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EDITORIAL

Antimicrobial Resistance: A Man Made Crisis

Background and Introduction

Antibiotics and similar drugs, together called antimicrobial agents, have been used for the last 70 years, since first world war to treat patients who had infectious diseases. Since the 1940s, these drugs have greatly reduced illness and death from infectious diseases. Antibiotic use has been beneficial when prescribed and taken correctly. Their value in patient care is enormous. However, these drugs have been used so widely and for so long that the infectious organisms against which the antibiotics are designed to kill, have adapted to them, making the drugs less effective. Infections caused by resistant microorganisms often fail to respond to conventional treatment, resulting in prolonged illness and greater risk of death. About 440 000 new cases of multidrug-resistant tuberculosis (MDR-TB) emerge annually, causing at least 150 000 deaths. Resistance to earlier generation antimalarial medicines such as chloroquine and sulfadoxine-pyrimethamine is widespread in most malaria-endemic countries. A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA).[1] Inappropriate and irrational use of antimicrobial medicines provide favourable conditions for resistant microorganisms to emerge, spread and persist. Resistance to antimicrobials is a natural and inevitable biological phenomenon that can be amplified or accelerated by a variety of factors and practices that facilitate " selective pressure". The microbes which adapt and survive carry genes for resistance which can be passed on to the next generation of microbes and also in some bacteria, across different species. The selection pressure is utmost when antimicrobials are used irrationally in health and veterinary sectors.[2, 3, 4]

Antimicrobial resistance (AMR) reduces the effectiveness of treatment because patients remain infectious for longer, thus potentially spreading resistant microorganisms to others. Many infectious diseases risk becoming uncontrollable and could derail the progress made towards reaching the targets of the health-related United Nations Millennium Development Goals set for 2015. When infections become resistant to first-line medicines, more expensive therapies must be used. The longer duration of illness and treatment, often in hospitals, increases health-care costs and the financial burden to families and societies. The achievements of modern medicine are put at risk by AMR. Without effective antimicrobials for care and prevention of infections, the success of treatments such as organ transplantation, cancer chemotherapy and major surgery would be compromised. The growth of global trade and travel allows resistant microorganisms to be spread rapidly to distant countries and continents.[5]

Global and Regional Status:

About 440 000 new cases of multidrug-resistant tuberculosis (MDR-TB) emerge annually, causing at least 150 000 deaths. Extensively drug-resistant tuberculosis (XDR-TB) has been reported in 64 countries to date.[6]

Resistance to earlier generation antimalarial medicines such as chloroquine and sulfadoxine-pyrimethamine is widespread in most malaria-endemic countries. Falciparum malaria parasites resistant to artemisinins are emerging in South-East Asia; infections show delayed clearance after the start of treatment (indicating resistance).[7]

A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci.[8]

Resistance is an emerging concern for treatment of HIV infection, following the rapid expansion in access to antiretroviral medicines in recent years; national surveys are underway to detect and monitor resistance.[9]

Ciprofloxacin is the only antibiotic currently recommended by WHO for the management of bloody diarrhoea due to Shigella organisms, now that widespread resistance has developed to other previously effective antibiotics. But rapidly increasing prevalence of resistance to ciprofloxacin is reducing the options for safe and efficacious treatment of shigellosis, particularly for children. New antibiotics suitable for oral use are badly needed. [10,11]

AMR has become a serious problem for treatment of gonorrhoea (caused by *Neisseria gonorrhoeae*), involving even "last-line" oral cephalosporins, and is increasing in prevalence worldwide. Untreatable gonococcal infections would result in increased rates of illness and death, thus reversing the gains made in the control of this sexually transmitted infection. There has been a substantial change in the antimicrobial susceptibility of *Neisseria gonorrhoeae.* Thirty years back, gonorrhoea used to respond effectively to penicillin. Now the resistance to penicillin and fluoroquinolones is widespread across the Region. [12]

New resistance mechanisms, such as the beta-lactamase NDM-1, have emerged among several gram-negative bacilli. This can render powerful antibiotics, which are often the last defence against multi-resistant strains of bacteria, ineffective.

Resistance to first-line anti-TB drugs has become a concern for national TB control programmes.The population weighted mean of multi-drug resistant tuberculosis (MDR-TB) in the Region is 2.8 per cent (1.9-3.6%) among new cases and 18.8 per cent (13.3-24.3%) among previously treated cases. It is estimated that around 180, 000 cases of MDR-TB reside/occur annually in this Region with more than 80 per cent of these being in Bangladesh, India, Indonesia, Myanmar and Thailand.The drugs needed to treat MDR-TB are over 100 times more expensive than the first-line drugs used to treat non-resistant forms. In some countries, the high cost of such replacement drugs is prohibitive, with the result that some of the MDR-TB cases can no longer be treated. [13]

The generic antiretroviral (ART) drugs available in the Region are contributing greatly towards improving the survival rate of patients worldwide and in rendering HIV as a chronic but a manageable condition. Although the response to ART drugs is excellent when these are delivered at health facilities, there are reports of the emergence of resistance that is a serious cause of concern.

Resistant malaria has already become a major issue for a population of 400 million living in areas that expose them to a high risk of contracting it. Artemisinin-based combination therapies (ACT) have recently been introduced in virtually all countries in which malaria is endemic. However, surveillance data from the Thai Ministry of Public Health indicate that clinical failures of artemisinin-based therapies exist in the Thai-Cambodian border, whereas efficacy with artesunate-mefloquine along the western borders of Thailand remains high. [14]

Pentavalent antimonials (SbV) have been successfully used for treatment of kala-azar since the last six decades. Since the 1970s, however, their conventional dosages have failed to achieve the desired results with 60 per cent unresponsiveness being reported with the WHO regimen in Bihar (India). Pentamidine initially used as a second-line drug, acquired resistance (25%) even with prolonged dosage. The newer oral drug, miltefosine is a potent antileishmanial drug with a longer half-life, a property likely to delay resistance. The evolution of resistance to this drug will cause havoc to the regional efforts to combat this disease. [15]

Cholera bacilli have acquired resistance to a number of antimicrobials. The resistance spectrum varies in different locales. In areas around New Delhi (India) extensive resistance to furazolidone, co-trimoxazole and nalidixic acid has been noted while tetracycline has remained effective. On the other hand, in Bangladesh, tetracycline resistance has been found to be frequent in prevalent *Vibrio cholera*.[11]

Streptococcus pneumoniae is the most common causative agent of pneumonias in children and adults in Asia. Till the1980s, almost all isolates of this organism used to be susceptible to penicillin. In 2006, in a hospital in Thailand, almost 69 per cent isolates of this bacterium were found to be penicillin resistant. [16,17]

Typhoid and paratyphoid fever continue to be important causes of illness and death, particularly among children and adolescents in the SEA Region where this disease is associated with poor sanitation and unsafe food and water. Shortly after the emergence of multidrug-resistant *S.* Typhi in this Region, case fatality rates approaching

10 per cent (close to 12.8% recorded in pre-antibiotic era) were reported.[18]

More than 50 per cent isolates of *Staphylococcus aureus* in hospital settings are now methicillin resistant. In a study undertaken in a 1000 bedded hospital in Thailand, 48 per cent patients with bacteraemia due to resistant *S. aureus* died. Methicillin-resistant *S. aureus* (MRSA) is a major problem in hospital-associated infections in almost all countries in the SEA Region.[19]

Multiresistant klebsiellae, *Pseudomonas* and *Acinetobacter* species have given new dimensions to the problem of hospital-associated infections. *A. baumannii* has become an important pathogen in intensive care units. In a study done in Thailand, mortality in admitted patients due to imipenem-resistant *A. baumannii* was 52 per cent as compared to 19 per cent in those who were infected with the sensitive variant. Presence of a drug resistant gene $bla_{\text{NDM-1}}$ in several members of the family *Enterbacteriaceae* has given rise to organisms that are resistant to a large number of commonly used antimicrobial agents.

Several salmonellae were isolated from chicken carcasses imported into Bhutan, 40 of 42 *Salmonella enteritidis* exhibited resistance to more than 2 drugs. From clinically healthy cows in Thailand, 68 per cent of isolates of *S. enterica* were resistant to at least one antimicrobial and 6 per cent were multiresistant. A spread of multiresistant *S. schwarzengrund* from chickens to humans in Thailand and from imported Thai food products to persons in Denmark and the United States has been well documented. [17,18]

Causes of AMR

Inappropriate and irrational use of medicines provides favourable conditions for resistant microorganisms to emerge and spread. For example, when patients do not take the full course of a prescribed antimicrobial or when poor quality antimicrobials are used, resistant microorganisms can emerge and spread. [19, 20, 21]

Underlying factors that drive AMR include:

- inadequate national commitment to a comprehensive and coordinated response, ill-defined accountability and insufficient engagement of communities;
- weak or absent surveillance and monitoring systems;
- inadequate systems to ensure quality and uninterrupted supply of medicines
- inappropriate and irrational use of medicines, including in animal husbandry:
- poor infection prevention and control practices;
- depleted arsenals of diagnostics, medicines and vaccines as well as insufficient research and development on new products.

Policy to combat AMR:

The emergence of AMR is a complex problem driven by many interconnected factors; single, isolated interventions have little impact. A global and national multi-sectoral response is urgently needed to combat the growing threat of AMR. [21,22]

WHO is engaged in guiding the response to AMR through:

- policy guidance, support for surveillance, technical assistance, knowledge generation and partnerships, including through disease prevention and control programmes;
- essential medicines quality, supply and rational use;
- infection prevention and control;
- patient safety;
- laboratory quality assurance.

WHO has selected combating antimicrobial resistance as the theme for World Health Day 2011. On this day, WHO issues an international call for concerted action to halt the spread of antimicrobial resistance and recommends a six-point policy package for governments.

WHO calls on all key stakeholders, including policy-makers and planners, the public and patients, practitioners and prescribers, pharmacists and dispensers, and the pharmaceutical industry, to act and take responsibility for combating antimicrobial .

Partners in AMR activities

Some organizations are engaged in several areas of prevention and containment of antimicrobial resistance. A synergy between these can yield better results.

Some of the active organizations with their networks spread over several countries are:

International Network on Rational Use of Drugs (INRUD)

ReAct
INDEPTH

Alliance for Prudent Use of Antibiotics (APUA)

Health Action International (Asia Pacific): HAIAP

GARP

The Member States in SEAR where some of these networks are active include Bangladesh, India, Indonesia, Maldives, Nepal and Thailand.

Research needs and perspectives for Antimicrobial Resistance

The issue of antimicrobial resistance requires research in following categories

- Basic research to bridge knowledge gap.
- Clinical/translational research to put new products into the health system.
- Operational/health systems research to convert information/knowledge into action.

Basic research in the following areas will benefit global efforts against antimicrobial resistance:

- Deciphering microbial genomics.
- How do the microbes cause disease?
- Ascertain dynamics of spread.
- Mechanism of antimicrobial resistance.
- Impact of agricultural/veterinary use.
- Discovery of new drug targets.
- Develop better diagnostics (viral vs bacterial).
- New vaccines.

Operational research on the following subjects is needed:

- Monitoring methodologies for antimicrobial resistance.
- Collect systematic data on compliance and proper public use.
- Understand impact of resistance on illness and economy.
- Determine factors that influence prescription habits.
- Elucidate behavioral aspects about self-medication and adherence and develop interventions to bring about change towards rational use.

The WHO Regional Strategy on Prevention and Containment of Antimicrobial Resistance and the initiative taken by the WHO Regional Office for South-East Asia. The following recommendations were made:

For the World Health Organization, WHO should:

1. Undertake advocacy with national authorities to establish national alliances against antimicrobial resistance;
2. Develop and disseminate generic protocols to facilitate generation of comparable epidemiological data on antimicrobial resistance and utilization of antimicrobials;
3. Facilitate cooperation between various players (government agencies, professionals, academia, NGOs, INGOs etc.) to enhance synergy between their actions and to obviate duplication of efforts;
4. Develop generic IEC material to create awareness amongst communities and obtain their active participation in the fight against AMR;
5. Through its WHO Collaborating Centre on AMR, collate and share global data and regional experiences on all aspects of antimicrobial resistance; The WHO CC should be supported to act as a Regional Clearing Centre and to coordinate multicentric studies in the Region.
6. Document and disseminate experiences gained within the Region and lessons learnt in combating AMR;
7. Support operational research on various aspects of antimicrobial resistance; and
8. Organize regional meetings on a regular basis for exchange of experiences within the Region.

For Member States in the South-East Asia Region Member States should:

1. Establish a national alliance against antimicrobial resistance with all key stakeholders as its members. The implementation of national efforts to prevent and contain antimicrobial resistance should be through a multisectorial national steering committee headed by the senior-most health executive and facilitated through advisory/ expert groups.
2. Designate a national focal point for antimicrobial resistance in the Ministry of Health.
3. Institute appropriate surveillance mechanisms in the health and veterinary sectors to generate reliable and actionable epidemiological information including baseline data and trends on antimicrobial resistance, utilization of antimicrobial agents and

impact on the economy and health through designated national and regional reference centers

4. Discourage non-therapeutic use of antimicrobial agents in veterinary, agriculture and fishery practices as growth-promoting agents.
5. Develop national standard treatment and infection control guidelines and ensure their application at all levels of health care and veterinary services through training, continuous educational activities and establishment of functional drugs and therapeutic committees and hospital infection control committees in health facilities (with the focus on proven, cost-effective interventions such as isolation, hand washing etc.).
6. Undertake operational research for better understanding of the technical and behavioral aspects of prevention and control of antimicrobial resistance and utilize the outcomes of these research studies/interventions in policy and programmer development/ improvement in the national context.
7. Launch educational and awareness programmers for communities and different categories of health care professionals.
8. Strengthen communicable diseases control programmers to reduce disease burden and accord priority to the discipline of infectious diseases in medical education and health services.

Recommendations and conclusions

Several issues hamper the prevention and containment of antimicrobial resistance and the efficacy of these drugs to maintain their "wonder" status.

Some of these are neglected problem with a profound impact on health and economy; inadequate visibility at decision-making level, lack of education amongst prescribers and users, weak collaboration between stakeholders; poor or no systematic surveillance of resistance and consumption of antimicrobial agents', ineffective regulatory mechanism; lack of economic potential for pharmaceuticals to invest in development of new drugs; and abysmal infection control practices.[4]

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Rising Trend of Caesarean Section in a Tertiary Hospital Over a Decade

R NAZNEEN[a], RA BEGUM[b], K SULTANA[c]

Abstract:

Background information: *Since the early 1990s, emergency obstetric care (EmOC) in Bangladesh has played important role to reduce the maternal mortality rate. Along with other indicators of improved maternal care, there is a trend of rising caesarean section rates over the last decade affecting the economy of the country. According to demographic and Health Surveys conducted between 1993 and 2004, rate of caesarean section has risen from 2% to 6% which is more pronounced in urban area.*

Objective: *To assess the indications and the trends of caesarean sections done over a 10-year period from 1995-2004.*

Study Design: *A retrospective observational study of the cases of caesarean sections over a decade.*

Study setting: *Holy Family Red Crescent Medical College Hospital.*

Results: *23748 women were admitted in department of Obstetrics and Gynacology. Total deliveries were 21149(89.05% of total admission). The caesarean birth rate increased from 45.85% to 70.55%. The indications varied a little in cases of malpresentation and eclampsia. APH and IUGR has risen a little (from 2.56 to 2.6 to 1.83 to 2.34%) respectively. But proportion of repeat caesarean section and that of presumed foetal distress (or less foetal movement) increased (from 25.99 to 31.45% and from 8 to 15%), recently the indication, as maternal choice is also coming up (from .43 to .8%). The proportion has fallen in prolonged labour for cervical dystocia (from 17 to 2.6%) and obstructed labour (from 4.6% to .36%). The data were compared and analyzed by Z Test and corresponding P value was calculated which was not significant.*

Conclusion: *Though caesarean section is a very safe intervention in obstetrics at present, crucial evaluation of the indications is advocated to reduce the rates of caesarean secion.*

Keywords: *Caesarean section rates, Indications.*

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Introduction:

Caesarean section rates have increased very rapidly over the past two decades both in developing and the developed countries[1]. The rates increased from 18% in 1997-1998 to 22% in 2000-2001 in England[2], from 10.7% in 1981 to 15.3% in 1995 in France[3] and from 5% in 1973 to 15% in 2000 in Sweden[4]. Although stable for more than 15 years, the rate is still high at 26.1% in 2002, in the United States[5]. This epidemic has also extended to the developing countries. Twelve Latin American countries have rates above 15%, with a highest rate of 40%[6].

