm, arterio-venous fistulae, haemorrhage and neurovascular compression due to haematoma are common.

Among these complications, one of the frequently occurring complication is pseudoaneurysm. A pseudoaneurysm is a pulsatile haematoma of traumatic origin. It communicates with an artery through a rent or disruption in the arterial wall. It occurs in 0.1 % - 0.2% of diagnostic angiogrames and

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3.5% - 5.5% of interventional procedures. Longer procedures, large bore catheters, anticoagulation and technical faults are associated with a higher incidence of femoral pseudoaneurysm[3].

Material and methods :

During the last 5 years (1997-2001), a total number of 4897 diagnostic and 413 therapeutic interventions were performed at NICVD. Out of those 5310 patients, 56 developed iatrogenic pseudoaneurysm of the femoral artery. These 56 patients with iatrogenic pseudoaneurysm are included in this prospective study.

Presenting complains in all the cases were pulsatile, painful mass in and around puncture sites at femoral triangle after angiographic procedures. On examination, subcutaneous groin haematoma of different sizes were noted. All were pulsatile, occasionally with thrill on palpation. Auscultation of the mass revealed continuous flow murmur in all patients. In addition whole limb swelling were noted in 06 and some degree of sensory loss in 03 patients. After initial diagnosis, 34 patients underwent duplex ultrasonography of the mass and lower limb vessels. This non-invasive and accurate diagnostic procedure allowed us to evaluate the pseudoaneurysm, its communicating tracts and adjacent veins. In addition we repeated this test as follow-up procedure in case of 16 non-operated, conservatively managed and 18 operated patients (Fig. 1, 2a & 2b). A total number of 38 patients having

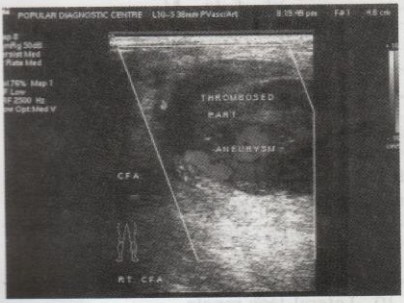


Fig.-1 : *Duplex Study. Common femoral artery (CFA) pseudoaneuryom with organized thrombus in the sac.*

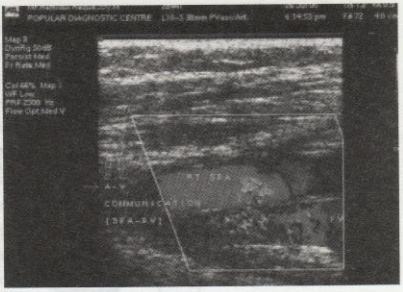


Fig.-2(a) : *Duplex Study. A-V fistula betweeun superficial femoral artery (SFA) and common femoral vein (FV).*

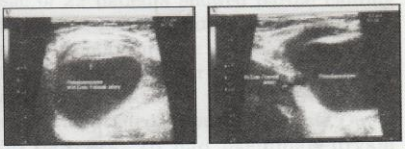
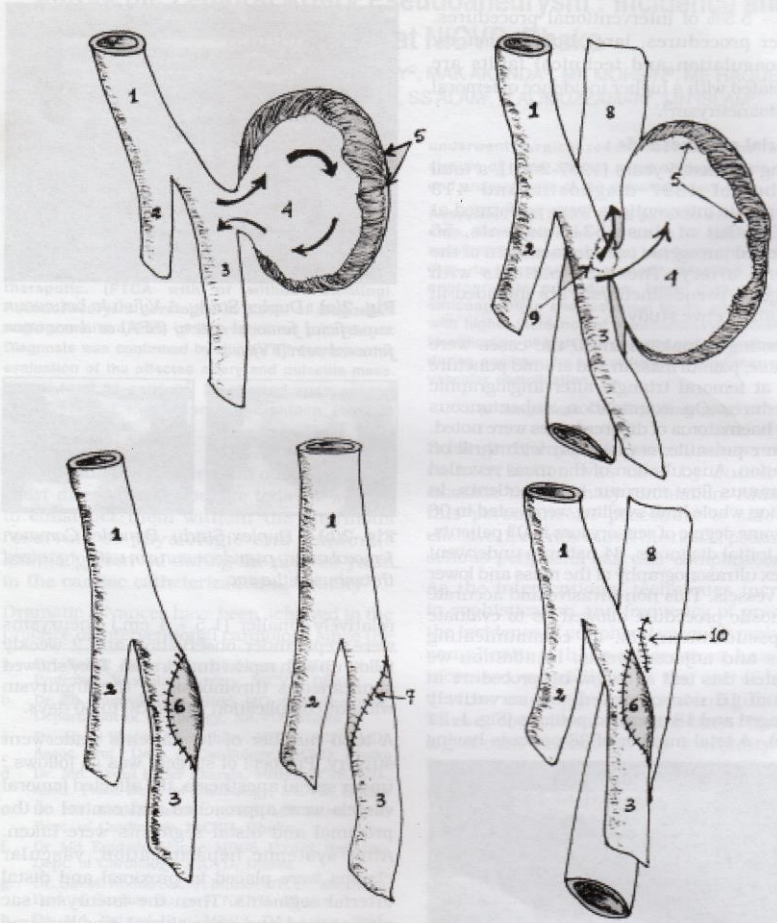


Fig.-2(b) : *Duplex Study. B-mode. Common femoral artery pseudoaneurysm with organized thrombus in the sac.*

relatively smaller (1.5 - 4 cm.) aneurysms were kept under observation and 2 weekly follow up with repeat duplex scan. They showed spontaneous thrombosis of the aneurysm without complication within 30 to 60 days.

A total number of 18 patients underwent surgery. Protocol of surgery was as follows : under spinal anesthesia, the affected femoral vessels were approached and control of the proximal and distal segments were taken. After systemic heparinization, vascular clamps were placed in proximal and distal arterial segments. Then the aneurysm sac was opened and arterial rent was repaired either by direct suture or vein patch angioplasty (Fig.-3) using great saphenous venous segment. Rents were repaired by interrupted 6/0 or 7/0 prolene sutures. Associated A-V fistulas were dismantled after taking proximal and distal control of venous segments, in addition to arterial segments. In all patients, rents in the lateral wall of



1. Common femoral artery
2. Profunda femoris artery
3. Superficial femoral artery
4. Pseudoaneurysm
5. Organised thrombus
6. Vein patch angioplasty
7. End-to-end anastomosis
8. Femoral vein
9. A-V fistula
10. Lateral tear repair

Fig.-3 : *Pseudoaneurysm of the superficial femoral artery and A-V fistula wih surgical management*

common femoral veins were repaired by interrupted 7/0 prolene sutures followed by arterial repair. In 2 patients the superficial femoral artery segment with aneurysm and A-V fistula were found grossly lacerated. Excision of about 1.5 cm. arterial segment was done in each patients followed by end to end anastomosis of the superficial femoral artery using 7/0 prolene making continuous suture.

Results :

Most of the patients with iatrogenic pseudoaneurysm of femoral artery were in the age group 51-65 years (64.2%), followed by 35-50 years (35.7%) (Table-I). Out of total 56 patients, 41.07% were male and 58.93% were female (Table-II). Four thousand eight hundred and ninety seven patients had history of diagnostic angioraphy and four hundred and thirteen patients underwent therapeutic procedures like PTCA with or without stenting (Table-II).