This continually rising caesarean birth rate is of increasing concern to both the professionals [7, 8] and the public.[9] Over the last 30 years, there has been a public health concern about increasing Caesarean section rates. In 1985, the World Health Organization issued a consensus statement suggesting there were no additional health benefits associated with a Caesarean section rate above 10 to 15%[10]. This also have generated wide spread concern and attempts to stop the reason to reduce this rate [11, 12, 13]. There are strong economic arguments for reduction of the rates[14]. Since early 1990s, emergency obstetric care (EmOC) in Bangladesh has improved to reduce the maternal mortality ratio. Along with other indicators of improved maternal care , there is a trend of rising caesarean section rates over the last

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decade affecting the economy of the country. According to demographic and Health Surveys conducted between 1993 and 2004, rate of caesarean section has risen from 2% to 6% which is more pronounced in urban area. In addition deficiency of adequate and efficient health care facilities in the rural settings increases the number of referral to the tertiary care centers. Analysis of the indications of these caesarean sections will reflect the causes of this increasing trend [15].

Objectives:

- To assess caesarean section rates over the past decade.
- To find out the indications of caesarean section.
- To compare between the rates of Caesarean section.

Materials and methods:

It is a retrospective study of all the cases of caesarean sections over the decade done in Holy Family Red Crescent Medical College Hospital. Data of all deliveries from 1995 to 2004 were collected from the yearly statistical record book produced annually by the department and the hospital. Patient's individual data were collected from the hospital record room. This included total obstetric admission, total numbers of vaginal deliveries, instrumental deliveries, caesarean sections, their indications for admission and caesarean section were noted. The major contributing factors were compared and their proportions were calculated. When two or more contributing factors were present only one major indication was taken. The rising trends were shown in graph. The data were compared between 1995 to1999 and between 2000 to 2004. Then Z Test was done for statistical analysis. Corresponding P value was calculated from the Tables.

Inclusion and exclusion criteria:

Figures contributing to a significant share in the indications of caesarean sections were included in the study. The rare and minor data were omitted.

Results:

The causes of caesarean sections were compared and shown in the tables and graphs. Table I shows that, total 23748 women were admitted in the obstetric unit over the decade. Numbers of the total deliveries were 21149 which comprised about 89% of total admission. The caesarean birth rate increased from 45.8% to 70.5% of total deliveries from 1995 to 2004. Spontaneous vaginal deliveries were reduced from 54.1% to 29.4%. **T**able II shows that, major indications of caesarean sections, which varied a little in cases of malpresentation but proportion of repeat caesarean section increased from 25.9% to 31.4% and that of presumed foetal distress (and reduced foetal movement) from 8.3% to 15%. Recently the indication as maternal choice is also rising up (from .4 to .8%). The proportion has been fallen significantly in prolonged labour for cervical dystocia (from 17.1 to 2.6%) & obstructed labour (from 4.6 to .4%). Proportion of IUGR has risen a little (from 1.8 to 2.3%) and that of post dated pregnancy from 1.8 to 2.8%. Percentage of APH remained unchanged (2.6%). Percentage of CPD and Eclampsia has fallen from 6.9 to 4% and .8 to .6% respectively over the years. Table III shows the comparative study of the total Caesarean sections and some important indications with their probability tests.

Figure 1a, shows the percentage of caesarean section rising from 45.8% in 1995 to 70.1% in 2004. Fig.-1b shows the percent of C/S due to presumed foetal distress was highest in 2000 and 2002 (18%) and lowest in 1997 (6.5%). Fig.-1c shows the percentage of caesarean section due to repeat C/S was lowest in 2001 (17.2%) and highest in 2004 (31.4%). Fig.-1d shows the

percentage of C/S due to IUGR was lowest in 1999 (1.5%) and highest in 2000 (4.2%).

Table-IV shows, the proportion of patients which contributes to caesarean section. This assessment form is adopted internationally and is known as 10 group classification of Caesarean section[10]. It shows, the more caesarean sections performed in group 1 and 2 are likely to result in a larger group 5 in future if those women have further pregnancies. That means occurrence of increased caesarean sections in first pregnancies will result in increased number of repeat sections in the subsequent pregnancies which actually happened in our cases.

The data of 2004 was taken for assessment in 10 group classification for cesarean section in our setting. The overall caesarean section rate was 70.5%. Out of these 5% were with spontaneous labour at term in first pregnancy; 4.3% were with spontaneous labour at term in their subsequent pregnancies; 22.15% were with repeat section at term; 14.46% were in subsequent pregnancies at term either induced or elective caesarean section. Primi breech was 1.6%, Multiparous breeches were 1.3%, abnormal lie were 2.4%, pregnancies at or above 36 weeks including previous caesarean section were 2.3%.

Table-I

Cumulative basic data from 1995 to 2004.
Values are shown as n (numbers), and figure in parenthesis shows the percentage.

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	Total
Total Obstetric cases	2285	2391	2646	2707	2239	2445	2404	1992	2255	2384	23748
Total deliveries	2257	2149	2356	2413	2213	2193	2060	1795	1777	1936	21149
Spontaneous vaginal Delivery %	1222 (54.1)	1028 (47.8)	1125 (47.7)	1155 (47.9)	987 (44.6)	802 (36.6)	693 (33.6)	571 (31.8)	611 (34.3)	569 (29.4)	8763
InstrumentalVaginal deliveries	13 (6)	7 (3)	7 (3)	9 (4)	3 (1)	7 (3)	2 (1)	0	2 (1)	1	51
Caesarean section%	1035 (45.8)	1123 (52.3)	1224 (52)	1249 (51.8)	1226 (55.4)	1392 (63.4)	1367 (66.3)	1224 (68.1)	1224 (68.8)	1366 (70.5)	12430

Table I - Shows that, out of 21149 deliveries, Cesarean section was 12430 that is almost 59% of total deliveries. It increased from 45.8% to 70.5% over the decade.

Table-II

Major Indications of Caesarean sections (C/S). Values are shown as n (numbers) and figure in parenthesis shows the percentage.

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Total C/S (%)	1035 (45.8)	1123 (52.2)	1224 (51.9)	1249 (51.8)	1226 (55.4)	1392 (63.5)	1367 (66.3)	1224 (68.1)	1224 (68.3)	1366 (70.1)
Repeat C/S	269 (25.9)	255 (22.7)	297 (24.2)	295 (23.6)	274 (22.3)	345 (24.8)	236(17.2)	293(23.9)	374(30.5)	429(31.4)
PET	131 (12.6)	102 (9.0)	222 (18.1)	233 (18.6)	149 (12.1)	212 (15.2)	298(21.7)	90(7.3)	133(10.9)	107(7.8)
Foetal distress	86 (8.3)	110 (9.8)	80 (6.5)	90 (7.2)	152 (12.4)	249 (17.9)	130(9.5)	220(18)	161(13)	205(15)
Prolong labour	36 (3.4)	29 (2.5)	59 (4.8)	58 (4.6)	60 (4.8)	63 (4.5)	74(5.4)	74(6.0)	27(2.2)	64(4.6)
Breech	41 (3.9)	55 (4.9)	63 (5.1)	61 (4.8)	100 (8.1)	70 (5.0)	45(3.3)	44(3.6)	21(1.7)	57(4.1)
Failed induction	38 (3.6)	76 (6.7)	56 (4.5)	46 (3.7)	47 (3.8)	74 (5.3)	33 (2.4)	61(5)	12(1)	37(2.7)
Cervical dystocia	177 (17.1)	121 (10.7)	69 (5.6)	55 (4.4)	12 (1)	16 (1.1)	108(7.9)	53(4.3)	33(2.7)	36(2.6)
PROM	23(2.2)	14(1.2)	17(1.3)	9(0.7)	21(1.7)	12(0.9)	31(2.2)	12(0.1)	19(1.5)	36(2.6)
IUGR	19(1.8)	23(2.0)	30(2.4)	26(2.0)	19(1.5)	58(4.1)	36(2.6)	33(2.7)	30(2.4)	32(2.3)
Obstructed. Labour	48(4.6)	31 (2.7)	22(1.7)	50(4)	40(3.2)	42(3.0)	24(1.7)	33(2.7)	3(0.2)	5(0.4)
Eclampsia	9(0.8)	17(1.5)	20(1.6)	19(1.5)	9 (0.7)	5(0.3)	12(0.9)	11(0.9)	6(0.5)	9(0.6)
APH	27(2.6)	12(1.0)	16(1.3)	29(2.3)	31(2.5)	36 (2.5)	25(1.8)	25(2.0)	27(2.2)	35(2.6)
CPD	72(6.9)	85(7.5)	83(6.8)	90(7.2)	94(7.7)	74(5.3)	62(4.5)	62(5.0)	52(4.2)	55(4.0)
Post Dated Pregnancy	19(1.8)	16(1.4)	23(1.8)	29(2.3)	22(1.8)	17(1.2)	32(2.3)	27(2.2)	37(3.0)	38(2.8)
Maternal choice	_	_	_	_	_	6(.4)	6(.4)	9(.7)	10(.8)	11(.8)

*PET- pre eclampsia, PROM- Prelabour rupture of membran, IUGR- Intra Uterine Growth Retardation, APH- Ante Partum Haemorrhage, CPD- Cephalo Pelvic Disproportion.

Table-III

Comparative study of the total C/S & some indications of C/S between 1995-1999 & 2000-2004

Parameter	1995-1999 (mean)	2000-2004 (mean)	Z Value (<1.96)	P Value (>.05)
Total C/S	1171.7	1314.6	1.84	
Repeat C/S	278	335.4	1.39	
C/S done for PET	167.4	168	.009	>0.05
C/S done for Post dated pregnancy	21.8	30.2	1.39	(Not significant)
C/S done for Foetal distress	103.6	122	0.39	
C/S done for Prolonged labour	48.4	60.4	.786	
C/S done for Obstructed labour	38.2	21.4	1.30	

Comparison of the above data showed that the value of z is not significant (<1.96), corresponding P value is >0.05 (not significant).

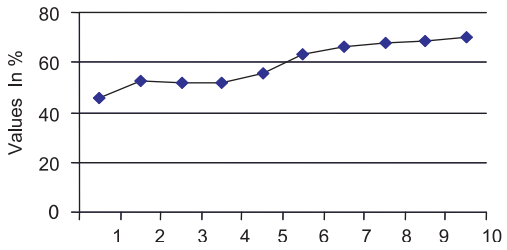

Fig.-1a : *Comparative study of the Percentage of total no. of C/S from 1995-2004.*

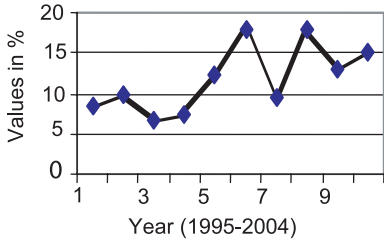

Fig.-1b: *Comparative study of the Percentage of C/S from presumed Foetal distress (1995-2004).*

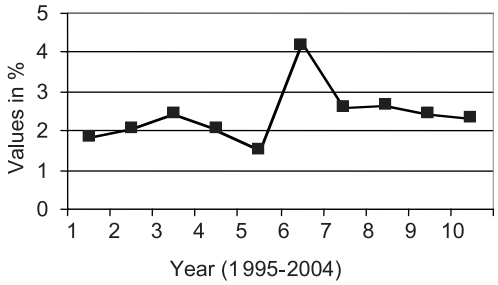

Fig.-1c: *Comparative study of the % of C/S due to IUGR (1995-2004).*

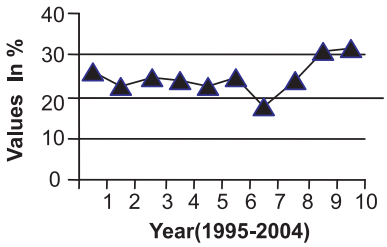

Fig.-1d: *Comparative study of the % of repeat C/S (1995-2004).*

Table-IV

Overall Caesarean Section (CS) rate (%)-1366/1936=70.55%

		No. CS over total No. Women in each group	Relative size of groups (%)	CS rate in each group (%)	Contribution made by each group to the overall CS rate of %
1.	Nulliparous, single cephalic, ≥ 37 weeks, in spontaneous labour	98/233	12% (233/1936)	42.06% (98/233)	5.06% (98/1936)
2.	Nulliparous, single cephalic, ≥ 37 weeks, induced or CS before labour	303/438	22.60% (438/1936)	69.17% (303/438)	15.65% (303/1936)
3.	Multiparous (excluding previous CS), single cephalic, ≥ 37 weeks, in spontaneous labour	84/348	17.97% (348/1936)	24.13 (84/348)	4.33% (84/1936)
4.	Multiparous (excluding previous CS), single cephalic, ≥ 37 weeks, induced or CS before labour	280/544	28.09% (544/1936)	51.47% (280/544)	14.46% (280/1936)
5.	Previous CS, single cephalic, ≥ 37 weeks	429/501	25.87% (501/1936)	85.62% (429/501)	22.15% (429/1936)
6.	All nulliparous breeches	31/43	2.22% (43/1936)	72.09% (31/43)	1.60% (31/1936)
7.	All multiparous breeches (including previous CS)	26/57	3% (57/1936)	45.61% (26/57)	1.34% (26/1936)
8.	All multiple pregnancies (including previous CS)	23/31	2% (31/1936)	74.19% (23/31)	1.18% (23/1936)
9.	All abnormal lies (including previous CS)	47/47	2% (47/1936)	1% (47/47)	2.42% 47/1936)
10.	All single cephalic, ≥ 36 weeks (including previous CS)	45/142	7% (142/1936)	31.69% (45/142)	2.32% (45/1936)

The 10 Group classification in 2004, Holy Family Red Crescent Medical College Hospital.

Discussion:

During the decade there was around 24.7% increase in the caesarean section rates in our setting which is comparable with an study done in our country[15]. Regarding the other findings, rate of instrumental deliveries decreased from 13 to 1 (.6% to 0%) which explains the rising trends of the caesarean sections. Yet this is becoming increasingly safe for women and children. The rate of pelvic floor problems (particularly urinary incontinence) is substantially higher in women who had vaginal deliveries than in women who had caesarean sections [16, 17, 18]. Although this evidence is discussed in the context of elective caesareans, it can be seen as challenging the professional perspective on the risk-benefit ratio for caesarean sections compared with vaginal delivery for specific indications[19]. Caesarean sections do involve certain risks, but the operation is much safer than in previous years. At the same time, the increased awareness of the complications of the vaginal delivery[20] and the increase in women's dissatisfaction with long labours of vaginal delivery have resulted in obstetricians having a lower threshold for advising delivery by caesarean section-[21-22]. In recent years, the incidence of Caesarean section for maternal request is gradually rising. Whether or not a Cesarean section should be carried out on a request is yet a controversial issue[23].

Studies shows that maternal request was one of the main indications for C/S (23%) in 1996[24]. Defensive

obstetrics is another common reason for high rates of caesarean section. It has been observed that 82% of physicians performed C/S to avoid negligence claims[25]. Repeat caesarean sections contributed 29%, presumed foetal distress contributed 22%, failure to progress in labour contributed 20%, 88% of breech babies, low birth weight 39%, and maternal choice **(**7%).

Other studies showed, the main indications of caesarean section were, repeat caesarean section (34.3%) , failure of progress (19.3%) and fetal distress 12.9% [23], another study done in our country showed repeat caesarean section decreased about 2.95% over the period of 8 years[15] . In our study the rate actually increased because the same patient attends the hospital for her successive deliveries. The rate of foetal distress and malpresentation in the same study showed a little increase (3.79% and 2.53% respectively) and considerably greater increase in caesarean section done for obstructed labour and eclampsia (2.79% , 3.75% respectively). But our study showed considerably greater increase in foetal distress and malpresentation (6.7%, .2%) and a decrease in obstructed labour and eclampsia (4.2%, .2%). The reason for this difference is the socio economical status of the patients attending both the settings. But overall there has been an increase in the rate of cesarean section in many countries of the world. The rising number of indications for cesarean section, the use of fetal monitors, the current medico-legal climate, and the indications for performing caesarean section has changed a lot in recent years and keep on changing for varied circumstances. Most caesarean section is currently performed to benefit the fetus, not the mother. This study was done to compare the changes in rates of caesarean section with a view to analyze and reduce the rates if possible. Although the reasons are multifactorial in most of the cases, and also the number of referral and workload pattern of the tertiary hospital, as well as the socio economical status of the patients , their demands for the service are the important factors for consideration, the findings of this retrospective study suggests that the rate of the caesarean section could be reduced in certain categories of patients.

The 10 group classification is currently being used internationally[10], and provides helpful information in the assessment of the causes of caesarean section rates. We have taken the data of 2004 for comparison. Unnecessary interventions in group 1 and 2 should, preferably be avoided. In '10 group classification', it has been shown that the category of pregnancy, the previous obstetric record of the woman, the course of labour and delivery, and the gestational age of pregnancy can add to the incidence of caesarean section. From these concepts and their parameters, the 10 groups were formed. Monthly critical analysis of these 10 groups is required including comparison with previous months in the same units and also in other units helps in analyzing the outcomes.

It is observed that the overall percentage of caesarean section has risen up. This could be due to the fact that more referral cases are appearing in commencing years. Also the less complicated population is being diverted elsewhere in nearby more inexpensive settings.

Conclusion and recommendations:

Caesarean section is undoubtedly a very safe intervention in obstetrics now a days. But yet, there is some morbidity even in tertiary care hospitals. With the advent of modern techniques of the procedure and also the safer anaesthesia, rates of caesarean sections has raised. More over patients with a previous caesarean sections are more likely to undergo a repeat section in the subsequent pregnancies mostly due to safety issues. As a result we have to perform a 3rd or 4th caesarean section which certainly carry a high morbidity risk. Also from the 10 group classifications we can categorize the cases which might undergo a caesarean section. So the situation definitely calls for an evaluation to catch hold the string of this rising trend.

Indications for doing caesarean section should be very cautiously evaluated. Mothers who opt for caesarean section just for their will needs be counseled properly. Labour analgesia also needs to be improved. Minimization of the costs of delivery can have a positive impact on the consumers. Trial for vaginal birth after caesarean section can also reduce the rate of repeat caesarean section, especially in tertiary care settings under proper vigilance. Periodic caesarean section evaluation sessions need to be more critically analyzed.

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Limitations of the study:

The study was a retrospective one and some of the indications did not reveal the actual proportion since only the main indication was documented out of multiple reasons for doing the operations. Also new tables regarding the complications of cesarean sections could not be given due to lack of raw data.

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Need Assessment for an Adolescent Clinic in a Periurban Hospital

S TASNIM

Abstract:

Background: Adolescents are a heterogeneous group with special reproductive health needs based on their age, sex, marital status and socioeconomic status. Existing health care system is not capable to respond to adolescents' demands.

Objective: To explore the idea regarding specific centre for adolescents and to identify the components of information and health services rendered through the centre.

Method: A cross sectional study was conducted with 70 participants in a half day workshop in the Institute of child and mother health (ICMH) on 9th August' 2006. The respondents filled up a set questionnaire containing both open and closed questions focusing different issues regarding functioning of an adolescent clinic. The responses were analysed using SPSS program

Result: Almost all respondents expressed the need for a separate clinic for adolescents, that should serve both boys and girls (84.3%), health providers at the centre should be doctors from both Paediatrics and Gynae & Obstetrics department (42.9%) and nurses (42.1%) and the working schedule should be similar to existing out patient hours. It was suggested that the clinic should provide counseling on sexuality issues, contraceptive services and special services as required in addition to general health care. About 75% opined that the cost of the services should be same as those of existing out patient services while 52.9% thought that the services should be free.

Conclusion: The need for an adolescent clinic was commonly felt and it is recommended to establish adolescent friendly services at ICMH.

Key words: Adolescent, Reproductive health, Adolescent friendly service

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Introduction:

Adolescents are between 10 to 19 years and in a transition of physical, mental and social development towards adulthood. They have special needs that will vary with their sex, stage of development, life circumstances and the socioeconomic condition of their environment[1]. Adolescents begin to experience new ideas, relationships and life styles. As they mature they are increasingly exposed to reproductive health risks such as sexually transmitted infections, unintended pregnancies and complications from pregnancy and childbirth[2] . It is necessary to provide care and support to them to cope up with the changes. They need proper guidance to become knowledgeable, confident and skilled to overcome the problems and develop as adults

International Conference on Population Development (ICPD) declaration states that countries must ensure that the programs and attitudes of health care providers do not restrict the access of adolescents to appropriate services and the information they need, including sexually transmitted diseases and sexual abuse. These services must safeguard the rights of adolescents to privacy, confidentiality, respect and informed consent, respective cultural values and religious values[3] .

In traditional society of Bangladesh sexuality is regarded as a private matter and often deliberately ignored to be discussed. It is difficult to obtain information on sexual behavior and practices specially those of unmarried adolescents. However, knowledge gap on reproductive health issues among adolescent was revealed in different studies[4-7]. As a consequence of the ignorance, adolescents may fail to protect themselves from unwanted and unsafe sexual practice[5]. It is well known that adolescents have limited access to reproductive health information and services[8,9]. However, parents, religious and other community leaders supported the idea of reproductive health education in the school curriculum[8]. The adolescent themselves express the need to include reproductive health information in the school curriculum[6,10] .

Adolescent reproductive health represents an area of tremendous unmet need worldwide. Existing health care system usually defers to respond to the reproductive health need of adolescent as social entity. They frequently fail to provide adolescents with specialized reproductive health information, counseling and services[1]. Lack of experience in social negotiation ,

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ignorance about their bodies and where to seek care, social stigma and poor treatment by providers often limit young peoples' access to services they need[11] . An adolescent's clinic is such that will attract, serve and retain adolescents for reproductive health needs[12].

A need assessment survey was done to explore the idea regarding a specific health centre for adolescents, to identify specific information and service areas and options for its implementation.

Method:

This was a cross sectional descriptive study with 70 participants conducted at Institute of Child and Mother health (ICMH). A half day workshop was arranged on 9th August '2006 where faculty members and junior doctors of Obstetrics & Gynecology, Paediatrics and allied specialty of ICMH participated. At the beginning a presentation was made by the researcher addressing a brief overview of adolescent reproductive health, characteristics of adolescent friendly services and gaps in providing the services. The potentials of establishing an adolescent clinic at ICMH was discussed in the workshop. The respondents filled up a self administered questionnaire consisting both open and closed questions focusing different issues regarding functioning of an adolescent clinic. Opinion of some nurses and adolescents were also collected through same questionnaire in a separate session. The responses were analysed using SPSS program.

Result:

The respondents were faculty members (12), junior doctors (28), nurses (20) and adolescents (10). The need for an adolescent clinic at the institute was expressed unanimously. They opined that it should serve both boys and girls (84.3%), remain open 6 days a week (54.3%), and (47.1%) said working hour should be same as the existing outdoor schedule (Table-I). Nearly half of them (42.9%) said that doctors from both Gynae and Paediatrics department and nurses should serve in the clinic (Figure-1).

Majority suggested that the clinic should provide general health care, pregnancy related care, counselling and communication on sexuality issues and 55.7% said that there should be provision for distribution of condoms (Table-II). Counseling topics as expressed were physiological changes of puberty, contraception, sexually transmitted infections, consequences of early marriage and pregnancy, substance abuse and adolescent rights (Table-III). To promote use of the clinic it was recommended to arrange health camps in local school and colleges (92.9%), distribution of leaflets (82.9%),

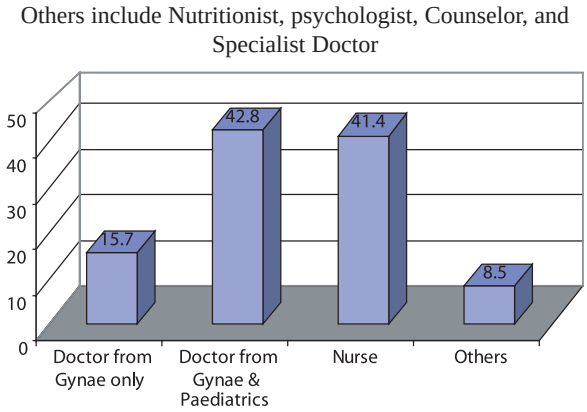

Fig.-1: *Percent distribution according to opinion regarding who should provide services in the adolescent clinic (n=70)*

and (71.4%). suggested making signposts in the hospital (Table-IV). Major constrains for establishing the clinic were shortage of manpower (47.1%), adolescents' unwillingness to attend the clinic (41.4%) and 47.4% thought it will be an extra burden for health care providers (Figure-2). About 75% opined that cost of services should be in accordance with the existing system of payment at outdoor, while 52.9% and 34.2% thought the consultation and any service required should be free respectively (Table-V).

Table-I

Distribution according to opinion regarding the characteristics of adolescent clinic in terms of providing services (n= 70)

Characteristics	Percentage
Beneficiaries at the adolescent clinic	
Adolescent boys only	0
Adolescent girls only	15.71
Both	84.28
Days the clinic should work in a week?	
One	25.71
Two	24.28
Daily (Six days)	54.28
For how many hours the clinic should work in a day?	
Same as existing OPD hours	47.14
2 hours in a day	11.42
4 hours in a day	30
What should be the timing of the clinic?	
Same as existing OPD hours	58.57
From 9-11 am	21.42
From 11-1.00 pm	5.7
From 2-3 pm	5.7

Table-II

Distribution according to opinion regarding type of services that should be provided in the clinic (n= 70)*

Characteristics	Percentage
Measurement of height	94.28
Measurement of weight	91.42
Clinical examination for anaemia/ malnutrition	94.28
T. T immunization	94.28
Distribution of anthelminthic	84.28
Antenatal care	85.71
Postnatal care	84.28
Reproductive health education session	91.42
Post abortion care	84.28
Treatment of infection and diseases	82.85
Contraceptive advise	84.28

Table-III

Distribution according to opinion regarding counseling issues in the clinic (n= 70)

Characteristics	Percentage
Physical change during Puberty	98.57
Mental changes during adolescence	91.42
Menstruation	100
Masturbation	75.71
Night emission	78.57
Conception	94.28
Contraception methods/ Emergency contraception	88.57
Violence	82.85
Sexually transmitted infection & HIV/ AIDS	98.57
Substance abuse (Cigarette, alcohol, drugs)	85.71
Danger sign of pregnancy	100
Consequences of early marriage and adolescent pregnancy	95.71
Adolescent rights	82.85
Nutrition	87.14
General hygiene	98.57
Sign symptoms of pregnancy	87.14
Others (ideal marital age etc)	31.42

*Multiple response

Table-IV

Distribution according to opinion regarding measures to be taken to increase the utilization of the clinic (n= 70)

Activity	Percentage
Making sign posts in the hospital	71.42
Arranging health camps in adjacent schools/College	92.85
Arrange a rally	51.42
Distribution of leaflet to parents, school teachers	82.85
Others (Give monthly magazine, extension of the clinic subsequently, adverting in media.)	37.14

*Multiple response

Table-V

Distribution according to opinion regarding the financial implication of its services (n= 70)

Cost of services at the clinic	
Consultation should be free	52.85
Existing system of paying for OPD tickets & Pathology	74.28
Iron, Folic Acid, Anthelminthic should be free supply	77.14
Any service required should be free of cost	34.28

*Multiple response

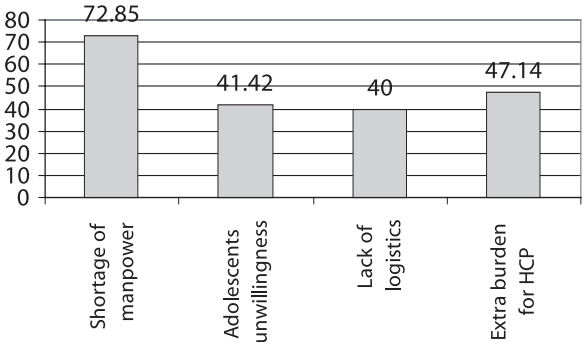

Fig.-2: *Percent distribution according to opinion regarding the limitations in establishing the clinic*

Discussion:

It was evident from this study that health care providers were well aware that adolescents are a special group and the need of separate provision to serve them was commonly felt. The idea of establishing an adolescent clinic in the outpatient department was well accepted and it was opined that both adolescent boys and girls should be served and doctors and nurses from multiple discipline should provide counseling and treatment according to individual needs through the special clinic. In another study the need of special clinic where adolescent can get information and service is a highly demanding issue that has been expressed by the adolescents themselves and their teachers[10].

Use of such adolescent clinics by the adolescents depends on various factors. Evidence shows adolescents avoid seeking reproductive health services unless confidentially is assured [13]. It is also that they do not want to expose their reproductive health problems in front of others such as in polyclinics where services are tailored to adults[14]. In a study from South Africa the young respondents expressed that the most important factor influencing their choice of a clinic were staff attitude, clinical environment, availability of the contraceptive methods and operating hours[13]. Study have revealed that adolescents are reluctant to use health centers because there are long waiting time, often the providers are rude, judgmental and do not show respect for adolescents privacy and confidentiality[15].

In this study the health care providers and the adolescents has opined to utilize existing policy of cost recovery and timing of out patient services that need to be evaluated for feasibility after implementation . Some non government organization that provides adolescent friendly services tailors their timing as per convenience of school going or working adolescents. For example, Marie stopes society runs youth friendly health clinics that accommodate adolescents separate from adults, logs and records are kept separately and adolescent specific hours are daily after normal clinic hours, generally from 4.00 to 6.00 p,m.[16]. Under a global fund project that aims to promote involvement of youth for prevention of HIV and AIDS Government of Bangladesh has established youth friendly corners in different district hospitals and Maternal and child welfare centres that use normal out patient hours[17].

Shortage of manpower was identified as a main constraint for adolescent friendly services in this study and that was an appropriate concern. According to the national standard the providers of adolescent friendly services must have good interpersonal and communication skill, motivated to work with adolescents, supportive, non-judgmental and devote adequate time to patient[18]. So capacity building of health care providers is also a prerequisite before establishing the clinic. There is evidence that training of health care providers on youth friendly services helped them to inform adolescents about where to obtain the health care services and can also convince them that services were more geared towards their needs[19]. Although it was a small scale study but it involved different levels of health care providers and also the potential users that is the adolescents and their recommendations will be utilized to formulate an action plan for establishment of an adolescent clinic.

Conclusion:

The need for a separate service corner for adolescents was commonly felt by the health care providers as well as the beneficiaries. Specific issues for counseling and type of services to be provided through an adolescent clinic was also suggested. .It is recommended that an adolescent clinic should be established at ICMH according to the need assessment.

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Solid-Pseudopapillary Tumor of the Pancreas: Our Experience in Bangladesh

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Abstract:

Background: Solid-pseudopapillary tumors of the pancreas (SPTPs) have been reported as rare lesions with "low malignant potential" occurring mainly in young women. This study was designed to understand clinicopathological characteristics of the disease, management strategy and outcome of this rare disease in Bangladesh.

Methods: A retrospective review from January 2001 to December 2009 was performed. Clinicopathological, peroperative, postoperative and survival data were obtained from record file. Our cases were discussed in the light of published literature.

Results: During this period, 31 patients were diagnosed as having SPTPs (6.9%). Twenty-four (77.4%) females and seven (22.6%) males were identified, with a median age of 24 years (range, 14–44). The median size of the lesions was 7.0 cm (range, 4.8–18). More than 90% presented with vague abdominal pain and lump. Twenty five patients had their primary tumors within the head of pancreas, the rest were in body and tail region. A total of 30 patients presented with local disease and underwent complete resection. One patient was found to have a very large tumor in the head with vascular invasion and underwent debulking of the tumor; which clinically reappear 1 year after debulking but still alive with episodic attacks of abdominal pain. All patients are surviving till date at a follow-up of 2 months to 9 years.

Conclusions: SPTP occurs predominantly in women although it can occur in men. Young and middle aged groups are affected. Complete resection or debulking of locally invasive tumor is associated with long-term survival.

(J Bangladesh Coll Phys Surg 2011; 29: 138-142)

Introduction:

Solid pseudopapillary tumor of the pancreas (SPTP) is a rare pathologic entity with low malignant potential[1] affecting primarily young women [2]. Recently there has been a steady increase in the number of SPTP of the pancreas. Despite the increase in recognition, the pathogenesis and apparent therapeutic algorithm remain unclear. Because of vague initial symptoms the tumor becomes very large on presentation. It is often seemed to be a locally invasive tumor on clinical and imaging evaluation and label the tumor as an irresectable one. This study was designed to examine the clinicopathological characteristics of the disease, management strategy and outcome by examining our institutional experience.

Patients and Methods:

We reviewed 451 patients with pancreatic malignancy those were admitted to Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh and other hospitals in Dhaka city, and underwent pancreatic resection during 2001 to 2009. Clinico-pathological, peroperative, and postoperative data were obtained from record file. The follow up records were obtained from out patient department follow up file and personal contact with the patient. This study was designed to understand clinical behavior, management plan and outcome of these rare tumors in Bangladesh

Results:

Out of the 451 patients with pancreatic malignancy histopathological report diagnosed 31 as having SPTP

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(6.9) (Table-I). There were 24 females and 7 males with a median age of 24 years (range, 14–44). The predominant presenting symptom was abdominal pain and lump (n=28, 90.3%); two patients had jaundice (6.7 %) and one patient was asymptomatic (3.0%).The tumor markers levels of all patients (CA19-9 & CEA) were within normal limits. The median size of the lesions was 7.0 cm (range, 4.5–18) (Table -II).