In addition to clinical examination 34 patients underwent duplex ultrasonographic examination of the aneurysm and adjacent lower limb vessels. The hallmark of the diagnosis by duplex scanning in our patients was the demonstration of an echofree space with evidence of swinging blood flow that communicated with the common femoral artery or one of its branches. We found echofree spaces anterior to the artery and just below the skin. Out of 34 patients undergone duplex scanning, 05 revealed communication with the common femoral artery and 13 with the superficial femoral artery. Size of the pseudoaneurysm varied from 1.5 to 10 cm. in diameter. Aneurysm sac of 22 patients showed partial clotting (organised thrombus). In 6 patients pseudoaneurysm were associated with A-V fistula between superficial femoral artery and common femoral veins. There was no case of associated venous thrombosis. Out of 56 patients, 26 had pseudoaneurysm measuring upto 3 cm., 14 had in between 3-5 cm., 04 had in between 5-7 cm., and 12 had in between 7-10 cm. (Table-III).

Table-I

Age group & Sex

Age group in years	Sex		Total
	Male	Female	
35 - 50	8	12	20
51 - 65	15	21	36
Total	23	33	56

Table-II

Relation of pseudoaneurysm formation with procedure performed

Sex	Diagnostic angiography	Therapeutic angiography	
		PTCA	PTCA +stent
Male	23	5	7
Female	33	9	6
Total	56	14	13

Table-III

Relation of size of pseudoaneurysm with management

Group	Size of Pseudoaneurysm (Diameter in cm)	Management	
		Conservative	Surgical
A	1.5-3	26	-
B	3-5	12	2
C	5-7	-	4
D	7-10	-	12
Total		38	18

Patients were first kept under observation and 2 weekly follow up with repeat duplex study. All patients of group A and 12 patients of group B showed spontaneous thrombosis without complication within 30 to 60 days. Rest of 02 patients of group B and all patients of the group C & D did not show spontaneous thrombosis and underwent surgery.

During surgery, it was found that 5 patients had puncture/rent site in the common femoral artery and 13 had in the superficial femoral artery (Table-V). Seven rents were repaired directly by 3-6 interrupted 6/0 or 7/0 prolene sutures and 03 rents needed vein patch angioplasty . Associated A-V fistula in 6 patients were also repaired accordingly. Grossly lacerated superficial femoral artery (SFA) segment of 2 patients were resected out and end to end anastomosis was done using 7/0 prolene continuous suture (Table-IV).

Postoperative period in 17 patients was uneventful and were discharged on 10-12th day of surgery. One patient had postoperative wound infection, for which hospital stay was prolonged up to 20 days.

Table-IV

Types of surgery performed

No	Types of Surgery	No. of patient
1	Direct suture repair of rent in arterial wall	7
2	Dismantling of A-V fistula, repair of venous wall rent and patch closure of arterial wall defect	6
3	Vein patch angioplasty of arterial wall defect	3
4	End to end anastomosis of artery	2
	Total	18

Table-V

Probable causes of pseudoaneurysm

Sl. No	Causes of pseudoaneurysm formation	No. of patient
1	Puncture site: a) superficial femoral artery	13
	b) common femoral artery	5
2	Continuation of anticoagulation in perioperative period	27
3	Difficult/faulty haemostasis	56

Discussion :

The explosive evolution of angiography and in particular coronary interventional technology over the last few years has carried with it an increased incidence of peripheral vascular complications. Pseudoaneurysm formation is one of them.

Reported incidence of pseudoaneurysm formation after angiography and interventional procedures varies widely. However, most of the authors report it to be in the range of 0.1- 0,2% for diagnostic angiographic series and 3.5 - 5.5% for interventional procedures[3,5]. In our series these figures are 0.59% and 6.5% respectively. It is to be mentioned here that most of the works done & reported in western literatures this subject are by truly professional interventionalists. On the other hand, the teaching institute NICVD, Dhaka is having young and relatively less experienced interventionalists. This is why ,there is increase in percentage of complications in comparison to western literatures. We hope that in course of time, it will definitely come down to international standard. .

The causes of pseudoaneurysm formation are low femoral artery puncture sites (e.g. SFA), inadequate compression following catheter or sheath removal or impaired clotting function[1,4]. In our series 13 patients had puncture sites at SFA. This faulty puncture resulted in pseudoaneurysm formation, probably due to deep anatomic location of SFA, which is less accessible to compression, following sheath removal.

Large bore catheters or introducers are associated with larger defects in the artery and are therefore more likely to be associated with the formation of pseudoaneurysm. This, in combination with anticoagulation, increases the chance of pseudoaneurysm formation. In our series 27 patients had pseudoaneurysm following longer interventional procedure like PTCA with or without stenting.

The diagnosis of iatrogenic pseudoaneurysm is not difficult and may be made at the bedside. A pulsatile tender haematoma with its other features are usually apparent. Duplex scanning and angiography or MRA confirm the diagnosis. Among these tools, duplex study is of particular use in this situation because the presence of blood flow into a perivascular haematoma detected by Doppler with colour flow imaging is diagnostic of a pseudoaneurysm[4] (Fig.-2). In our series none of the patients had angiography or MRA for the diagnosis of pseudoaneurysm. Duplex study adequately served the purpose. Moreover it was used for follow up during pre and postoperative period without any harm to the patient.

Treatment of pseudoaneurysm may be of two types.

a. Conservative or non-surgical technique

Pseudoaneurysm of less than 3 cm. in size can often be followed clinically for spontaneous thrombosis[5]. In our series 38 patients having pseudoaneurysm of varying size (1.5 to 5 cm) had spontaneous thrombosis within 4-8 weeks of observation. Newer non-surgical techniques like progressive graded mechanical compression using a C-clamp is performed, with duplex Doppler control to obliterate flow in the aneurysm sac, while maintaining adequate flow in the main femoral artery are popular in different series[6,7]. This procedure is yet to be introduced and not so far reported in our country.

b. Surgical repair

It is the traditional and invasive method of treatment for pseudoaneurysms. It is not at all a difficult job for an experienced vascular surgeon with a good support team. Usually it is done under spinal or epidural anesthesia.

All patients of our series, undergoing surgical intervention were without any perioperative complication except one wound infection and postoperative hospital stay upto 20 days.

Peripheral vascular complications like pseudoaneurysm formation is one of the causes of significant morbidity following diagnostic and therapeutic interventional angiographic procedures. The initial fault in compression for haemeostasis is being tackled by mechanical and pneumatic compression devices. In addition, extravascular collagen haemostatic devices and haemostatic puncture closure device with intraluminal anchor are recently introduced devices[2]. We hope that in time all these will be introduced in our setup also. But the most important is the prevention of the complication. The identification of those patients at high risk and meticulous care during angiographic procedure may help to reduce vascular complications.

Conclusion :

Femoral artery pseudoaneurysm is one of the acceptable complications of angiographic procedures. Puncture site at lower level, inadequate compression following catheter or sheath removal or impaired clotting are the probable case. Diagnosis may be made clinically at bedside and confirmed by duplex scanning. Small sized rent heals with conservative treatment but the larger rents head surgical intervention. Identification of high risk patients and meticulous care during angiographic procedures may prevent this sort of vascular complication to some extent.

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Pregnancy Outcome in Patients with Nonreactive Nonstress Test

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Summary :

Cardiotocography or electronic foetal heart rate monitoring has proved to be a sensitive tool for detecting foetal distress[1]. With the advent of electronic foetal heart rate monitoring, a relationship between foetal movement and foetal heart rate was observed and this relationship formed the basis for the non stress test (NST)[2].

In total 60 patients were selected randomly for inclusion in this study .Those patients exhibiting non reactive NST (n =30) were included in study group. Those exhibiting reactive NST (n = 30) were included in control group with same inclusion and exclusion criteria (of two groups) were evaluated by : (1) Perinatal death . (2) Umbilical arterial blood pH, gas values at birth (acidemia in newborns umbilical arterial blood pH <7.20). (3) Apgar score <7 at 1&5 minute.(4) Needs for neonatal admission in special care baby unit (SCABU)/ Intensive care unit due to respiratory distress for more than 24 hours. (5) Congenital anomalies (6) Neurological signs like convulsions, hyperreflexia, hypertonia and hypotonia in neonatal period.

In non reactive NST group 14 (46%) neonates were found to be normal & reactive NST group 30(100%) neonates were normal. In this study, in non reactive NST 15 newborns (50%) were found to be low Apgar score <7 at 1 minute and 8 (26.66%) neonates were found to be low Apgar score at 5 minutes. In non reactive NST group no newborn was found to be low Apgar score. From 15 neonates of low Apgar score at 1 minute 14 neonates were admitted in (SCABU)/ intensive care unit for respiratory distress. Their mean hospital stay were 11 days. Perinatal mortality In non reactive NST group were found to be 2 (66.66 per 1000) one still birth & one early neonatal death. No perinatal death in reactive NST group. In non reactive NST group 12 (40%) newborns were acidemic and all the newborns were normal in reactive NST group.

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Introduction :

The rationale for the use of the non-stress test for the antepartum evaluation is the presence of acceleration of FHR associated with foetal movement indicates intact responsive CNS mechanisms that are reflected by these FHR changes[3]. It has been established that FHR accelerations associated with foetal movements are reliable indicator of the foetal wellbeing[4]. A foetal heart rate pattern, non reactive in the absence of extreme prematurity, gross congenital anomalies, maternal fasting or pharmacological influences accurately identifies a compromised foetus likely to be acidotic or preacidotic at delivery. Such NST patterns signal the urgent need to consider delivery delay many result in intrauterine foetal death.

Determining the pH of blood in umbilical artery has become an important measure of the infants condition at birth. Foetal umbilical venous blood gas values are similar to maternal intervillous oxygen and acid base status because oxygen and carbondioxide can equilibrate between these two compartments whereas umbilical arterial blood represents the foetal status[6]. Metabolic acidosis reflects foetal distress and asphyxia[7].

Subjects & methods :

This prospective case control study was carried out from July 1998 to December 1999 in the department of Obstetrics & Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka and Bangladesh Institute of Research Disorder of Endocrine & Metabolism (BIRDEM), Dhaka.

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In total 60 patients were selected randomly for inclusion in the study. Gravid women 34 weeks and onwords were included in this study. Those patients exhibiting non reactive NST (n=30) were included in this study group-group 1. Those exhibiting reactive NST (n=30) were included in control group- group 2 with same inclusion and exclusion criteria.

Inclusion Criteria:

All gravid women of 34 weeks and onwards, both primigravida and multigravida were included.

Exclusion criteria:

Patients who had just recently been exposed to :

- Tranquilizers.
- Barbiturates.
- Atropin.
- Cigarette smoking.
- Corticosteroid.

The obstetrics course after performing NST, delivery and immediate neonatal staffs were observed and the characteristics were recorded prospectively. Pregnancy outcome (of two groups) were evaluated by following parameters:

i) Perinatal death ii) Umbilical arterial blood p^H and gas values at birth (acidema in newborns-umbilical arterial blood p^H <7.20). iii) Apgar score <7 at 1 and 5 minute iv) Needs for neonatal admission in special care Baby Unit/Intensive care unit due to respiratory distress for more than 24 hours. v) Congenital anomelies. vi) Neurological signs covulsions, hyperreflexic, hypotonia.

Methods :

After informed consent had been obtained all tests were performed with the patient in lateral tilt position. No smoking or drugs (as mentioned in exclusion criteria) were permitted during the preceding 2 hours. Foetal heart rate recording was made with a Meridion 800 Sonicaid foetal monitor. Tracings were observed & interpreted, non reactive tracings were done for more than 40 minutes & reactive tracings were done for 20 minutes.

With utmost aseptic measure umbilical cord arterial blood (0.5cc) samples were drawn from a clamped umbilical cord immediately after delivery into a heparinized 3ml syringe. The umbilical arterial blood samples were placed in ice. The blood p^H and gas analysis were done within 30 minutes of collection. p^H values and blood gas values were determined with 238 p^H blood gas analyzer at 37°c.

Observations and Results :

During the study period, 60 pregnant women of gestational age ranging from 34-42 weeks were randomly selected from the inpatient department of Obstetrics and Gynaecology, BSMMU and BIRDEM, Dhaka.

Age of patients, parity and gestational age (weeks) of two groups were matched.

Cases where NST were performed within 48 hours preceding delivery were included in this study. Delivery was monitored and immediately after birth of the baby, umbilical cord was clamped and umbilical cord arterial blood sample was collected & blood pH & gas analysis were done. The newborn infants were studied as regards Apgar score, birth weight, any congenital anomalies were recorded immediately after birth. Apgar scoring was done at 1 and 5 minutes.

Mean birth weight of newborn infants are 2.76kg (n=30) in non reactive NST group and 2.93 kg (n=30) in reactive NST group.

Umbilical arterial blood p^H and gas values at 37°C of the two groups

	Non reactive NST group (n=29)	Reactive NST group (n=30)
	Mean ± SD	Mean ± SD
pH	7.21±0.14	7.41±0.03
Pc02	61.71 ± 14.94	44.90 ± 13.68
P02	21.81 ± 7.06	29 ± 4.50
HC03	25.32 ± 7.38	25.69 ± 2.88
BE	0.92 ± 7.35	1.45 ± 1.89

In group 1 (non reactive NST group) 15 (50%) newborns were found with low Apgar score (<7) at 1 minute and 8 (26.66%) newborns were found with low Apgar score at 5 minute. In group 2 (reactive NST group) no newborn was found Apgar score <7 at 1 and 5 minutes.

In group 1 still birth occurred in 1(3.33%) cases, 1(3.33%) early neonatal death occurred 42 hours after birth who had multiple congenital anomelies (Meningomyelocele, clept lip, clept palate, polydactile). The neonate became acidotic and died due to respiratory failure. But no still birth or perinatal death in group 14 neonates (46.66%) in group 1 required admission into SCABU/neonatal intensive care unit for respiratory distress and their mean length of hospital stay were 11 days. No neonate of group 2 was required admission.

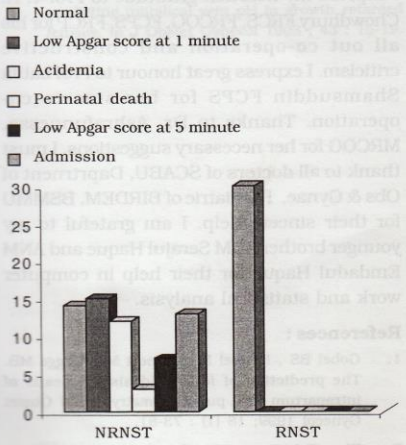

Figure: Perinatal Outcome

Umbilical cord arterial p^H <7.2 was considered as neonatal acidemia.

Correlation of umbilical arterial blood pH with 1 minute & 5 minute Apgar score were found to be 0.8309 & 0.8585 both were a strong positive correlation & both were statistically highly significant (p <0.001). Correlation of $P0_2$ with 1 minute Apgar score & 5 minute Apgar score were found to be 0.6104 & 0.7548, both had moderate positive correlation and were statistically highly significant (P< 0.001). Correlation of $HC0_3$ with 1 minute Apgar score were found to be 0.6370 & 0.6238 both were statistically highly significant. Correlation of p^H & $P0_2$ was found to be 0.7527 & this moderate positive correlation was also statistically highly significant (p <0.001).