Table-I

Types of pancreatic tumor underwent resection in BSMMU and other Hospitals of Dhaka City from 2001 to 2009

Sl no	Types of pancreatic tumor	Number (%)
1	Adenocarcinoma	418 (93.7)
2	Solid pseudopapillary tumor of pancreas (SPTP)	31 (6.9)
3	Non Beta cell tumor	1 (0.2)
4	Non Hodgkin tumor	1(0.2)
	Total	451 (100)

Table-II

Clinical data of patients with solid pseudopapillary tumor of pancreas

Total patient	31
Male : Female	7 : 24
Median Age (years)	24 (range: 14 to 44)
Clinical Presentation	25
Abdominal pain and lump	28 (90.3%)
Jaundice	02 (6.7%)
Incidental	01 (3.0%)
Tumor size (Median)	7.0 cm (range: 4.5 to 18)
Tumor location	
Head	25 (80.6%)
Body	02 (6.5%)
Tail	04 (12.9%

Twenty five patients had their primary tumors within the head, 2 in the body and 4 in the tail of the pancreas (Fig-1) Preoperatively, CT guided FNAC of the lump in initial few cases were inconclusive; therefore FNAC was abandoned in later cases. Laparotomy was planned for resection of the tumor; however triple bypass and tissue biopsy from the lesion was taken into consideration in case of irresectable tumor. A total of 30 patients presented with local disease underwent resection. Twenty four patients underwent pancreaticoduodenectomy (Fig 2a), four patients underwent a distal pancreatectomy (Fig. 2b) and two patients underwent enucleation of the tumor. One patient was found to have a very large tumor in the head with vascular invasion (Fig.-3) and underwent debulking of the tumor. Postoperatively, 23 patients (74.1%) had an uneventful course; rest 8 patients (25.9%) had minor complications; wound infection and wound dehiscence in 2, atelectasis in 1, thrombophlebitis in 2 patients.

Tumors were generally large, varied from tan to yellow, and showed irregular cystic cavities lined by soft, friable tissue. Foci of hemorrhage were common. Some examples also demonstrated firm, fibrotic regions within the tumor. Most cases appeared to be grossly well circumscribed or even partially encapsulated. The microscopic appearance of all the cases demonstrated the characteristic microscopic features of SPTP. The solid areas were composed of monotonous polygonal epithelioid cells, often with minimal intervening stroma, accompanied by innumerable capillary-sized vessels. Some areas showed more extensive stromal fibrosis, with round aggregates of perivascular hyalinized stroma imparting a cylindromatous appearance. In the pseudopapillary regions, the cells located away from the small vessels appeared to have dropped away, leaving an irregular cuff of cells surrounding each vascular core. There was evidence of cellular degeneration, including aggregates of foamy histocytes, cholesterol clefts, and cytoplasmic vacuolization. Clusters of cells demonstrated large eosinophilic cytoplasmic globules. The nuclei were generally uniform and round to oval, with longitudinal grooves. The microscopic interface between the tumors and the adjacent pancreas commonly showed an infiltrative growth pattern, with islands of non-neoplastic pancreatic parenchyma entrapped within the tumor and nests of tumor cells extending into the adjacent pancreas (Fig-4).

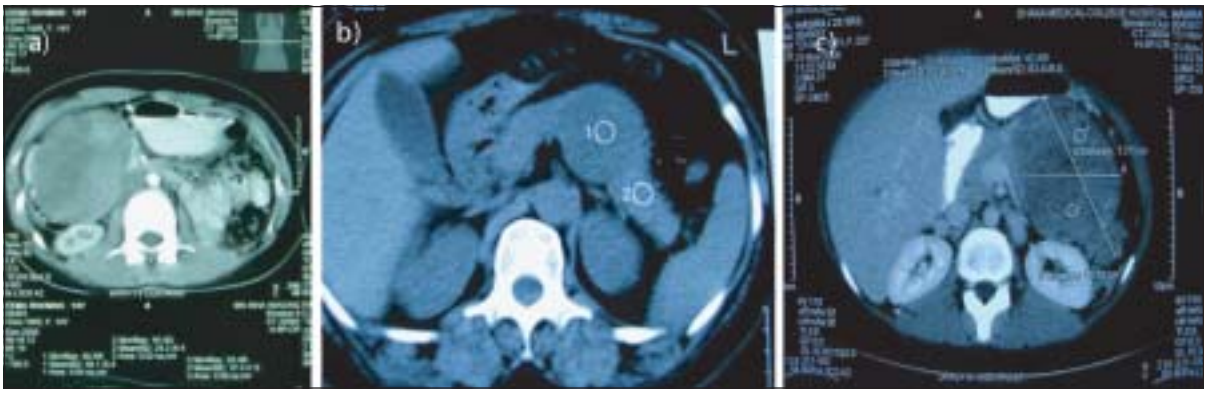

Fig. 1: *Location of the tumor a) Head of the pancreas, b) Body of the pancreas, c) body and tail of the pancreas*

Fig.-2: *Specimen of a) pancreatoduodenectomy and b) distal pancreatectomy*

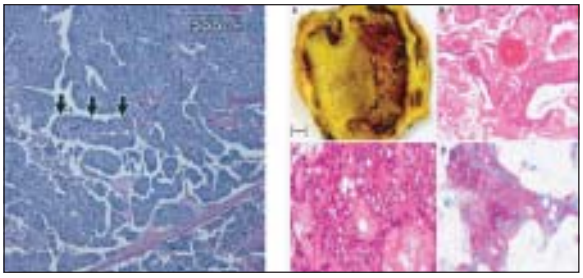

Fig.-4: *Histopathology of Solid Pseudopapillary Tumor of Pancreas*

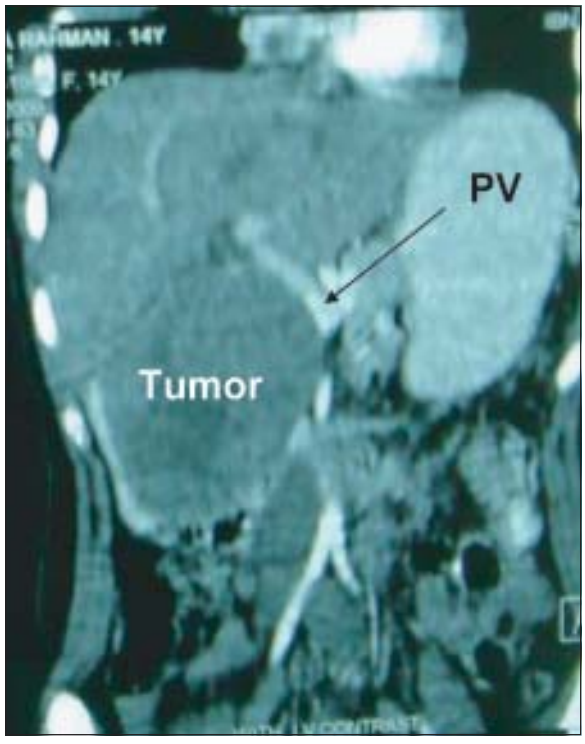

Fig.-3: *Tumor compressing the portal vein (PV)*

At a follow-up of 2 months to 9 years, all patients are surviving till date; no patients had any evidence of recurrence except one who underwent debulking of the tumor. This patient's tumor clinically reappears 1 year after debulking, and the patient is still alive with episodic attack of abdominal pain

Discussion:

SPTP is a very rare variety of pancreatic tumor. It was first described in 1959 by Frantz[3]. World Health Organization named this tumor as SPTP in 1996.[4] Before that it has been described by many other terms, such as papillary epithelial neoplasm, solid and cystic acinar cell tumor, papillary cystic neoplasm, papillary cystic carcinoma, solid and cystic tumor, low-grade papillary tumor, and Frantz's tumor. It has also been misdiagnosed as adenocarcinoma, islet cell tumors, cystadenomas, papillary cystadenocarcinoma, or cystadenocarcinoma.

A total of 719 cases of SPTP of the pancreas have been reported in the literature since it was first described in 1959 [5,6]. There has been an increasing incidence of this

entity in recent years. A possible explanation of increasing incidence is greater awareness of this disease, as well as better understanding of pancreatic pathology with the 1996 new classifications of pancreatic neoplasms from the World Health Organization[7].

SPTPs of the pancreas have been diagnosed most commonly in young women. The series has demonstrated the incidence of male patients diagnosed with this disease similar to the series of Memorial Sloan-Kettering Cancer Center, New York[8]. A majority of reports have found the greatest incidence of SPTP of the pancreas in the third decade of life; however, our patients presented with a median age of 24 years, which is similar with two large single institutional series and in the total number of cases reported (median age of 26 years)[9,10]. However Robert C et al reported SPTP with a median age of 39 years.

More than 90% patients in this series presented with vague abdominal pain and abdominal lump. Symptoms, when they occur, are often vague and nonspecific, leading to a delay in diagnosis. As a result of these subtle symptoms, tumor presentation can be quite large. But size of the lesion is not a predictor of unresectability, as seen in this series with maximum size of 18 cm and in others, with lesions 20 to 30 cm in size still being resectable[11,12]. These lesions rarely invade contiguous structures or occlude the bile ducts as occurred in only two of our patients presenting with jaundice. Vascular invasion, although uncommon, does occur, as evidenced by one of our patient who presented with portal vein encasement.

The cell of origin of the solid –pseudopapillary tumour is uncertain and has not yet been clarified. It is a low malignant potential tumor, complete resection or enucleation whenever possible and even debulking of the tumor provide a good survival time. In our series all patient survived 2 month to 9 years without recurrence except one patient who underwent debulking of the tumor still surviving one year after operation.

Metastatic disease does occur with SPTPs, with 20 previously reported cases[13,14]. The most common site of distant disease is the liver; very rare cases of lymph node and peritoneal spread have been reported. Disseminated disease is also not a negative predictor of survival. Long-term survival, 7 to 10 years, has been reported in patients undergoing complete resection, but it is more important to note that it has also been reported in patients with residual disease[11,14]. In Robert C et al series, two patients with liver metastasis had significant overall survival, with one alive at 11 years and the other alive with liver recurrence at 4 years.

In most studies of the clinical outcome of SPTPs, no pathologic factors predictive of prognosis have been identified. In the largest clinicopathological study to date (published only in abstract form), pathologic factors including mitotic rate, nuclear pleomorphism, and vascular invasion were not found to correlate with prognosis[15].

Adjuvant therapy has been used only in a small number of patients as published in the literature. Many different regimens of chemotherapy have been used without any demonstration of response. One patient of a series[8] was treated with complete cycles of 5-fluorouracil, doxorubicin, and streptozocin and interferon, cisplatin, and topotecan without any response to the primary lesion. Radiotherapy has been used infrequently. Only one case report indicates significant success in a locally advanced lesion involving the porta hepatis; it responded to 4000 cGy over 6 weeks with a 3-year follow-up[16]. Other reports have also looked at estrogen receptor status and have found no indication that over expression exists in these lesions[10].

Summary:

Our experience with SPTP showed young adult female are commonly sufferer. Because of vague initial symptoms, tumor becomes large at presentation. Aggressive treatment with attempts made for complete resection, even if this requires metastasectomy can provide long-term survival for SPTP. Adjuvant therapy did not show any improvement of survival in such patients as per literature review.

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Clinical and Bacteriological Profile of Neonatal Septicaemia at A Community Level Medical College Hospital

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Summary:

Septicaemia is a significant cause of morbidity and mortality in neonates. Meningitis is a serious problem in newborns with high mortality and frequent neurological sequelae. In neonates, signs and symptoms of infections are often obscure and clinical examination cannot distinguish septicaemic babies with or without meningitis. Therefore, lumbar puncture is often not done in time and thus diagnosis of meningitis is missed. Our aim was to see the association of bacterial meningitis in neonatal septicaemia and their clinical and bacteriological profile. This study was performed at the neonatal ward of Kumudini Women's Medical College Hospital from August 2007 to July 2009. All admitted newborns diagnosed as septicaemia clinically were enrolled prospectively. Detailed history was taken, thorough clinical examination performed, and blood culture, CSF study and other relevant investigations were done. Patients received standard medical care and followed-up daily till discharge/death. Among 86 suspected cases, 30 (34.9%) had positive blood culture. Common clinical presentations of culture-positive cases were poor feeding (86.7%), lethargy (70%), respiratory distress (56.7%), fever (46.7%), jaundice (33.3%), seizure (26.7%) and cyanosis (20%). Male child outnumbered the baby girls (1.7:1). Other risk factors were maternal fever during delivery, prolonged rupture of membranes, birth asphyxia and poor socio-economic status. Majority (63.3%) of the cultures isolated gram-negative bacilli, most commonly Klebsiella pneumonia (16.7%), Pseudomonas sp. (16.7%), and Acinetobacter (10%). Staphylococcus aureus (20%) was most common among gram-positive organisms, followed by Streptococcus pneumoniae (10%); no Group B streptococcus was isolated. Associated meningitis was present in two cases (6.7%) and nine out of 30 culture-positive cases (30%) died. This study confirms that neonatal septicaemia is a major problem in perinatology with high case fatality. As associated meningitis is difficult to distinguish clinically, CSF study needs to be included in septicaemia screening. An alarming finding of the study is that high proportion of the organisms are resistant to most of the commonly used antibiotics, again emphasize the importance of judicious antibiotic use.

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Introduction:

The World Health Organization (WHO) estimates that 4 million neonatal deaths occur around the world every year[1]. Approximately 98% of these deaths occur in developing countries, and are attributable to infections, asphyxia, and consequences of prematurity and low birth weight[2]. Overall, neonatal mortality accounts for nearly two-thirds of infant mortality and one-third of under-five childhood mortality worldwide[3-5]. Serious bacterial infections are major contributors to newborn morbidity and mortality. An estimated 20% of all children born in developing countries, or 30 million annually develop an infection during the neonatal period, and infectious diseases account for an estimated one-third of all neonatal deaths[1,6].

Meningitis is a serious problem in newborn infants with a high mortality and frequent neurological sequelae in survived patients. About 20-30% of neonatal septicaemia, whether early or late, is complicated by bacterial meningitis[7,8]. One study from Saudi Arabia showed 21 per 1000 admission at NICU had bacterial meningitis[9]. In a two-year (1985-87) prospective study of acute meningitis in England and Wales in infants; the incidence of neonatal meningitis was 0.32 per 1000 live

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births[10], another study done in Oxford showed 0.38 per 1000 live births[11]. Reviews from USA,[7,12] Europe[10,13] and Australia[14] have shown 0.2 – 0.5 cases of bacterial meningitis per 1000 live births. In our country we do not have much data, but two prospective studies done at Dhaka Shishu Hospital have shown that 13-27% of neonates with septicaemia had concurrent meningitis[15,16].

Several studies report that prematurity, low birth weight, prolonged rupture of membranes and maternal infections are most common perinatal factors associated with septicaemia and meningitis in the newborn period[7,8,12,13,17]. Clinical examination cannot distinguish septicaemic babies with meningitis from those without meningitis. Blood culture may also be negative in meningitis. One study showed 13% of bacterial meningitis with positive CSF culture had negative blood culture[13], another study showed 15% case of meningitis with negative blood culture[18].

The causative agents of neonatal septicaemia and meningitis vary between geographical areas and with time in any particular locality. To our knowledge, there has been no documented survey on causative agents of neonatal septicaemia and meningitis at community level from our country. During 1975-91, the leading causes of neonatal bacterial meningitis were Group B streptococcus (34.1%) and *Escherichia coli* (28.5%), which accords with the patterns of causative organisms reported from UK[10], USA[19] and Australia.[14] Another study done at Saudi Arabia shows *Klebsiella pneumoniae* and *Serratia marcescens* as the important organisms of neonatal meningitis[9]. In North America and Europe, the prevalent bacterial agents of late-onset septicaemia include coagulase negative staphylococcus, Klebsiella sp. and *Escherichia coli*.[20] The two studies done at Dhaka Shishu Hospital showed *Escherichia coli, Klebsiella pneumonia* and *Pseudomonas aeruginosa* as the common organisms of neonatal septicaemia and meningitis[15,16].

Materials and methods:

Study site: This hospital based prospective study was conducted at the neonatal ward of Kumudini Hospital in a cohort neonates admitted between August 2007 and July 2009. Kumudini Hospital is a 70 years old, 750-beded non-profit private hospital, with laboratory and radiology facilities in Mirzapur, a rural sub-district (Thana) of Bangladesh, located 60 km north of Dhaka. Mirzapur has an estimated total population of 400,000, distributed in 13 unions and 219 villages. The hospital is staffed by specialists of all disciplines. A medical college, Kumudini Women's Medical College, is affiliated to the hospital. As the major referral hospital, Kumudini Hospital serves most patients throughout the Mirzapur sub-district.

Study Population: All admitted newborns diagnosed as septicaemia clinically on admission or at any stage of hospitalization were considered for enrolment. Septicaemia was suspected based on the presence of one or more clinical sign consistent with possible serious bacterial infection including lethargy, refusal of feeds, abdominal distension, vomiting, groaning, grunting, facial grimace, respiratory distress, hypothermia, hyperthermia or sclerema with or without supporting evidence of risk factors such as prematurity, low birth weight (LBW), birth asphyxia, maternal chorioamnionitis (maternal fever and/or foul smelling vaginal discharge) and prolonged rupture of membranes. Meningitis was suspected from a history of irritability, convulsions, high-pitched cry and full, tense anterior fontanel along with other features of septicaemia. We excluded babies in moribund condition and those who had active bleeding for which lumbar puncture could not be done.