In this study NST was found to have a sensitivity of 100% for detection of low Apgar score of newborns, needs for admission of neonates in SCABU. Intensive neonatal care unit, perinatal death, acidemia in newborns.

NST was found to have a positive predictive value of 50% for the detection of low Apgar score for newborns, 46.66% needs for admission of neonates, 6.66% for the detection of perinatal death, 40% for the detection of acidemia of newborns.

NST was found to have a specificity of 66.66% for the detection of low Apgar score, 65.21 % for the detection of needs for admission of neonates, 51.72% for the detection of perinatal death, 62.5% for the detection of acidemia in newborns.

Discussion :

NST is a useful test, where there is poor maternal surveillance, sudden intrauterine

foetal death remains one of the most disturbing situations faced not only by the treating obstetrician but also by the family of the affected patient[8]. Many regard cord blood gas analysis as an additional and objective method to check for acidosis of the newborn immediately after birth[9]. The foetal metabolic status can be assessed directly by analysis of foetal blood samples for pH and gases[10]. We assessed the predictive value of acidosis at birth at 1 minute and at 5 minute Apgar score[11]. We applied the Apgar score in our study because it remains as a simple clinical index of the condition & behavior of newborn babies[12].

There was a striking similarity between the Apgar score and rates of neonatal admission to special care nursary. In this study acidemia was found to be 40% in group 1. This study well corresponds with the study of Henson et al[13,14].

In this study, perinatal mortality in non reactive NST group were found to be 2 (66.66 per 1000), no perinatal death occurred in reactive NST group. Similar study result was also found in perinatal mortality of 60 per 1000 in non reactive NST group[14]. There was a significant relationship between CTG and neonatal outcome. All babies with a normal CTG survived and had a good perinatal outcome[15]. Borrett et al mentioned stillbirth rate of 6.4 per 1000 in non reactive NST. They conclude it clearly that a foetus with a non reactive NST is at much higher risk of stillbirth than a foetus with a reactive NST[16].

In non reactive NST group correlation of umbilical arterial blood pH and 1 minute & 5 minute Apgar score has strong positive correlation and statistically highly significant. Umbilical artery blood pH was found to correlate best with the Apgar score regardless of wheather at 1 minute, 5 minute[17].

Similar study by Shelev at al also found that for the detection of acidemia in newborns, NST have sensitivity of 100%, specificity 84.2% and positive predietive value 57.1%[18].

Conclusion :

Increased perinatal mortality and morbidity among foetuses with non reactive NST than reactive NST. This study reflects that non reactive NST was associated with increased number of newborn with low Apgar score, acidemia increased need for admission and increased perinatal mortality as well.

One of the major goal of the antepartum foetal surveillance is the appropriate and timely identification of the compromised foetus, requiring immediate intervention improved perinatal outcome. An equally important goal is the correct identification of the foetus who is well and require immediate intervention. Avoidance of unnecessary intervention with risk and cost for both mother and foetus must be appreciated as basic to any protocol of high risk pregnancy surveillance.

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REVIEW ARTICLE

Motor Neuron Disease and Glutamate

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Summary :

MND is a neurodegenerative disease due to chronic loss of motor neurons (both upper and lower motor type). The "glutamate hypothesis" is one of the major pathophysiological mechanisms of motor neuron injury. Motor neuron expresses a unique molecular profile of glutamate receptors. There is a great diversity in the glutamate receptor family. Abnormal activation of glutamate receptors is one of the main candidates as a final common pathway of neural death. The concept of excitotoxicity may be particularly relevant to a chronic neurodegenerative disease such as MND where cellular injury by glutamate is triggered by disturbances in neuronal energy status. In classical acute excitotoxicity there is influx of Na^+ and Cl^- and destabilization of intracellular Ca^{++} homeostasis, which activates a cascade of harmful biochemical events leading to neuronal death. Two important molecular features of motor neurons have been identified which may contribute to their vulnerability to neurodegeneration. The low expression of calcium binding proteins and the low expression of GluR2, AMPA receptor subunit by vulnerable motor neuron groups may render them unduly susceptible to calcium-mediated toxic events following glutamate receptor activation. The links between abnormal activation of glutamate receptors and other potential mechanisms of neuronal injury, including activation of calcium mediated second messenger system and free radical mechanisms are emphasized. Riluzole, which modulate the glutamate neurotransmitter system, has been shown to prolong survival in patients with MND. The goal of future research is the development of subunit specific therapeutic targeting of glutamate receptors and modulation of downstair events within motor neurons.

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Introduction :

The primary pathogenetic processes underlying motor neuron diseases (MND) are likely to be multifactorial and the precise molecular mechanisms underlying selective cell death in the disease are, at present unknown. A complex interplay between genetic factors, toxic activation of glutamate receptors and oxidative stress may result in damage to critical target proteins and organelles[1-4]. Other processes like auto immune mechanism may contribute to motor neuron injury in some MND patients[5,6]. The present article will highlight the present state of knowledge relating to glutamate neurotransmission in the human motor system; the concept of excitotoxicity and how this might apply to a chronic neurodegenerative disease such as MND; current knowledge of molecular profile of glutamate receptors on human motor neurons; possible reasons for the selective vulnerability of motor neurons to glutamate; the links between glutamate receptor activation and free- radical mediated damage.

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Normal glutamate neurotransmission :

Glutamate is a major excitatory neurotransmitter in the mammalian nervous system. It is an important neurotransmitter in several pathways in the human motor system, including the corticospinal tracts[7], cortico-cortical association pathways[8] and excitatory inter neuronal pathways in spinal cord[9]. Postsynaptic glutamate receptors have traditionally been classified into two major categories; metabotropic receptors and ionotropic receptors. Ionotropic receptors are ligand-gated ion channels and metabotropic receptors are coupled through G proteins to second messenger systems

The ionotropic receptors have been sub-divided into three sub-types; N-methyl-D-aspertate (NMDA) receptors; Alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptors; and kainate receptors[10]. Fourteen genes have been identified which encode different ionotropic glutamate receptors sub-units (figure 1)[11-13]. The existence of multiple sub-unit genes and variations of sub-unit assembly to form receptor complex in vivo contribute to the diversity of receptors[14]. A given glutamate receptor gene product and splice variant may be further modified by post-transcriptional RNA editing. This may have significant functional consequences; for example, the change of single amino acid in the second trans membrane domain of the glutamate receptor channel can determine whether or not the channel is permeable to Ca^{++} [15]. In addition, multiple sub-unit variants can be generated from a single gene by alternative splicing of adjacent axons of glutamate receptor genes, as exemplified by the flip and flop variants of the AMPA receptors sub-units[16]. Thus, the potential number of different sub-types of glutamate ionotropic receptors is very large and it is quiet conceivable that a given population of neurons, within the CNS such as motor neurons, will be characterized by a relatively unique molecular profile of glutamate receptors.

During normal glutamate neurotransmission (fig 2), glutamate is released from the pre-synaptic neuronal terminal and travels across the synaptic cleft to act on postsynaptic receptors. The excitatory signal is terminated by active removal of glutamate from the synaptic cleft by several types of glutamate reuptake transporter proteins, which are situated on both perisynaptic astroglia and presynaptic terminals. Four human glutamate transporters have recently been cloned ($EAAT_1$, $EAAT_2$, $EAAT_3$ and $EAAT_4$)[17,18].

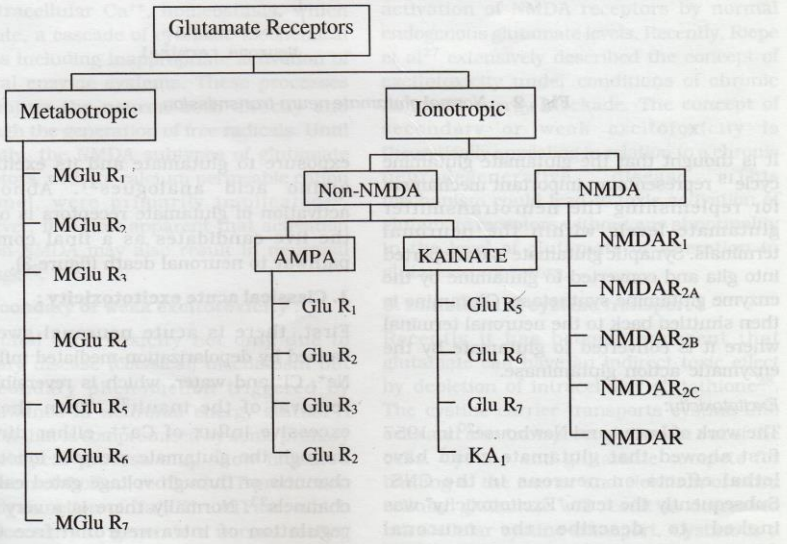

Fig . 1 : *Showing the different types of Glutamate receptors.*

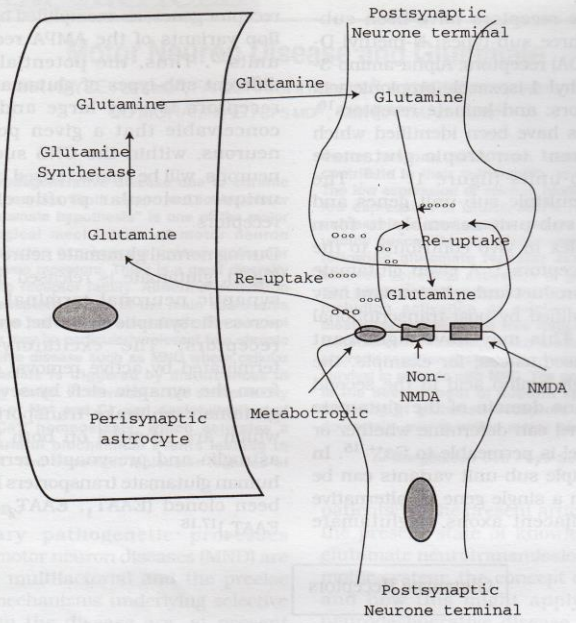

Fig . 2 . *Normal glutamate neuro-transmission*

It is thought that the glutamate glutamine cycle[19] represents an important mechanism for replenishing the neurotransmitter glutamate levels within the neuronal terminals. Synaptic glutamate is transported into glia and converted to glutamine by the enzyme glutamine synthetase. Glutamine is then shuttled back to the neuronal terminal where it is converted to glutamate by the enzymatic action glutaminase.

Excitotoxicity:

The work of Lucas and Newhouse[20] in 1957 first showed that glutamate could have lethal effects on neurons in the CNS. Subsequently the term "Excitotoxicity" was inoked to describe the neuronal degenerative change resulting from exposure to glutamate and its excitatory amino acid analogues[21]. Abnormal activation of glutamate receptors is one of the five candidates as a final common pathway to neuronal death (figure 3).

1. Classical acute excitotoxicity :

First, there is acute neuronal swelling caused by depolarization-mediated influx of Na^+, Cl^- and water, which is reversible on removal of the insult[22]. Then there is excessive influx of Ca^{++}, either directly through the glutamate receptor ionotropic channels or through voltage gated calcium channels[23]. Normally there is a very tight regulation of intra-neuronal free Ca^{++}, maintaining the level of free Ca^{++}, below 0.1

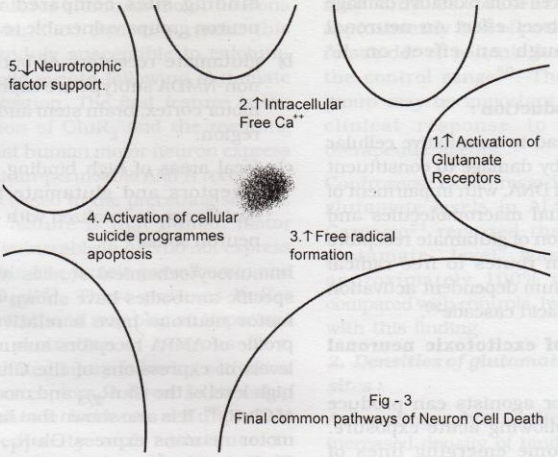

Fig - 3
Final common pathways of Neuron Cell Death

μM[24]. After excessive stimulation of glutamate receptors, there is destabilization of intracellular Ca^{++}, homeostasis, which activate, a cascade of cytotoxic biochemical events including inappropriate activation of several enzyme systems. These processes can injure the neuron both directly and through the generation of free radicals. Until recently, the NMDA subtypes of glutamate receptors, with its calcium permeable cation channel, were primarily implicated[25]. However, it is now apparent that activation of non-NMDA may also result in neuronal damage[26].

2. Secondary or weak excitotoxicity :

Neuronal excitotoxicity not only due to primary disease (classical) mechanism but a secondary phenomenon triggered by disturbance in neuronal energy status. A neuron that is compromised by some primary pathological process may show impaired glucose metabolism, reduced ATP production and dysfunction of Na^+/K^+ - ATPase, which are necessary to generate a normal resting membrane potential. For example, the voltage dependent Mg^{++} block of the NMDA receptor channel may be eliminated, resulting in over activation of NMDA receptors by normal endogenous glutamate levels. Recently, Riepe et al[27] extensively described the concept of excitotoxicity under conditions of chronic neuronal energy blockade. The concept of secondary or weak excitotoxicity is theoretically appealing in relation to a chronic neurodegenerative disease. This mechanism could lead to toxic activation of glutamate receptors without any abnormality in the level of glutamate or alteration in glutamate receptors.

3. Inhibition of cystine transport :

Recently it has become apparent that glutamate can have an indirect toxic effect by depletion of intracellular glutathione[28]. The cystine carrier transports cystine into cells and also transports glutamate out of the cells. Cystine and glutamate compete for binding to the carrier and elevation of extra cellular glutamate will result in decreased intracellular cystine transport. Cystine is a vital precursor of intracellular glutathione,

which protects the cell from oxidative damage and also has a direct effect on neuronal excitability through an effect on K^+ conductance.

4. Free radical production :

Free radical can lead to cumulative cellular injury and death, by damage to constituent proteins, lipids and DNA, with impairment of function of essential macromolecules and organelles. Activation of glutamate receptors is one of the main routes to free radical production by calcium dependent activation of the arachidonic acid cascade[29].

5. Time course of excitotoxic neuronal death :

Glutamate receptor agonists can produce neuronal death following acute exposure. There are also some emerging lines of evidence that excitotoxic mechanism can potentially produce chronic neuro-degenerative pathology. Excitotoxicity in rat brain neurons have been shown in low dose expose to EAA agonist quinolinic acid[30]. Prolonged pharmacological blockade of glutamate reuptake system results in degeneration of motor neurons over weeks[31]. Activation of glutamate receptors under physiological condition result in change in synaptic efficiency[32] and under pathological/ physiological condition may alter gene expression in a long lasting manner[33].