Babies were categorized according to the following risk factors for septicaemia: birth weight (<1500 g, 1500 – 2500 g, >2500 g), gestational age (<37 weeks, 37 – 42 weeks, >42 weeks), birth-place (home, hospital/clinic), and mode of delivery (normal, forceps-assisted, Caesarean section). Study patients were also categorized as having early- or late-onset septicaemia depending upon whether the onset of symptoms was within 7 days (early-onset) or 8 to 28 days of life (late-onset).

After enrolment, patients underwent the following diagnostic procedures: complete blood count, blood culture, CSF study (cytology, biochemistry and culture) and other relevant investigations as necessary. A diagnosis of definitive septicaemia was made when the clinical suspicion was confirmed by a positive blood culture. Similarly bacterial meningitis was diagnosed depending on clinical suspicion and positive CSF culture. Of the total 86 cases evaluated during the study period, 30 had a positive blood culture; 2 of them also

had positive CSF culture. The presenting symptoms and signs, agents of infection and outcome of the 30 culture positive cases are described here.

Culture methods: A blood sample was taken from each patient with suspected septicaemia after careful preparation of the skin site with 70% isopropyl alcohol. The site chosen was a peripheral vein, preferably the antecubital vein. Blood (~2 ml) was withdrawn using a sterile disposable syringe and transferred using sterile technique to 5 ml of Tripticase Soy broth. In the laboratory, subculture was done on days 1, 2, 3 and 5 of incubation onto blood agar, chocolate agar and MacConkey's media. Cerebrospinal fluid was plated on the same media as the blood. Antimicrobial sensitivity testing of all isolates was performed on Muller Hinton Agar (MHA) plates by the Kirby Bauer diffusion method.

Patient management: All patients received the standard treatment for neonatal septicaemia followed in the hospital. Cefotaxime and gentamicin were started at enrolment and changed later, if needed, depending on the culture sensitivity report as well as the clinical condition. Other supportive therapy such as correction of acidosis, maintenance of fluid and electrolyte balance, ventilatory assistance, phototherapy and blood transfusion was given as required. Infants enrolled in the study were evaluated on a daily basis while hospitalized.

Data collection: At enrolment a detailed history was taken and thorough physical examination was performed and recorded on standard forms. The parents of the neonates were explained about the study and then witnessed verbal consent was taken.

Statistical analysis: The data were subjected to statistical analysis according to standard procedure. SPSS version 12.0 for Windows (SPSS Inc, Chicago, IL, USA) software was used for data recording and analysis. Results of the findings were verified by conducting standard tests for significance, including unpaired student T-test and Chi-square (c_{-}^{2}) tests, as appropriate. A p-value of < 0.05 was considered as statistically significant.

Results:

Among 86 cases of clinically suspected neonatal septicaemia, 30 (34.9%) had a positive blood culture; 12 (40%) had early- and 18 (60%) late-onset infection. Blood culture positivity was significantly lower in those with early- (25.5%, 12/47) compared to late-onset (46.1%, 18/39) disease ($p<0.05$). Although males with positive blood cultures (63.3%, 19/30) outnumbered females (36.7%, 11/30), there were no gender differences in culture positivity rate (males 32.7%, 19/58; females (39.3%, 11/28) or proportion of early- (males 42.1%, 8/19; females 36.4%, 4/11) and late-onset (males 57.9%, 11/19; females 63.6%, 7/11) disease. Forty percent of neonatal septicaemia cases were preterm and 18 (60%) were term babies. Blood culture positivity rate was equivalent, however, for preterm (30.0%, 12/40) and term (39.1%, 18/46) infants; and for very LBW (30.8%, 4/13), LBW (36.8%, 14/38) and normal birth weight (34.3%, 12/35) infants. (*Table I*).

Table-I

Blood culture-positivity and mortality rates of sub-categories of neonates with suspected sepsis (n=30)

Category		Number enrolled cultures (n)	Positive blood positivity (%)	Blood culture	Mortality (n)	Mortality (% of blood culture positive cases)
Onset	Early	47	12	25.5	3	25.0
	Late	39	18	46.1	6	33.3
Gender	Male	58	19	32.7	6	31.6
	Female	28	11	39.3	3	27.3
Gestational age	Pre-term	40	12	30.0	4	33.3
	Term	46	18	39.1	5	27.8
Birth weight (g)	<1,500	13	4	30.8	2	50.0
	1,500 – 2,500	38	14	36.8	4	28.6
	>2,500	35	12	34.3	3	25.0
Monthly income (Tk.)	<5,000	50	16	32.0	5	31.2
	5,000 – 10,000	25	9	36.0	3	22.2
	>10,000	11	5	45.4	1	20.0

Majority of the deliveries of septicaemic neonates in this study were conducted at home (70%, 21/30) and 9 (30%) took place in a hospital or clinic. Five culture positive cases (16.7%) were delivered by caesarean section, and 11 (36.7%) had a history of birth asphyxia. Neonates with septicaemia more often were from low socio-economic classes (family income < 5,000 Taka per month) (53.3%, 16/30) than middle (5,000 to 10,000 Taka) (30%, 9/30) or higher income (> 10,000 Taka) (16.7%, 5/30) groups. There was a trend for the culture positivity rate to be lower in the low (32%, 16/50) than the middle (36%, 9/25) or high (45.4%, 5/11) income groups, although the difference was not significant statistically. (*Table I*) Prolonged rupture of membranes for more than 18 hours was present in 20% (6/30) cases and maternal fever during delivery in 10% (3/30), one of them had both (4%).

The most frequent clinical presentations of patients with culture-proven serious neonatal bacterial infection were poor feeding (86.7%, 26/30), lethargy (70%, 21/30), respiratory distress (56.7%, 17/30), fever (46.7%, 14/30), jaundice (33.3%, 10/30), seizure (26.7%, 8/30) and cyanosis (20%, 6/30). Jaundice and convulsion were more common in early-onset and fever was more common in late-onset disease, though not statistically significant ($p>0.05$); other presenting signs were almost similar in both groups. (*Table II*) Meningitis cases were presented with features of septicaemia; there were no specific symptoms or signs related to meningitis.

Of the 30 organisms isolated, about two-thirds (63.3%, 19/30) were gram-negative bacilli; 11 (36.7%) were gram-positive. Among the gram-negative bacilli, *Klebsiella pneumonia* (16.7%, 5/30), Pseudomonas sp. (16.7%, 5/30), and Acinetobacter (10%, 3/30) was the most common and *Staphylococcus aureus* (20%, 6/30) and *Streptococcus pneumoniae* (10%, 3/30) was most common among gram-positive organisms, The pattern of organisms isolated was similar, regardless of time of onset of disease, birth weight or gestational age. (*Table III*) A large number of the organisms are resistant to all of the commonly used antibiotics. Ampicillin virtually has no effect except against *Streptococcus pneumoniae* and *H. influenza*. Gentamicin, third generation cephalosporins and ciprofloxacin showed mixed sensitivity pattern. Imipenem and netilmicin are found most effective against majority of the organisms. (*Table IV*).

Of the 30 culture-positive cases, 9 (30%) died. The case fatality rate was inversely related to birth weight (<1500 g: 50%, 2/4; 1500-2500 g: 28.6%, 4/14; >2500 g: 25%, 3/12)**,** and was highest in neonates infected with *E. coli* (50%), followed by *Klebsiella pneumoniae* and Pseudomonas sp. (40%) and no mortality in neonates infected with *H. influenza*, Streptococcus sp, Enterobacter and Salmonella sp. *(Fig. I)* Case fatality was not influenced by time of onset (early-onset: 25%, 3/12; late-onset: 33.3%, 6/18) or gender (males: 31.6%, 6/19, females: 27.3%, 3/11). (*Table I*).

Table-II

Common Clinical Manifestations of the Blood Culture Positive Cases of Neonatal Septicaemia (n=30)

Clinical features	Prevalence (%)			p-value
	All	Early-onset	Late-onset	
Poor feeding	86.7	91.7	83.3	NS
Lethargy	70.0	66.7	72.2	NS
Respiratory distress	56.7	66.7	50.0	NS
Fever	46.7	33.3	55.6	NS
Jaundice	33.3	41.7	27.8	NS
Seizure	26.7	41.7	16.7	NS
Cyanosis	20.0	16.7	22.2	NS
Vomiting	13.3	16.7	11.1	NS
Hypothermia	10.0	16.7	5.6	NS
Apnoea	10.0	16.7	5.6	NS

NS=Non-significant

Table-III

Organisms Isolated in Relation to Onset of Disease, Birth Weight and Gestational Age (n=30)

Organisms	Total	Age of onset		Birth weight (g)			Gestational age	
	(percentage)	Early	Late	<1500	1500 -2500	>2500	Pre-term	Term
Staphylococcus aureus	6 (20.0)	2	4	1	2	3	3	3
Klebsiella pneumoniae	5 (16.7)	2	3	-	3	2	1	4
Pseudomonas sp.	5 (16.7)	1	4	1	2	2	1	4
Acinetobacter	3 (10.0)	1	2	1	1	1	2	1
Streptococcus pneumoniae	3 (10.0)	2	1	-	2	1	1	2
Streptococcus sp.	2 (6.7)	-	2	-	1	1	1	1
Haemophilus influenzae	2 (6.7)	1	1	-	1	1	1	1
Escherichia coli	2 (6.7)	1	1	-	1	1	1	1
Enterobacter sp.	1 (3.3)	1	-	1	-	-	1	-
Salmonella sp.	1 (3.3)	1	-	-	1	-	-	1
Total	30 (100)	12	18	4	14	12	12	18

Table-IV

Antibiotic Resistance (%) of Organisms Isolated (n=30)

Antibiotic	*Staph. aureus*	*Kl. pneumoniae* (n=6)	Pseudomonas sp. (n=5)	Acinetobacter (n=5)	*Str. pneumoniae* (n=3)	*Streptococcus* (n=3)	*H. influenzae sp.* (n=2)	*E. coli* (n=2)	Enterobacter sp. (n=1)	Salmonella sp. (n=1)
Ampicillin	83.3	100	100	100	0	50	0	50	100	100
Gentamicin	16.7	60	80	66.7	0	0	0	0	0	0
Cefotaxime	16.7	60	80	33.3	0	0	0	0	0	100
Ceftriaxone	16.7	60	60	33.3	0	50	0	0	0	100
Ceftazidime	33.3	20	40	33.3	0	0	0	0	0	100
Ciprofloxacin	16.7	40	40	33.3	0	0	0	0	0	100
Imipenem	0	0	20	0	0	0	0	0	0	0
Netilmicin	0	0	60	0	0	0	0	0	0	0

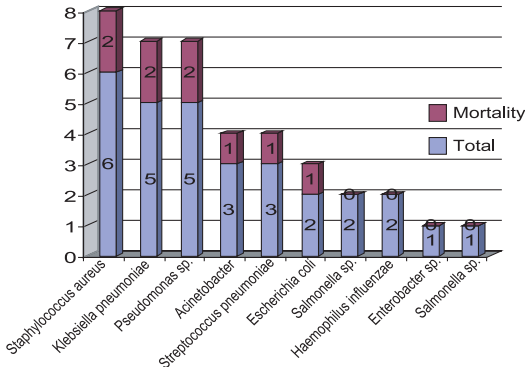

Fig.-1. *Mortality of the 30 Blood Culture Positive Cases of Neonatal Septicaemia in Relation to Bacterial pathogens. (Total no of deaths n=9)*

Of the 30 culture-positive cases, 2 also had meningitis with culture-positive CSF; among them, 1 patient (50%) died. *Streptococcus pneumoniae* caused meningitis in early-onset and *Klebsiella pneumoniae* in late-onset disease.

Discussion:

In this study, at a community level medical college hospital in Bangladesh, we found that late-onset neonatal septicaemia was more common than early-onset disease; in contrast to other reports in which early-onset septicaemia generally has been more common[21,22]. Perhaps this discrepancy is due to the fact that mortality in early-onset cases is relatively high[23], and thus, some

neonates in the catchment area of our hospital, which largely serves a low socioeconomic status community with poor communication facilities, might have died prior to arrival at the hospital. Although males have been reported to be 2- to 6-fold more likely than females to develop septicaemia[23,24], the 1.7:1 ratio of male-to-female infants in our study, while seemingly consistent with this data, could also reflect a gender bias in presentation to the hospital for care. Population-based studies would be needed to address this important question. The clinical features, culture positivity rates, and case fatality rates, however, were equivalent across gender, suggesting that the males and females in the study overall had a similar degree of illness.

The majority of the study population was poor, and delivered at home, largely in the hands of untrained birth attendants. Home deliveries are common in Bangladesh[25], and typically are conducted in poor standards of asepsis[26]. History of unclean vaginal examination was associated with a 10% incidence of deep infection in one study[27]. Home deliveries also are significantly related to birth asphyxia[28], which was highly prevalent in our study population, and which, in turn, is associated with an increased risk of serious neonatal infection[29].

The clinical features of neonatal septicaemia seen in this series are similar to those previously reported in other studies[30,31]. In majority of cases early clinical presentation was nonspecific simulating other common neonatal problems. Poor feeding was present in majority of the cases (86.7%). Other common presentations were lethargy (70%), respiratory distress (56.7%), fever (46.7%), jaundice (33.3%), seizure (26.7%) and cyanosis (20%). Jaundice and convulsion were more common in early-onset and fever in late-onset disease, though the difference was not statistically significant ($p>0.05$); other presenting signs were almost similar in two groups. Apnoea and hypothermia was mostly seen in preterm babies. The more non-specific symptomatology of disease and the relatively greater tendency to over-diagnose illness in the younger age group may have contributed to the lower percentage of positive cultures in neonates with early- compared to late-onset disease. Nonetheless, negative blood culture does not rule out septicaemia. Squire et al[32]. reported 7 cases with negative culture, fatal outcome and post-mortem evidence of infection. The possibility of infection with anaerobes also cannot be ruled-out as anaerobic culture was not performed in this series. Chow et al[33]. reported that 26% of all neonatal septicaemia was caused by anaerobes.

Of the organisms isolated 19 (63.3%) were gram negative and the rest (11,36.7%) gram positive. Increasing prevalence of gram negative septicaemia has been reported from other studies in India[34,35] and Pakistan[23,36] as well as previous studies in our country[15,16,37]. Earlier study showed prevalence of *E. coli*, followed by *Klebsiella pneumonia* and Pseudomonas sp.,[15] later studies showed preponderance of Klebsiella, followed by Pseudomonas sp. and Acinetobacter[16,37]. In the present study, *Klebsiella pneumonia* was also the most prevalent organism (16.7%), followed by Pseudomonas sp. (16.7%) and Acinetobacter (10%) and only 2 (6.7%) *E. coli*. This supports the changing trend of bacterial etiology in neonatal septicaemia[38]. Group B Streptococcus was not isolated in this study, unlike western, developed countries where it is the major agent of neonatal septicaemia[21,22,39] The insignificance of GBS as a pathogen in many developing countries is supported by a number of other studies[34,40-46]. This may be attributable to low prevalence of GBS colonization of pregnant mothers in this area, or, possibly, to the presence of strains with low virulence[47].

An alarming finding in this study is the high proportion of the organisms are resistant to all of the commonly used antibiotics. Imipenem and netilmicin are found most effective against majority of the organisms. Gentamicin, third generation cephalosporins and ciprofloxacin, which previously had good sensitivity, also becoming resistant. This observation shows that the problem of antibiotic resistance is a serious threat for treating serious bacterial infections in neonates and to control antibiotic resistance, practice of prudent or judicious use of antibiotics is very important.

The present survey confirms the high case fatality rate in neonatal septicaemia, despite care in a medical college hospital and use of appropriate antimicrobial therapy. The death rate was higher in preterm LBW, highlighting the importance of anticipatory guidance for parents at home, particularly those with a LBW infant, and early clinical suspicion on the part of practitioners. The survey also showed epidemiological features of neonatal

septicaemia that may have direct future preventive measures. But due to small sample size the study identified the need for continuing evaluation at different levels of local patterns and antibiotic sensitivities of pathogens of neonatal septicaemia to formulate rational antibiotic policy. There also is a need for community-based case-control studies with larger sample sizes to identify risk factors and preventive measures for neonatal septicaemia.

Conclusion:

The present survey confirms that neonatal septicaemia is a major problem in perinatology and paediatric infectious disease with high case fatality. To identify risk factors for adverse outcome and preventive measures, case-control studies with representative sample size is recommended. High incidence of antibiotic resistance amongst the various organisms again emphasizes the importance of judicious antibiotic use.

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Pregnancy in Addison's Disease

N AKHTAR

Summary:

Pregnancy with Addison's disease is very rare. Addison's disease is caused by destruction or dysfunction of the adrenal cortices. A 25 years old lady with Addison's disease receiving chronic treatment with prednisolone (5mg) 1+½+0 tab daily was admitted in 0bs & Gynae Department, BSMMU on 25th October,'09 with 2nd gravida , 38 wks of pregnancy. Caesarean section was done on 26th October, '09. A male baby of 2.5 kg was delivered. Her peroperative and postoperative periods were uneventful. Inj. Hydrocortisone was given peroperatively and postoperatively. Patient was discharged on 7th P.O.D. with above dose of Tab prednisolone.

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Introduction:

Autoimmune destruction of the adrenals is the most common cause of Addison's disease which must involve more than 90% of the glands before adrenal insufficiency appears [1]. It is characterized by chronic deficiency of cortisol, aldosterone and adrenal androgens and causes skin pigmentation that can be subtle or strikingly dark. Volume and sodium depletion and potassium excess eventually occur in primary adrenal failure.At one time, the commonest cause was tuberculosis, with autoimmune destruction of adrenal gland accounting for a minority of cases. The situation is now reversed and patients may have other autoimmune conditions such as pernicious anemia [2]. It usually appears by age 15 years. Partial or late expression of the syndrome is common. The symptoms may include weakness, fatiguability, weightloss, myalgia, arthralgia, fever, anorexia, nausea, vomiting, anxiety and mental irritability due to excess ACTH. Pigmentary changes consist of diffuse staining over nonexposed as well as exposed parts or multiple freckles; hyperpigmentation is especially prominent over the knuckles, elbows, knees, posterior neck, in palmar creases and nail beds. Nipples and areolas tends to be darker. The skin in pressure areas such as the belt or brassiere lines and the buttocks also darkens. The diagnosis of Addison's disease in pregnancy is difficult, because so many of the features of Addison's disease may be associated with normal pregnancy. However, persistence of nausea and vomiting after 20 wks gestation and weight loss should be considered abnormal [3]. On laboratory investigations the WBC count usually shows moderate neutropenia, lymphocytosis and a total eosinophil count over 300/ mcL. Among patients with chronic Addison's disease, the serum sodium is usually low (90%) while the potassium is elevated (65%). Low plasma cortisol(<3mcg/dl) at 8a.m. is diagnostic, especially if accompanied by simultaneous elevation of plasma ACTH level(usually >200pg/ml). Serum DHEA levels are under 1000ng/ml in 100% of patient with Addison's disease. Replacement therapy should include a combination of corticosteroid and minerolocorticoids. In mild cases hydrocortisone alone may be adequate. Most addisonian patient are well maintained on 15- 25 mg of hydrocortisone orally daily in two divided doses, two thirds in the morning and one third in the late afternoon or early evening. Some patients respond better to prednisone in a dosage of about 2-3 mg in the morning and 1-2 mg in the evening. A proper dose usually results in a normal differential white count. Fludrocortisone acetate has a potent sodium retaining effect. The dosage is 0.05-0.3mg orally or every other day. In the presence postural hypotension, hyponatremia, or hyperkalemia the dosage is increased. During pregnancy the prepregnancy dose of cortisone must be maintained unchanged throughout pregnancy, as a reduction, even late in the third trimester, will be followed by the return of Addisonian symptoms. Furthermore any additional stress such as vomiting, infection or haemorrhage must be met by a temporary increase in maintainance dose[4]. For women undergoing elective surgery , stress doses of cortisol should be administered. On the day of surgery , 300mgm of cortisol can be administered, and this dose can be reduced by 50 mg daily until oral glucocorticoid replacement is reinitiated[5]. Before glucocorticoid replacement therapy becomes available, pregnancy in

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patients with adrenal insufficiency was associated with a maternal mortality rate of 77%; when extracts of the adrenal cortex became available, maternal mortality reduced to 30 %. Now with the use of full steroid replacement therapy, pregnancy should be no excess cause of maternal mortality. In patients with treated autoimmune Addison disease, conception, fetal development and delivery should not be problematic. The only consistently recorded fetal complication is intrauterine growth retardation[6].

Case Report:

A 25 years old lady, 2nd gravida was admitted in BSMMU on 25th Oct, 2009 with 38+ weeks of pregnancy with known case of Addison's disease for 6 years .During her antenatal period she was jointly managed by obstetrician (fetomaternal) and endocrinologist. She was on Tab Prednisolone 15 mgm daily. According to the advice of endocrinologist, S. electrolyte, S.cortisol level and APTT was done monthly from 28weeks onwards. Her APTT was high 41.7 sec (control-28sec).Other parameters were normal. Her pregnancy period was uneventful till 34 weeks then she developed diarrhea and went into adrenal crisis and was managed Inj.Hydrocortisone 200mgm I/V stat and 100mgm I/V 8 hourly for 24 hrs. Since then she has been carrying with her an adrenal crisis card. During her first pregnancy she was on Tab Prednisolone. She went into labour at term and developed shock at second stage of labour, delivered a stillborn female baby. She developed postpartum haemorrhage that was managed by condom catheter , inj.oxytocin, prostaglandin E1and shock was managed by volume replacement, blood transfusion and Inj.Hydrocortisone. During this pregnancy elective caesarian section was done at term to avoid stress of labour. A male baby of 2.5 kg was delivered. Adrenal crisis was prevented with Inj.Hydrocortisone 200mg I/V preoperatively and then 100gm I/V 8 hourly for 72hours followed by Tab Prednisolone(5mg daily). In 2003 she developed diarrhea and vomiting and was admitted into ICDDRB. Diarrhoea was not controlled by ORS or I/V fluid. After investigations she was diagnosed as a case of Addison's disease. Since then she is on Tab Prednisolone 7.5 mg daily. She also complaints of red to blackish rash on and off in her body. Her elder sister is suffering from SLE which is also an autoimmune disease.

Discussion:

Pregnancy in Addison's disease is rare. These patient usually suffer from subfertility. Cortisone appeared to cure this patient subfertility. On the other hand modern antibiotics eliminate the spread of tuberculous infection to adrenals, previously the source of one-half of the cases.However , simple atrophy will still provide new cases and irrespective of the causes, cortisone will so enhance the wellbeing , fertility and expectation of life.

The well being and life span of patients with Addison's disease have been greatly improved by cortisone & allied substances. Prior to 1951 their average expectation of life was only two and a quarter years or three and a half years depending on whether tuberculous infection or atrophy was the cause but women with Addison's disease can now expect to survive the entire reproductive period and to enjoy almost normal fertility. Pregnancy and in particular labour and its complications were hazardous in the past[7,8]. In one study on 13 cases where cortisone was given[9]. One case reported maternal death among these 13 cases. Two cases reported vomiting at 8 weeks of pregnancy led to admission in crisis and managed by cortisone [10]. Our patient went into crisis at 34 weeks of pregnancy because of diarrhoea and managed with Inj. Hydrocortisone in endocrinology department. One case reported development of post partum haemorrhage three hours after delivery[10]. The patient collapsed and recovery was slow inspite of adequate blood transfusion and large doses of deoxycortisone and aqueous adrenal extract. Cortisone 25 mg was given intramuscularly. In our patient during her first delivery, went into adrenal crisis during 2nd stage of labour. Even after forceps delivery she delivered a stillborn baby and developed postpartum haemorrhage immediately and patient was luckily saved because of prompt management with Inj.Hydrocortisone and Blood transfusion. The pre-pregnancy dose of cortisone must be maintained unchanged throughout the pregnancy, as reduction even late in the third trimester,will be followed by the return of Addisonian symptoms[11]. Furthermore, any additional stress such as need by a temporary increase in the maintainance dose. Studies shows that the adrenals of patients with Addison's disease are unable to secrete additional corticosteroid which are recovered from normal patient during pregnancy[12]. During the last trimester there is a reduction in the demand for additional sodium chloride. When

maintenance therapy has included a mineralocorticoid, this should be curtailed but prompt resumption is required after delivery. This suggest some mineralocorticoid production by the placenta. An adrenal crisis is more likely to develop during the first twenty-four hours after delivery than any other time during the child bearing incident[7]. This results from inability of the adrenals to meet the stress of labour.The loss of biologically active placental steroids has been suggested as an additional factor, but is as yet improved. The muscular exertion of labour may be an important factor. To prevent this reaction cortisone 200mg daily during labour and first 48 hours after delivery is recommended. It should be given as 50mg six hourly, intramuscularly during labour and orally thereafter. The blood pressure as determined by hourly reading is the best guide to the adequacy of the dosage, a fall indicating the need for further cortisone. After the first two days of the puerperium the dose of cortisone is gradually reduced to the previous maintainance level, the blood pressure being checked four hourly [9].

Conclusion:

Patient with Addison's disease can expect a normal life expectancy if their adrenal insufficiency is diagnosed and treated with appropriate replacement doses of corticosteroids and if required with mineralocorticoids. Adrenal crises can occur in patients who stop their medication or who experience stress such as infection, trauma, surgery, pregnancy. Pregnancy with Addison's disease should be managed by obstetrician and endocrinologist. Vomiting and diarrhoea should be managed promptly with injection hydrocortisone. Patient should always carry addisonian crisis card. The delivery must be in tertiary hospital, where stress should be managed by inj. hydrocortisone and postpartum haemorrhage should be managed properly to save the life of the mother.

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Caudal Regression Syndrome - A Case Report and Literature Review

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Abstract:

Background and Purpose: Caudal regression syndrome (CRS) is a rare congenital abnormality in which a segment of the spine and spinal cord fails to develop. The severity of the morphologic derangement inversely correlates with residual spinal cord function. The caudal regression syndrome is frequently associated with maternal diabetes. The exact etiology is elusive, though maternal diabetes is one of the important factor; genetic factors, and hypoperfusion might play roles. Recently, the role of teratogens has been studied in animal. Here we report a case of CRS of a newborn baby of diabetic mother.

Methods: The history of the patient was taken from parents and physical examination was done. Plain radiographs, USG of abdomen and other investigations were done for evaluation.

Results: Agenesis of lower three thoracic, lumbar and sacral vertebrae with multiple congenital anomalies were observed. Lower limbs showed hypoplastic and talipes equinovarus. Hip joints were fixed, flexion contracture of the knees and webbing of Popliteal fossa were present. Other anomalies were dextrocardia and duplex right kidney.

Conclusion: CRA is a rare congenital anomaly associated with maternal diabetes. Control of diabetes is necessary to reduce the risk of occurrence.

(J Bangladesh Coll Phys Surg 2011; 29: 166-169)

Introduction:

Incidence of CRS varies from 1:7500 to 1:60,000 live births[1]. The majority of cases of CRS are sporadic, partial genetic contribution has been reported[2]. However it occurs in about one in 350 infants of diabetic mothers, which is about 200-fold increase incidence in diabetic patient than general population[3].

The syndrome has been occurring more frequently in the offspring of diabetic than non-diabetic mothers. Although hyperglycemia in the early stages has been implicated, the pathogenesis remains unknown. Trauma, nutritional problems, toxic agents and genetics are the other factors suggested in the aetiology[4].

It has also been hypothesized that hyperglycemia leads to release of free radicals from the influx of glucose across injured cell and mitochondrial membranes. These excess free radicals can be teratogenic; prostaglandin imbalance, amino acid abnormalities ultimately leading to disruption in signal transduction[5]. Animal experiments have shown that CRS could be induced by retinoic acid, diethylpropion, lithium, sulfamide, cadmium, lead, ochratoxin A, radiation, hyperthermia, organic fat solvents, and 6- aminonicotinamide. In addition vitamin A deficiency may be responsible for CRS. Familial occurrence of CRS has been reported, but no Mendelian pattern of inheritance has been established[2]. A recent study provides evidence of the homeobox gene HLXB9, but a possible role for this gene has not been established yet[6].

CRS is thought to arise from a defect in induction of caudal elements of the embryo before the 7th week of gestation[7]. The exact process leading to the development of CRS has not been established, although it has been proposed that one or more processes of primitive streak migration, primary or secondary neurulation, or differentiation are compromised[4,5]. Bohring et al.[8] postulate that the spectrum of congenital malformations observed in CRS represents abnormalities in blastogenesis and is due to disturbances of a primary embryonic field. The defects of the primary field lead to failure of axis formation, midline, primitive node and streak, gastrulation, segmentation of the paraxial mesoderm, laterality determination and cardiac formation.

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CRS is characterized by agenesis of spine to a variable degree. The orthopedic, gastrointestinal, genitourinary and cardiac anomalies are commonly seen with this condition[9]. CRS may range from absent coccyx as an isolated finding without neurologic sequelae to sacral or lumbosacral agenesis[10]. Akhter et al. have described a syndrome of sirenomelia in which the baby had limb fusion, tracheoesophageal fistula and absent genitalia[11]. In less complete varieties there may be only sacral hypoplasia and urinary tract infection; therefore it has been suggested that the sacrum should be examined in all cases of urinary tract infections in the child born to diabetic mothers[12].

Diagnosis of CRS can be made in the first trimester by noting the short crown – rump length. Sonography in second or third trimester can also demonstrate the absence of sacrum and shortened femurs. The legs may be flexed and abducted at the hips, and there may be clubfeet. Sonography may detect associated urinary anomalies, such as renal agenesis, cystic dysplasias, caliectasis and gastro-intestinal anomalies, such as duodenal atresia. Diagnosis is usually made on routine prenatal ultrasound examination. In cases with oligohydramnios in whom diagnosis is not clear, an MRI examination may be performed[13,14]. We are reporting this case because of rarity.

Case report:

A 30 year-old diabetic mother gave birth to a female baby following 37 weeks gestation by caesarean section . Indication of caesarean section were gestational Diabetes mellitus, pregnancy induced hypertension and breech presentation.

Maternal diabetes was detected at third trimester. She was on irregular antenatal check up. Her HbA_1C was 9.1%. Antenatal ultrasound done on single occasion showed oligohydromnious but no fetal abnormalities were detected.

At birth, we noted multiple abnormalities in the baby. Her weight was 2511g (AGA), length 40 cm (below third centile). Head circumference was 35 cm (AGA) but dolicocephalic with normal anterior fontanelle. She had low hair line and low set ear. Chest examination showed broad chest with wide apart nipples, apex beat was on right 4th intercostal space, heart sounds were more prominent on right side and no murmur was present. Lower limbs showed hypoplasia muscle wasting and talipes equinovarus. Lower thoracic, lumbar and sacral vertebrae could not be palpated. Hip was also hypoplastic and there were dimples on the lateral aspect of both thighs overlying the greater trochanters. Hip joints were fixed in position of flexion, abduction and external rotation. There was flexion contracture of the knees and webbing of Popliteal fossa. Movement of joints were restricted in lower limbs. The bladder was not distended and the anus was normal in position. Her upper limbs were normal. X-Ray of skeleton showed 8th & 9th thoracic hemi vertebrae, agenesis of lower three thoracic, lumbar and sacral vertebrae, anterior widening of all ribs, anterior forking of right 6th & 8th ribs, rudimentary hip bones, non ossification of left fibula and fracture of left femur and tibia. were noted. Chest x-ray showed dextrocardia, USG of abdomen revealed duplex right kidney.