Glutamate receptors profile of human motor neurons :

Human motor neurons contain a high density of glutamate receptors[34] and are susceptible to toxic effects following NMDA or non-NMDA glutamate receptors activation[35]. Receptor distribution in human motor neurons has been studied using quantitative autoradiography with specific radio ligands. The important findings are –

a) motor neuron groups that tends to be spared in MND (eg: 3rd nerve nucleus) express a low density of NMDA receptors binding sites and high density of AMPA binding sites compared with motor neuron groups vulnerable to the disease.

b) glutamate receptors of both NMDA or non-NMDA subtype are expressed in the motor cortex, brain stem and spinal cord region.

c) focal areas of high binding with NMDA receptors and glutamate transporter system are co-localized with lower motor neuron soma[36,37].

Immunocytochemical studies with subunit specific antibodies have shown that human motor neurons have a relatively distinct profile of AMPA receptors subunit with low levels of expressions of the $GluR_1$ protein, high level of the $GluR_{2/3}$ and moderate levels of $GluR_4$[38]. It is also shown that human spinal motor neurons express $GluR_1$, $GluR_3$ and $GluR_4$ but have no detectable expression of mRNA for $GluR_2$[39]. The $GluR_2$ subunit has a very important role in determining the calcium permeability of AMPA receptors[40]. Most native AMPA receptor subunits are the edited from of $GluR_2$, which render them impermeable to calcium[41]. Only a few groups of cells in the mammalian CNS appear to express calcium- permeable AMPA receptors. It has been shown that neuronal subpopulations expressing atypical AMPA receptors that lack $GluR_2$, which gate calcium-permeable ion channels, exhibit heightened vulnerability to non-NMDA agonist toxicity[42]. Thus the lack of $GluR_2$ expression by human motor neuron and the resulting likely permeability to their AMPA receptors could potentially render the cell group vulnerable to excitotoxic injury by increasing calcium influx during glutamate receptors activation.

Selective vulnerability of motor neurons :

Motor neurons differ from many other groups of cells in the CNS by their large size, high ratio of axonal length to cell soma diameter, high metabolic rate, high content of neurofilament proteins and free radical scavenging enzymes[43,44]. Two cells specific

molecular features of human motor neurons have been identified that may render this cell group unduly susceptible to calcium-mediated toxic events following glutamate receptor activation. The first feature is the low expression of $GluR_2$ and the resulting likelihood that human motor neuron express atypical calcium-permeable AMPA receptors, which is discussed in the preceding section. The second feature is that human motor neurons are vulnerable in ALS do not express the calcium binding protein parvalbumin and calbindin $D_{28}K$[45]. These proteins buffer intracellular Ca^{++} and may play an important role in the protection of neurons from calcium-mediated injury following activation of glutamate receptors. A direct relationship has been shown between cellular Ca^{++} buffering capacity and resistance to glutamate neurotoxicity[46]. These two molecular features may in combination, render human motor neurons particularly susceptible to calcium toxicity following AMPA receptor activation.

Evidence of dysfunction of the glutamate neurotransmitter system in MND :

The evidence that a disturbance of glutamate transmission may be present in MND has been discussed in several recent reviews.

1. Glutamate level in CNS tissue, CSF and plasma of MND patients – several groups have found significant reduction in the levels of glutamate, aspartate, N-acetyl-aspartyl-glutamate and N-acetyl-aspartate in several CNS regions of MND patients[47]. In other study it has been shown that glutamate in the CSF is increased in MND patients[48]. This lead to the hypothesis that there may be an underlying defect in the metabolism, transport or storage of glutamate. Again the reason of discrepancies in glutamate level may relate, in part, to heterogenety of the MND patients and also to technical difficulties in measuring glutamate in biological samples[49]. A recent study has indicated that the elevation of CSF glutamate may only be present in a subset of approximately 30% of patients with MND, the remainder of patients having levels within the control range[50]. The high glutamate group may be important in evaluating the clinical response to anti glutamate therapeutic agents.

Controversy exists regarding fasting plasma glutamate levels in ALS. Plaitakis and Caroscio[51] reported that fasting plasma glutamate level was increased by approximately 100% in MND patients compared with controls. Iwasaki et al[52] agreed with this finding.

2. Densities of glutamate receptor binding sites :

Autoradiographic studies have shown an increased density of binding site for NMDA and non-NMDA receptor ligands in MND, particularly in the intermediate grey matter of the spinal cord and the deep layers of the motor cortex[53].

3. Abnormalities of glutamate transport :

Inefficient synaptic clearance of glutamate could result in excessive activation of EAA receptors with resulting toxic damage of motor neurons. Rothstein et al[54] showed that the motor neurons of affected regions of CNS in MND have a specific functional defect in the Na^+dependent glutamate uptake system. It has been shown that "knockout" of the glial glutamate transporters GLT –1 and GLAST using chronic antisense oligonucleotide administration in vivo produces elevation of extra cellular glutamate levels, excitotoxic neurodegenerative changes and progressive paralysis. Studies using antibodies to synthetic peptides from three of the clone's glutamate transporters showed a substantial loss of the astroglial GLT-1 immunoreactive protein in MND. There was a 70% decrease in GLT-1 expression in motor cortex from ALS patients, and in about 25% of the MND cases the loss of expression of the GLT-1 protein was dramatic, with no accompanying

depletion of another glial specific protein, glial fibrillary acidic protein or GLT-1 m-RNA[55]. This proves that in a proportion of patients with MND there is an abnormality in the synthesis or turnover of the protein. Alternatively GLT-1 could be selectively damaged by other pathophysiological processes, such as oxidative stress, given the known sensitivity of glutamate transport to damage by free radicals[56].

4. Experimental studies :

Using tissue culture model in which organotypic rat spinal cord is maintained under conditions of chronic glutamate uptake inhibition, motor neuron toxicity is produced with a subacute time course[31]. Intrathecal injection of the EAA agonist kainic acid in mice preferentially injuries anterior horns cells and induce formation of abnormally phosphorylated neurofilaments, a cytoskeletal abnormality that has been documented in MND[57]. It appears that drugs which inhibit glutamate release, which block glutamate synthesis or which act as non MNDA receptors antagonist are the most potent neuroprotective agents, and certain oxidants or inhibitors of nitric oxide synthesis can also exert a modest neuroprotective effect[58].

5. Exogenous excitotoxins :

Several excitotoxins have been identified which are responsible for excitotoxic damage of motor neurons. These are : B-N-oxalyl-amino-L-alanine (BOAA), excitotoxin of sago palm, B-N-methyl-amino-alanine (BMAA), domic acid etc. BMAA is a constituent of cycad seeds, which is a potent excitotoxin capable of activating several types of glutamate receptors. It can also exert other neurotoxic effects, including disruption of mRNA metabolism[59]. Domoic acid is also an excitatory toxin, which is a selective kainate receptor agonist, responsible for outbreak of food poisoning. It affects mainly the hippocampus an amygdale and some of the affected individuals develop limb weakness, suggestive of either lower motor neuron injury or a motor polyneuropathy[60]. BOAA, a glutamate analogue presents in the Lathyrus satibus. Victim of this disease develop upper motor neuron signs predominantly in the lower limbs due to degeneration of the cortico spinal tract. Seven percent of the patients have clinical evidence of lower motor neuron dysfunction and inclusion bodies have been described within the anterior horn cells of victims of lathyrism[61]. Until recently, one of the major hypothesis for the high incidents of MND and Parkinsonism-dementia in the Western pacific was that neurotoxicity may have been resulted from the use of the seed of falls sago palm for food.

6. Positron emission tomography studies :

In the MND groups there was significantly greater activation in several cortical areas, implying inappropriate activation of pyramidal tract neurons, outside the normal somatotropic representation of the moving upper limbs. This suggests an imbalance between excitatory and inhibitory neurotransmission in the cortex in MND patients. Abnormalities in the contra-lateral cortical area increase in cerebral flow caused by freely selected upper limb movements have been shown in MND patients compared with controls[62].