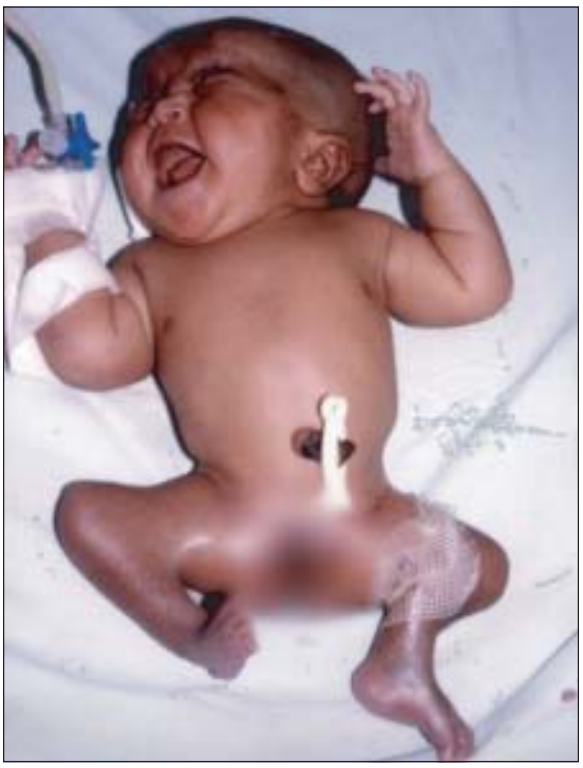

Fig-1: *Shows flexion contracture of the knees, webbing of Popliteal fossa and talipes equinovarus.*

Fig-2: rudim

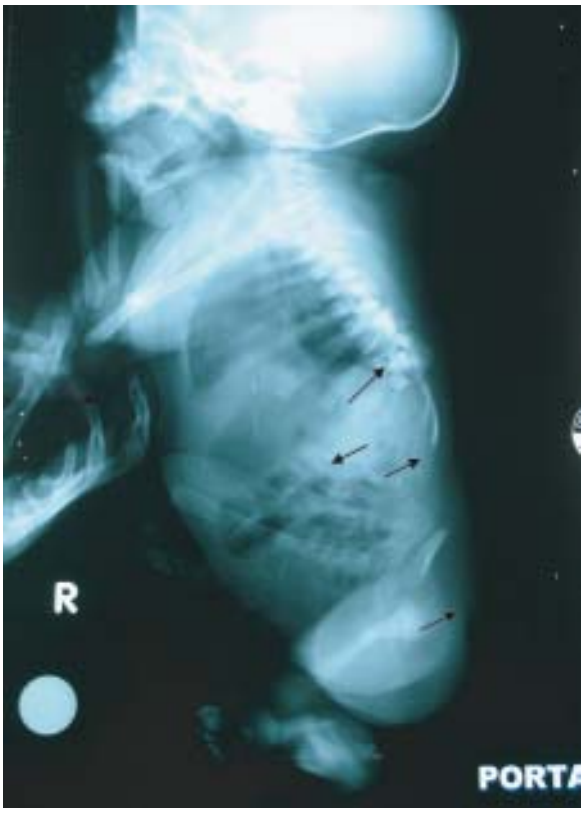

Fig-2: *Shows 8th & 9th thoracic hemi vertebrae, agenesis of lower three thoracic, lumbar and sacral vertebrae and rudimentary hip bones.*

Discussion:

CRS occurs in 0.2 to 1% of pregnancies of women with diabetes, and about 15–25% of cases of CRS are associated with either type I or type II diabetes mellitus in the mother[15]. Women with diabetes who are dependant on insulin are 200–400 times more likely to have a child with CRS than women without diabetes. Thus making CRS the most characteristic foetal abnormality of diabetic embryopathy[16].

In patients with good diabetic control during the first few weeks of pregnancy, the risk of congenital malformations is not significantly different from that of the general population. However, history of maternal diabetes is present in only 16% to 22% of infants with CRS indicating an environmental contributing factor[17]. In our case CRS was probably due to maternal uncontrolled diabetes; although diabetes was diagnosed in third trimester but we can not be very sure about the glycaemic control in first trimester as the glucose profile and HbA_1C could not be done as needed due to the poor compliance of the patient.

Depending upon the extent of spinal malformation, five types have been described by Renshaw, the most severe being sirenomelia[18]. According to Renshaw the patient in this study can be classified as Type III.

Orthopaedic anomalies like gluteal anomalies, scoliosis, and talipes deformities in 12%, and progressive deficits like back and leg pain present in 30% cases in different study[7], But in our patient lower limbs was hypoplastic with muscle wasting and talipes equinovarus. There was also fixed flexion, abduction and external rotation of hip joints; webbing of popliteal fossa and restricted movement of joints of lower limbs in our patient. In one study, hip-knee-flexion contracture, equinovarus deformity of foot associated with popliteal webbing were the prominent orthopaedic abnormalities, there was no associated upper limb abnormalities which was similar to our study [19]. In same study radiographic documentation showed total agenesis of the sacrum with subtotal lumbar agenesis and the lowest lumbar vertebrae were resting above an iliac amphiathrosis[19]; in the present study lower thoracic, lumbar and sacral vertebrae could not be shown radiologically. In another study, a baby girl was delivered whose lower limbs were hypoplastic and held in a position of flexion both at the hips as well as the knees. She had bilateral talipes equinovarus[20].

Congenital cardiac disease was found in 24% cases with CRS in which Tetralogy of Fallot is the most common cardiac anomaly[1]. Martinez-Frias presented data suggesting that the incidence of transposition of the great vessels was significantly increased in the offspring of diabetic mothers[21]. Dextrocardia was detected on postnatal examination in present study that was different from other study.

Other malformations such as Chiari I malformation is associated with caudal regression syndrome[22]. In the present case, no cerebral anatomical abnormality was seen. Genito-urinary disease like hydronephrosis, renal agenesis, epispadias and hypospadias was present in 24% cases, but in our patient duplex kidney was detected by ultrosonography[4,5].

The prognosis depends on the extent of spinal abnormalities. The greater the extent of spinal anomalies, the greater the neurological deficits and

consequently the greater orthopaedic and neurological support is required. The main cause of morbidity is usually neurogenic bladder causing urologic impairment and progressive renal failure[4]. The prognosis in this neonate was unlikely to be good as there was high termination of spine and fixed flexion of both the lower limbs; long-term neurological, urologic and orthopaedic complications may develop.

Conclusions:

It has been known that diabetes in pregnancy can have severe adverse effects on foetal and neonatal outcomes. CRA is an uncommon abnormality, the associated disabilities can be severe and genetic counselling is necessary. In this case maternal diabetes may be inciting agent. Treatment is difficult and multidisciplinary, largely supportive, need intensive and long-term attention, so prevention the ultimate goal. Control of diabetes before conception and in early pregnancy is presumed to reduce the risk of occurrence.

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Giant Schwannoma of Median Nerve at Forearm

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Abstract:

Schwannomas are common benign nerve tumors occurring in the peripheral nerves. A very large schwannoma of more than 7 years duration, originating from the median nerve in the forearm in a 40 years old woman, is reported. There was numbness and tingling sensation in the forearm and hand. It was 18 cm in length and 8 cm in diameter. On the palm, there were signs of sensory disturbance with atrophy on the thenar muscles. Surgical removal was performed under operating microscope by separating the nerve fascicles from the tumor. There were 2 more tumors (1.5x2cm) on median nerve at elbow above the mentioned one. Histological examination revealed schwannoma. At 3.5 year follow-up, the patient was asymptomatic with excellent relief of symptoms with good forearm and hand motor function, though thenar atrophy persisted. The tumor did not recur. Although cases have been reported in the literature, this is probably the largest ever described with 2 more adjacent schwannomas.

Key words: ***Median nerve, Giant schwannoma, Forearm***

(J Bangladesh Coll Phys Surg 2011; 29: 174-176)

Introduction:

Schwannomas are benign neoplasm arising from schwann cells of peripheral nerve sheath. In 1935, Stout [1] first described this as fibrosarcoma, though he changed his opinion in 1949 after observing the outgrowth of schwann cells in vitro from such tumors. Median nerve is one of the common sites for schwannoma. Pain and paresthesias may occur when the tumor reaches large size. Surgical removal of a Schwannoma is usually curative. Although cases have been reported in the literature, this is probably the largest ever described with 2 more adjacent schwannomas of median nerve.

Case report:

A 40 year-old female presented with gradually enlarging swelling in her forearm for last seven years. There was numbness, tingling sensation with recent onset pain in right forearm and hand for last 03 years. On examination there was a mass in whole front of right forearm measuring about 18x8 cm, seem to be fixed with muscles, non tender and firm to cystic in consistency. There was a scar over skin due to herbal application (Figure-1A). There was thenar muscle atrophy on right side with mildly reduced modalities of sensation in hand along the distribution of median nerve. The patient had no stigmata of neuro-fibromatosis. Preoperative percutaneus FNAC revealed schwannoma. The tumor was exposed by long anterior forearm incision (Figure-1B&2A). Under operating microscope widely spreaded median nerve fascicles over the tumor surface were preserved carefully during dissection of the tumor(Figure-1B). After removal of the tumor median nerve was examined proximally and distally. Two small tumors (1.5x2cm) were found proximally at the elbow and just above the elbow. These two tumor were also removed carefully under the microscope. There was cystic degeneration in the large tumor, found after sectioning before sending for histopathology. Histology revealed schwannoma in all tumors (Figure-2B). Post operatively(3.5 years after operation),patients all symptoms disappeared, her motor function is good both in forearm and hand, sensation is normal but thenar atrophy still persisted without any recurrence of tumor.

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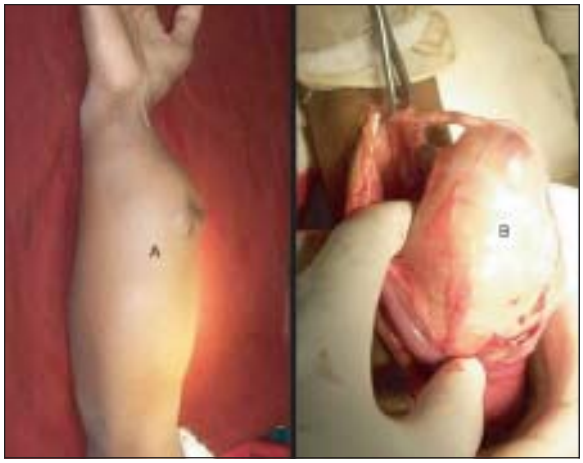

Fig.-1:*A-preoperative picture of forearm and hand; B-Per-operative picture(Tumor and median nerve seen).*

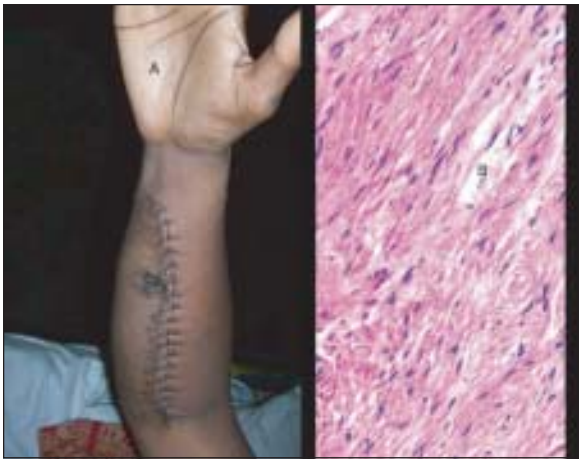

Fig.-2:*A-postoperative picture of forearm and hand; B-Microphotograph of histopathology(arranged and wavy tumor cells in long fascicles);[H&E, X200]*

Discussion:

Schwannomas are benign, slowly growing and encapsulated[2] tumors arising from the neurilemmal sheath, common in all ages, without obvious preference to either sex[3]. Most patients are 40 years old and their lesions ordinarily are soli-tary.[3] Most schwannomas are found in peripheral nerve fibers in the limbs, head, and neck. In a small proportion of cases obvious stigmata of Von Recklinghausen's disease are accompanied[3,4].

Cut section of schwannoma shows grey white in color, whorled with areas of hemor-rhage[4]. Histologically, schwannomas consist of compact cellular lesions (Antoni type A tissue) and loose, hypocellular myxoid lesions with microcystic spaces (Antoni type B tissue)[5,6].

Malignant transformation has only been reported on rare occasions[7]. Most Schwannomas

occur as a solitary lesion, but they can occur as multiple lesions and can affect one or several nerves[8]. In the extremities, they may arise from any of the peripheral nerves, with a predilection for the peroneal and ulnar nerves[7]. The tumor is usually first seen as a painless, asymptomatic mass and is present several years before it is noticed. The tumor is usually less than 5cm in diameter. Pain and paresthesias may occur when the tumor reaches sufficient size to compress the involved nerve[7].

Surgical excision is the treatment in schwannoma. The first priority in the treatment of benign nerve sheath tumors is to prevent axonal damage[9]. In contrast to a neurofibroma, the schwannoma can be separated from the involved nerve. Initially, the tumor may appear attached to nerve fibers, and on occasion, a few nerve fibers may need to be resected with the tumor. The nerve should be inspected for the possibility of additional tumors[10] as we found additional two tumors on the same nerve.

In our case we found that the tumor was slow growing, initially asymptomatic and later it produced symptoms due to bigger size. Even in such a big tumor nerve fibers were easily identified, separated from the tumor and well preserved using microsurgical techniques .Without microsurgical techniques preservation of nerves fibers and fascicles are seem to be difficult. Careful proximal and distal checking of involved nerve is very important to identify the existence of other smaller schwannoma that we found here. In this long standing huge tumor degenerative changes and rarely malignant changes can take place but here fortunately only cystic degeneration took place.

Surgical removal of a Schwannoma is usually curative. Recurrence is rare and relief of symptoms is common[7].

Conclusion:

In benign schwannoma, even in very big and long standing tumor very good result can be achieved with proper microsurgical treatment.

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Wilson's Disease in a Young Girl with Abnormal Behavior

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Abstract:

Wilson's disease is an inborn error of copper metabolism caused by a mutation to the copper-transporting gene ATP7B. Epidemiologic clustering of mutations to the ATP7B gene based on ethnicity has been observed. Diagnosis of the condition is made primarily on the basis of clinical findings, presence of the Kayser–Fleischer ring, and biochemical and radiological parameters. The young patient's usual presentation is through liver involvement. Uncommonly the young group can present with neuropsychiatric manifestation. Behavior disorder like bizarre activity, personality change, affective or schizophrenic presentation may be the initial presentation of Wilson's disease. Choreoathetoid movement although not common can also be presented in such patient. A young girl with abnormal behavior with atypical presentation was recently observed in one of the medicine unit of Dhaka Medical College.

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Introduction:

Wilson's disease (WD) is an inborn error of copper metabolism caused by a mutation to the copper-transporting gene *ATP7B.* The disease has an autosomal recessive mode of inheritance, and is characterized by excessive copper deposition, predominantly in the liver and brain[1]. The majority of patients with WD present with either predominantly hepatic or neuro psychiatric symptoms, and with either clinically asymptomatic or symptomatic liver involvement[2]. About half the patients with Wilson's disease have neurological or psychiatric problems. Most patients initially have mild cognitive deterioration and clumsiness, as well as changes in behavior. Specific neurological symptoms then follow, often in the form of parkinsonism (increased rigidity and slowing of routine movements) with or without a typical hand tremor, ataxia (lack of coordination) or dystonia (twisting and repetitive movements of part of the body) and or choreoathetoid movement[1,2], Psychiatric problems due to Wilson's disease may include behavioral changes, depression, anxiety and psychosis[1,2]. Psychiatric features include emotional lability, impulsiveness, disinhibition, and self-injurious behavior. Kayser-Fleischer rings are observed in up to 90% of individuals with symptomatic Wilson disease and are almost invariably present in those with neurologic manifestations[1,3]. Kayser-Fleischer rings are a useful diagnostic sign and they are considered pathognomonic of Wilson's disease when accompanied by neuropsychiatric manifestations[3]. Here is a case report of a young girl with abnormal behavior who had multiple psychiatrist consultation before and ultimately confirmed as a case of Wilson's disease.

Case Report:

Miss. S. 13 year-old class VI student from Jinjira, Dhaka presented with complaints of progressive behavioral disorder for 8 months characterized by undue smile, recurrent transient mutism, self neglect, somnambulism and occasional cry. There was no prior psychiatric illness. Although she was euphoric and easy going child with normal upbringing and routine school activity, her academic success was not up to the mark. An episode of fever with complete recovery was observed at the initiation of her illness. There is consanguinity in her parents but no first-degree family members are having any physical or psychiatric illness. Her premorbid personality was normal except she was found introverted but elated and maintained disciplined life.

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Her home life, relations with peer, leisure activity were quite normal. On query there was no sexual abuse, conflict, illicit drug history or criminal act. Since the abnormal behavior started, she is reluctant to take food and start loosing weight. There was no history of anorexia, abdominal pain, nausea, vomiting, diarrhoea during food withdrawal period. There was no dysphagia or regurgitation of food material. Her sleep pattern was normal except occasional somnambulism when she tried to get up from sleep and walk around home. She took advice from general practitioner and psychiatrists repeatedly for following 3 to 4 months and was treated with multiple antipsychotics and anidepressant drugs without any significant benefit. As there was no improvement, parents took her to a specialist private hospital where she was diagnosed as mental retardation and anticonvulsant was added with antipsychotics. Her status remains unchanged.

For the last 5 months she experienced intermittent purposeless, repetitive movements of limbs (more on left upper limb) and repeated scalp scratching

which fluctuates from time to time. There is no history of head or neck trauma, headache, convulsion, unconsciousness, jaundice, bony or joint pain or ENT ailments. There is also no history of alimentary, cardiovascular or respiratory symptoms during any period of her illness. On examination she is undernourished (BMI-14.78) with stable vital sign. She is well groomed, euphoric with undue smile. Occasional mutism with complete spontaneous recovery was observed. There was no abnormality like thought disorder, preoccupation, perception, cognitive difficulty. Although concentration was lacking, she is well oriented with a remarkable memory. Her mini mental state score was 9.

She had a clumsy gait with choreoathetoid form of abnormal movement and repeated scalp scratching. There was no dystonia, akathisia, tremor, rigidity or bradykinesia. There is Kayser –Fleischer (K-F) rings present in both eyes (Fig.-1). The naked eye finding was confirmed with slit lamp examination. Rest of neurological examination was unremarkable. Fundoscopic examination revealed no cataract and with high power, K-F ring was observed. All other systemic examination was normal.