7. Neurophysiologic studies :

The presence of hyper excitability of motor neurons of MND patients was proved by transcranial magnetic stimulation of the motor cortex[63].

8. Therapeutic modulation of glutamate neurotransmission :

The recently published clinical trial of riluzole showed a 35% increase in survival at 18 months in the group receiving the optimal dose of riluzole compared with placebo[64]. Riluzole interferes with pre- and post-synaptic glutamate neurotransmission via a complex mechanism of action involving the blockade of voltage-sensitive Na^+

channels, ionic flux through NMDA channels possibly also interaction with G proteins[65]. Riluzole inhibits glutamate release, decreases EAA-evoked firing of rat facial motor neurons and exerts neuroprotective effects in experimental models of acute and chronic neurodegenerative disease[66]. An interesting property of riluzole is that its binding affinity is several hundred-fold higher for the inactivated state of Na^+ channels compared with the activated state [67]. This state-dependent drug affinity means that riluzole can be expected to preferentially block depolarized hyperactive neuron, because their Na^+ channels are more often in the inactivated state compared with Na^+ channels of normal neurons.

Links between glutamate receptor activation and free-radical mediated damage:

Free radicals are one of the main potential causes of age related deterioration in neuronal damage and accumulation of oxidative damage may contribute to the delayed onset and progressive nature of neurodegenerative disease[68]. Activation of glutamate receptors and subsequent calcium dependent second messenger systems is an important pathway of free radical production within neurons. There is considerable interest in the role of free radicals in motor neuron injury following the discovery that some patients with familial MND have point mutations in the gene on chromosome 21 that encodes super oxide dismutase (SOD). The normal role of SOD is to catalyze the removal of super oxide radicals that can contribute to cellular oxidative damage[69]. The molecular mechanism of selective motor neuron injury is the presence of SOD mutations are not understood. But recent evidence suggests that the mutant protein has acquired some "toxic gain-of-function". One hypothesis for this toxic effect is that the mutant SOD protein may alter the sensitivity of motor neurons to glutamate neurotransmission by mitochondrial dysfunction.

Conclusion:

Whatever the primary pathophysiological process underlying the motor neuron in MND, the glutamate neurotransmitter system is likely to remain an important target for therapies aimed at retarding the pathological progression of the disease.

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CASE REPORTS

Secretory Carcinoma of Breast : Report of a Rare Case

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A HOSSAIN M.PHIL[d], KM NAZRUL ISLAM M .PHIL[e]

Summary :

A 34 years female presented with an irregular breast lump which was persistent for five months . It was excised and histopathological examination showed features of a secretory carcinoma which is a very uncommon tumour of breast with a relatively favourable prognosis

Introduction: **Carcinoma of breast is a common and important tumour the female. Different types of carcinomas are described in different texts and articles. A rare distinctive type of carcinoma was first described in 1966 by Mc Divitt and Stewart in seven patients whose age ranged from 3 to 15 years, averaging 9 years[1]. Oberman and Stephens reported four more such cases in adult and elderly women[2]. 19 patients were studied in Armed Forced Institute of Pathology USA, with a median age of 25 years and reported as secretory carcinoma[3]. A number of reports of secretory carcinoma in children including male were also published[4,5,6].**

Here, we report a case of secretory carcinoma of breast in a female patient of 34 years.

(J Bangladesh Coll Phys Surg 2003; 21 : 43-45)

Case report :

The patient presented with an irregular right breast lump which was gradually increasing in size and persisted for five months. The lump was surgically removed. It measured 4.5 x 3.5 x 3.0 cm. The cut surface was soft and markedly slimy.Microscopic examination showed a carcinoma composed of atypical epithelial cells forming glandular and microcystic pattern.The tumour cells, glands and microcystic spaces contained abundant secretion, which was pale pink in appearance on Haematoxylin and Eosin stain. (Fig-1& 2). Some of the tumour cells contained bubbly cytoplasm. The secretion was positive for Periodic Acid Schiff (PAS) stain.

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Fig.-1 : *Microscopic appearance of secretory carcinoma of breast showing cribriform appearance (H & E x 150).*

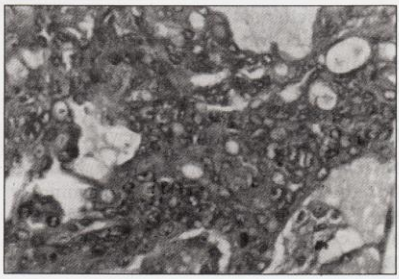

Fig.-2 : *High power view of secretory carcinoma showing pleomorphism of tumour cells(H & E x 450)*

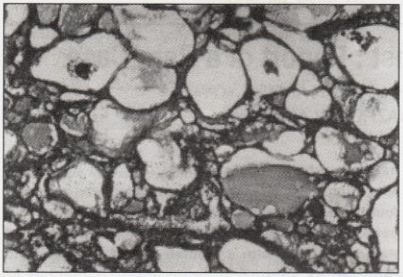

Fig.-3 : *Microscopic appearance of secretory carcinoma of breast (PAS stain) showing PAS positive secretion within the lumina.*

Discussion :

Secretory carcinoma is a rare cancer of breast, first described in 1966. It is mostly seen among very young female. The tumour is uncommonly noted in adult and elderly. [6] To our knowledge, secretory breast carcinoma has not been reported in Bangladesh.

A number of cases have been reported from different areas of the world [4,5,7,8,9,10,11].

The tumour appears in the form of a well defined mass. Usually circumscribed, firm and sometimes lobulated .The tumour may have infiltrative margins. Usually the tumour is small but occasionally larger lesions of 12 cm or more may be seen in adults[7,8,9].

Subareolar lesions have been associated with nipple discharge. No clinical evidence of hormonal abnormality has been described to explain the secretory characters of the tumour. It is never associated with pregnancy. Oestrogen receptors are negative in most of the cases except a few. [5]

Microscopically secretory carcinoma has an intraductal component, which commonly shows cribriform appearance but solid foci and comedo necrosis may be seen. Microcalcification are rarely seen in neoplastic glands or in stroma. Tumour cells, glands and microcytic spaces contain abundant secretion, which is usually pale pink with a vacuolated appearance. The secretion is positive with the mucicarmine and PAS stain.[12]

Ultrastructurally, secretion has been found in membrane-bound secretory vacuoles within the cytoplasm of tumour cells and in intracytoplasmic lumina. Cytologically the tumour has abundant pale to clear cytoplasm and small round nuclei. In some areas more granular eosinophilic cytoplasm is seen suggesting apocrine carcinoma. [13]

In the majority of patients secretory carcinoma has a low-grade clinical course and a favorable prognosis. Axillary nodal metastases have been described. The risk of nodal involvement is as great in children as it in adults. [5]

Surgical excision and biopsy is necessary for diagnosis of secretory carcinoma although the lesion may be suspected in a fine needle aspiration specimen[8].

Local excision is the preferred initial treatment .In postmenarchal girls wide local excision may be sufficient for small lesion but quadrantectomy may be helpful for larger tumours. Axillary dissection is indicated if there is evidence of nodal involvement[5,6].

Conclusion :

The case is first time reported in Bangladesh. Secretary carcinoma of breast is an unusual breast tumour found in childhood as will as in adult life. Prognosis of the tumours good if diagnosed early. So lump is the breast in the younger patients should be explored to have a early diagnosis & proper treatment.

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Primary Ovarian Pregnancy with Ovarian Hyper Stimulation Syndrome

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Summary :

A thirty years old married lady after ovulation induction, presented with the history of one & a half month amenorrhoea along with lower abdominal pain for four days without any per-vaginal bleeding. Her vital signs were within normal limit & uterus was of ten weeks size. Serum BhCG was high and USG revealed viable right ovarian pregnancy. Laparotomy followed by histopathology of the specimen confirmed the diagnosis.

(J Bangladesh Coll Phys Surg 2003; 21 : 46-48)

Introduction :

A case of an intact ovarian pregnancy following ovulation induction resulting, ovarian hyperstimulation syndrome is presented. Ovarian pregnancy is rare. Among all the ectopic pregnancies , it accounts 1-3% and seen in 1: 700 maternities[1]. Ovarian pregnancy may be primary or secondary. In case of primary one, it is presumed to result from the rare fertilization or trapping of the ovum within the follicle just at the time of rupture or in the process of leaving the follicle. Pregnancy then develops within a capsule of ovarian tissue with corpus luteum immediately alongside it. In case of secondary one -pregnancy is caused by an extruded tubal pregnancy becoming adherent to the surface of the ovary. Although the ovary can accommodate itself more than the tube to the expanding pregnancy, rupture or erosion at an early period (2-3 wks.) is the usual, but there are records of ovarian pregnancy continued upto term [2].

Case Report :

A 30 years old housewife, married for 2 years presented with history of amenorrhoea for one and a half months and lower abdominal pain for 4 days. She had no vaginal bleeding. About one year back she had an abortion at 1st trimester which was incomplete and required D &C. She was on ovulation inducing drugs for last 3 months.

On examination-her vital signs (Pulse-78/minute, Temperature 98.5^{0}c, Respiration 14/minute and Blood pressure –110/70 mm Hg) were within normal limit. She was not that much pale, uterus was about 10 weeks size and free. Per vaginal examination reveals very tender fornix but there was no P/V bleeding.

Beta hCG was high. Ultrasonography reveals a viable ectopic pregnancy sac in the right tubo-ovarian region. Foetal cardiac pulsation was present and gestational sac corresponds with 6 weeks & 4 days of pregnancy. Left ovary was moderately enlarged in size. No mass or cyst was found in left tubo-ovarian region. Uterus was bulky and the cavity was empty i.e. no intrauterine pregnancy. Endometrium was about 18.1 mm in thickness and has mixed echo-meaning decidual reaction. Small amount of clear free fluid was present in the cul-de-sac.

She got admitted in a private hospital on the same day of consultation and laparotomy was done under general anaesthesia through a small pfennensteil incision.

Operative findings :

There was fresh blood in the peritoneal cavity. Uterus was about 10 weeks size, homogenously enlarged. Both the tubes were apparently healthy and intact. There was no bleeding from the free ostium. Pouch of

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Doughlas and uterovesical pouch was free. Left ovary was bigger in size but to some extent congested. There was an intact pregnancy sac on the right ovary at its medial end, near the attachment of the ovarian ligament but there was an abrasion on the lower end of the prominence with oozing of blood. Resection of the pregnancy sac and reconstruction of the ovary was done by 3/0 atraumatic chromic cat gut. Then after thorough toileting of the peritonial cavity abdomen was closed in layers. Postoperative period was uneventful.

Histopathological examination of the resected specimen shows sections of the ovary with trophoblastic tissues. A corpus luteum was also seen and diagnosed as a case of ovarian pregnancy.

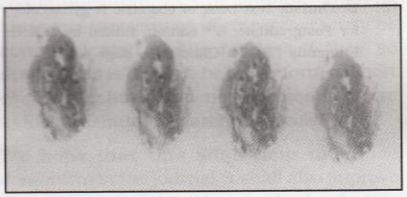

Fig.-1 : *Histological findings of ovarian pregnancy*

Discussion :

Ovarian pregnancy falls under the umbrella of ectopic or extrauterine pregnancy. Ectopic pregnancy can be diagnosed before going for laparotomy in 63% patient. Today's improved image resolution ultrasonography, its careful use and interpretation of the images and patient's acceptability of transvaginal ultrasonography (TVS) has revolutionised the correct diagnosis as many as 90%, before development of life threatening haemorrhage from rupture of the ectopic pregnancy [3-6].

Ultrasonographic finding of ovarian pregnancy includes empty uterus, intact or distorted pregnancy sac in either adnexae, cardiac pulsation may or may not be present. In the ovary formation of double or thick hyperechoic ring which is surrounded by irregular hypoechoic structure suggest ovarian pregnancy. Peritubal haemorrhage and blood clot may be present. Even then definite diagnosis is made after laparotomy/laporoscopy by varifying the Spiegelberg's criteria of ovarian pregnancy which dictates :

a) The tube and fimbrae should remain intact and seperate from the pregnancy sac on the affected side.

b) The foetal sac must occupy the position of the ovary.

c) The ovary must be connected to the uterus by ovarian ligament.

d) Definite ovarian tissue must be present in the sac wall around the pregnancy sac.

But in case of advanced ovarian pregnancy, the parenchyma of the ovary is compressed, distorted and laminated by the gradual increase in the size of the foetus and adnexae, the abscence of placenta being adherent to other organs than the ovary can be kept as a worthwhile criteria of ovarian pregnancy[7]. At operation the condition is likely to be confused with, haemorrhage from the corpus luteum of menstruation/ Pregnancy, ovulation haemorrhage, or haemorrhage in the cyst. These conditions can only be excluded by histopathology [8,9].

The reported case fulfills all the criteria of primary ovarian pregnancy. Treatment includes wedge resection of the part of the ovary containing gestational sac, leser ablation or ophorectomy. The use of methotrexate has been reported with successful results[10].

Conclusion :

Primary ovarian pregnancy is a varient of ectopic pregnancy. Pre-operative diagnosis is difficult though careful history taking and meticulous examination along with high resolution transvaginal ultrasonography may provide a near concluding diagnosis, even than laparotomy or laparoscopic procedure

followed by histopathological examination of the specimen is the final answer.

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COLLEGE NEWS

Communications

Dear Colleagues

The Editorial Board of the Journal has introduced a new column where we encourage free communications among the readers and the authors of the published articles. Opinions / comments and constructive criticisms have always been the tool of development and we expect to make use of it. Your opinion / comments and constructive criticisms are welcome and we shall make every effort to publish them in subsequent issues.

The board has also decided to publish personal communications in this column whereby ideas and innovations of researchers may be communicated to the readers if they so desire. This is likely to be in the form of short communications and not necessarily have to follow definite research protocols.

We hope that this shall help to infuse dynamism in the journal & shall also improve communications and provide for better understanding among the readers.

We look forward to your continued interest in the journal.

Editor-in-Chief

Fellowship and Membership Examinations :

The Fellowship Part-I and II and Membership examinations of the college for January 2003 has commenced on scheduled, from the 1st January 2003. As in previous years a number of senior and reputed academicians of Royal Colleges of United Kingdom, National University of Singapore and College of Physicians & Surgeons Pakistan have been invited to examine the students of the above mentioned examinations along with their Bangladeshi counterparts.

Annual General Meeting :

The Annual General Meeting of the College for 2003 will be held on 28th February at the college premises. A number of agenda along with the annual budget will be placed before the meeting.

Election of the Councillors :

Biennal election of the College to elect eight councillors will be held on the same day of annual general meeting. Fellows of the college will elect eight new councillors for coming four years. The newly elected councillors will join the existing twelve councillors to form the twenty member college council.

Publications :

I) The college council has published a pocket diary of the college for the first time. The diary has been sent to the fellows at their addresses available in the college. The fellows yet not received the diary are requested to contact with the college office.

II) The Council has decided to publish fellows directory for 2003. In this regard a prescribed form of information details has been sent to the fellows. The fellows are requested to fill up the form and send to the college within 31st January 2003.