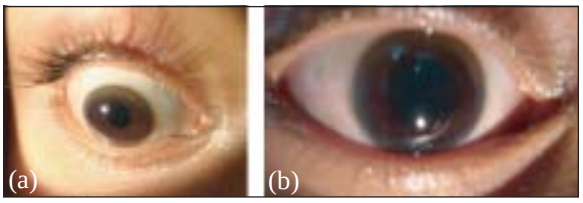

Fig.-1 : *a) The Kayser–Fleischer ring around the cornea b) This is a characteristic finding observed in most periphery of the cornea caused by deposition cases of neuropsychological Wilson's disease of copper in Descemet's membrane.*

Investigations of the patient revealed Hb 10.3 gm/dl, ESR in first hour 8mm total count of WBC 3100/cmm, Poly 43%, Lympho 53%, Monocyte 03% Eosino 01%, Basophil 00%, Platelet count 1,20,000/cmm. Peripheral Blood film showed Leucopenia and thrombocytopenia. S.Creatinine 1.10 mg/dl.

Urine routine examination was Normal, Blood sugar (2 hrs ABF) was 7.06 mmol/L, SGPT- 27u/l, S albumin-36 gm/l, S Globulin-34gm/l, A:G ratio 1.05:1, Prothombin time was 18.8 sec(INR-1.53). Chest X ray revealed no abnormality, Upper GIT endoscopy was normal. USG of whole abdomen revealed Liver is normal in size with coarse hepatic parenchymal echotexture consisted with sonographic features of early change of chronic parenchymal liver disease. Serum ceruloplasmin was 0.02 g/L (normal range-0.2-0.6 g/L).Analysis of copper in urine- 197±1 pgm/24 hours (normal range<100 pgm/24 hours). MRI of brain shows in T2W and FLAIR images of hyperintense areas in pons, both basal ganglia regions and splenium of corpus callosum. There is distinct "the face of the giant panda" and occasionally "the face of the miniature panda" sign suggestive of Wilson's disease (Fig.-2). MRI of liver to estimate the copper content could not be done due to lack of facility. The diagnosis was confirmed as Wilson's disease'.

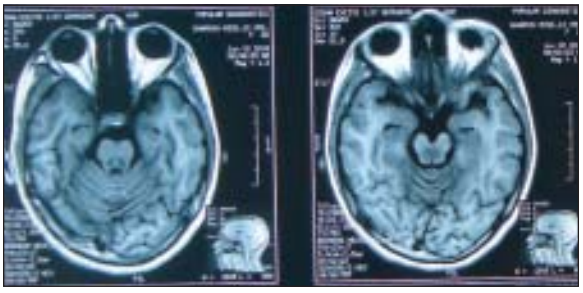

Fig.-2 : *MRI showing the distinct "the face of the miniature panda"*

Case summary:

Characteristics and unusual features in this patient of Wilson's disease is her initial presentation of bizzare behavior and which let her to be consulted by half a dozen psychiatrist. The disease was not suspected as the common psychiatric manifestation of psychosis, depression or personality changes were not prominent rather somnambulism, mutism, undue smile and self neglect. These features are uncommon in Wilsons disease.

The common neurological manifestation of Wilson's disease like dystonia, parkinsonism, scelorotic type or cerebellar type was also not seen in this patient. Her choreoathetosis pattern of neurological sign are also an uncommon presentation and thus the suspicion was not sought for 8 months before she was seen comprehensively in medicine unit of DMCH. The patient was treated with Penicillamine (250 mg slowly escalating to maximum dose of 1000 to 1500 mg) and zinc acetate(75 mg/day) with pyrodoxine and vitaminE. She was initially followed up on every two weeks for two months with partial recovery of her neuropsychiatric manifestations and plan to follow up to see the complete response. Her family screening was done and no presymptomatic patient was observed in the family.

Discussion:

The mean age of onset of 'neuropsychological WD' is in the second to third decade, although it has been reported as late as 72 years of age[4]. The majority of patients become symptomatic before the age of 50[5]. In the Indian subcontinent, the disorder tends to manifest one decade earlier, which is possibly related to the traditional practice of cooking and eating food using copper utensils[6].The statement is characteristically seen in this young girl as she is only 13 yrs of age derived from lower middle class family and home environment of similar practice of cooking. The reported percentage of patients with psychiatric symptoms as the presenting clinical feature is 10-20%[7]. The range of psychiatric abnormalities associated with Wilson disease has been divided into 4 basic categories as behavioral, affective, schizophrenic like and cognitive.

About one-third of patients experience psychiatric disturbances[8]. These disturbances can manifest as changes in school-related or work-related performance, attention deficit hyper activity disorder, impulsivity, paranoid psychosis, obsessive behavior, depression, suicidal tendencies or bizarre behavior, and can occur early or late in the disease course[7,8].In this case report the patient have transient mutism, undue smile, somnambulism, occasional cry and self neglect indicating the bizarre form of behavior as early presentation. In neurological presentation there may be variable of presentation in Wilson's disease. Patients commonly present with extrapyramidal, cerebellar and cerebral-related symptoms,[5,9] in either a subacute or a chronic fashion. An acute presentation is seen in rare cases. The most common initial presentation is bulbar symptoms characterized by difficulties with speech and swallowing, and drooling[9].

These symptoms are related to dystonia of the bulbar muscles, or pseudobulbar palsy. Abnormal posturing caused by limb dystonia interferes with writing and walking, and features of parkinsonism commonly occur in combination. A few patients present with cerebellar features such as unsteadiness of gait, and in coordination of speech and limbs [10]. Rarely, patients exhibit chorea or choreoatheroid movement(10% cases) of generalized or localized distribution over one half of the body[11]. In this case report we observed choreoathetoid movement indicating a rare form of presentation.

The most important sign in Wilson's Disease is the KF ring (Fig.-1), which is best visualized with the use of a slit lamp. The presence of the KF ring reflects copper deposition in the brain. Wilson's Disease is also associated with sunflower cataract brown or green pigmentation of the anterior and posterior lens capsule. In our patient the K-F ring was ovious in naked eye; Slit lamp confirmed bilateral symmetrical K-F rings which is diagnostic in neuropsychiatric presentation of Wilson's Disease. There was no cataract. Levels of ceruloplasmin are abnormally low (<0.2 gram/liter) in 80-95% of cases[2]. The Wilson's disease can be diagnosed confirmly in a patient with K-F ring when the ceruloplasmin level is <0.2gram/liter when the patient present with neuropsychiatric manifestation[1,2,7] . The diagnostic criteria fullfilled in this case report Urine copper are elevated in Wilson's disease and levels above 100 μg/24h (1.6 μmol/24h) confirm the diagnosis[2,7]. The urinary copper in this case report was 197±1 pgm/L spot collection.

Most patients who present with neuropsychiatric manifestations have cirrhosis of liver which may or may not be clinically evident. Biochemical and radiological

evidence may be obvious in such cases. In our patient the prothombin time was 18 sec with INR 1.53 and ultasonography of hepatobilliary system revealed features of cirrhosis. Imaging plays an important role in both the diagnosis of Wilson's Disease and the monitoring of patients during therapy. MRI of brain is more sensitive and it shows hyperintensity in lentiform nuclei, pons, midbrain and occasionally in cerebral cortex. Some WD-related changes exhibit characteristic features on MRI, for instance 'face of the giant panda', which is seen in T2-weighted images of the midbrain [12], and 'face of the miniature panda'(Fig 2), which can be seen in the tegmentum region of the pons in the same sequence. In our patient MRI of brain revealed features of face of giant panda. MRI copper content estimation of liver could not be done due to lack of facility. Family screening was done and no presymptomatic patient was observed in the family. A possible new mutation related Wilson's diseases was thus observed in this case report.

Consent process: Written informed consent from the legal guardian was done for imprinting her case report including pictorials.

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Positron Emission Tomography (PET) in Clinical Medicine and Bangladesh Perspective

MSH MAJUMDER

Summary:

Positron emission tomography (PET) imaging devices were first developed in the 1970. In the last thirty years PET imaging has been extensively used in research, but only in the last few years the technology has become more widely available for clinical applications. Most of the early works with PET focused on brain metabolism, partly because of the smaller size of detector needed to study head. With the introduction of improved instruments and suitable radionuclide, applications in oncology have developed into the major clinical uses of PET. Myocardial viability is usually assessed using perfusion studies with Signal photon emission computed tomography (SPECT) but in case of inconclusive result, metabolic assessment with short-lived PET tracers may be more decisive. PET allows study of body function; it helps detection of alterations in biochemical processes that suggest disease before changes in anatomy are apparent with other imaging tests, such as computed tomography (CT) or magnetic resonance imaging (MRI). The future of PET imaging is bright. New geometries are being studied especially to develop organ specific imaging devices, new detector materials are being developed and techniques for reconstruction are improving. However, perhaps the most important need for further utilization of PET imaging is the development of new radio-pharmaceuticals or radiotracer compounds and better understanding of cellular physiology and metabolism in disease states. Until recently, Bangladesh had no positron emission tomography scanner, though the neighboring countries like India, Pakistan, Thailand & Singapore have PET scanning for last several years. PET scanning in Bangladesh has been introduced by a multidisciplinary tertiary level private hospital – United Hospital, Gulshan, Dhaka recently.

Key Words: Position emission tomography Positron 18 Flurodeoxyglucose

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Introduction:

The existence of the positron in the atom was predicted by British physicist Paul Dirac in the year 1928. Rutherford (1910) established solar atomic model - a positively charged nucleus surrounded by a cloud of negatively charged electrons; later, it was redefined by Bohr (1913) that stated electrons travel in discrete orbits circling around the dense nucleus. Paul Dirac arrived at his prediction by applying the theory of relativity of physicist Albert Einstein to observations of the motion of particles with electric charge. Based on Einstein's theory and mathematical analyses of the motion of electrons, Dirac assumed the existence of a new kind of particle that was identical to the electron in all ways except the sign of its electric charge[1, 2]. Dirac's theoretical particle received the name positron, although the scientific community was reluctant to accept this finding. This reluctance was vanished in 1932, when American physicist Carl David Anderson discovered the same particle while tracking the paths of subatomic particles. Some of the paths Anderson analyzed had the same curve as electron paths but with positive charge. Thus, he indicated the existence of particles that possessed the characteristics Dirac had predicted earlier mathematically[2, 3].

Positron is an elementary or fundamental particle identical to the electron except for its electric charge and its magnetic moment (a property that determines how it behaves in a magnetic field); and it can not be divided into smaller units. All elementary particles have basic characteristics called mass, charge and spin. The positron has the same mass - amount of matter - as the electron, and the same spin. The two particles also have the same amount of electric charge, but the positron's charge is positive and the electron's is negative. For this reason, the positron is sometimes called a positive electron. Although positrons and electrons have a measurable mass, charge, and spin,

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they have no measurable size, shape, or structure. They are considered as point like. Other point like elementary particles includes neutrinos and quarks. Every elementary particle has an equal and opposite antiparticle. The positron is the antiparticle of the electron. Just as particles combine to form ordinary matter, antiparticles combine to create antimatter. When a particle and its antiparticle collide, they destroy each other releasing energy. This feature makes positron useful in creating Positron Emission Scan. Tomography is a special X-ray or imaging technique that blurs out the shadows of superimposed structures to show more clearly the principal structures being examined. To create a Positron Emission Tomography scan, positron emitting substances are injected into the body. Computers track the energy released inside the body by positron- electron collisions and use this information to form images. Positrons, as positron emission tomography scan, have uses in medicine and in industry. PET scans, as shown in Figure-1A & B are especially helpful in identifying and locating brain tumours, lesions in brain and other parts of the body [2, 3,4,5,6].

Positron sources can be natural as well as artificial. Positrons are naturally produced within stars and by collision of cosmic rays. They can also be produced artificially, called positron-emitting radionuclide in the laboratory in a cyclotron machine by interaction of gamma rays with a very heavy atom[2]. The radionuclide emit positron which after moving a very short distance,

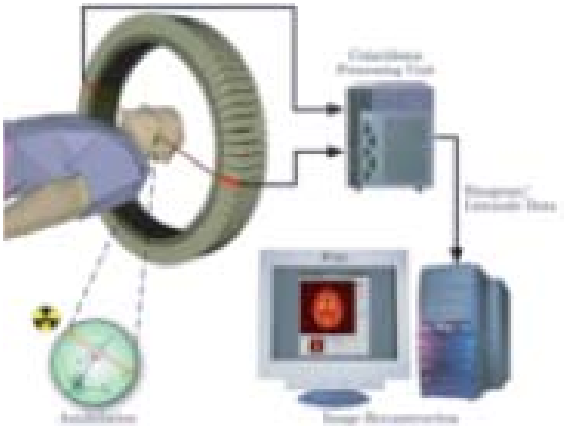

Fig.-1A: *PET acquisition process.*

Fig.-B: *Typical PET facility.*

encounter and combine a nearby electron; and destroy each other. The destruction of both positron and electron leads to simultaneous production of two 511 kev (killoelectron volt) photons that travel in opposite direction at an angle of 180^0. This is called annihilation reaction or radiation(Figure 2). Such coincident pairs of photons are to be recognized by detector placed on opposite sides of position of source of radiation[2,3].

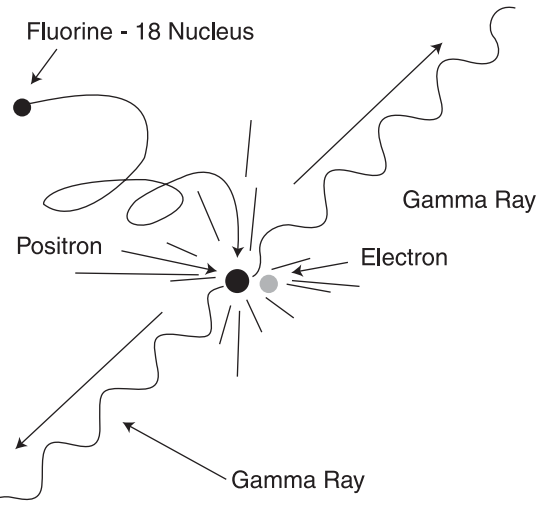

Fig.-2: *Positron emission and annihilation radiation, producing 2 gamma photons which travel in opposite direction.*

Radiopharmaceutical Development For 'PET' Imaging

Positron emitting radionuclides were discovered in the 1940. The only isotopes of carbon, nitrogen, and oxygen that are suitable for imaging in vivo are the positron

emitters such as ^{11}C, ^{13}N, and ^{15}O. Unfortunately, all these nuclides are short lived, so that they can only be used in close proximity to the cyclotron in which they are produced. Even so, they have been used to label a wide range of naturally occurring small organic molecules for physiological research and larger molecules for pharmacological investigations, but none are yet in routine clinical use. PET imaging was initially based on the use of ^{15}O labeled to O_2, CO and CO_2 primarily because the Allis Chalmers cyclotron was a deuteron machine and was primarily used to producing ^{15}O. ^{15}O labeled carbon monoxide (CO) provided a means of measuring regional blood volume and blood flow in research tool. Ter-Pogossian and Power had demonstrated that ^{15}O labeled water could be used to measure blood flow in brain and other organs long before PET was developed[7, 8].

One of the prime reasons for the importance of PET in medical research and clinical practice is the existence of positron emitting isotopes of elements such as carbon, nitrogen, oxygen and fluorine which may be processed to create a range of tracer compounds similar to naturally occurring substances in the body. The tracer compounds are carbon monoxide, carbon dioxide, water, methionine, ammonia, flurodeoxyglucose, etc. The physiological processes or functions involved by these radiotracer compounds are blood perfusion, protein synthesis, glucose metabolism, receptor binding's etc[9]. One of the factors most responsible for the acceptance of positron imaging was the development of radiopharmaceuticals, particularly the development of ^{18}F labeled flurodeoxyglucose (18-FDG), which expanded the scope of PET imaging (Figure 3). Flurodeoxyglucose is basically a glucose analogue molecule, where one oxygen atom is replaced by an atom of fluorine[9, 10]. Currently, the mainstay of clinical PET is deoxyglucose labeled with Fluorine-18 (18-FDG). In a normal subject about half of the injected dose is excreted in the urine in 2 to 2.5 hours after injection. The half-life of Fluorine-18 is 110 minutes, so a daily production is required, and the location of imaging needs to be within 1 to 2 hours of the cyclotron production site. Absolute measurement of glucose uptake into lesions or specific organs is difficult because of differences in the size and body composition of the patients, and individual variations in glucose metabolism. Approximate quantitation is achieved by using the Standardized Uptake Value (SUV), which is an estimate of the uptake of FDG into the lesion or organ of interest compared with the mean uptake in the rest of the body[8].

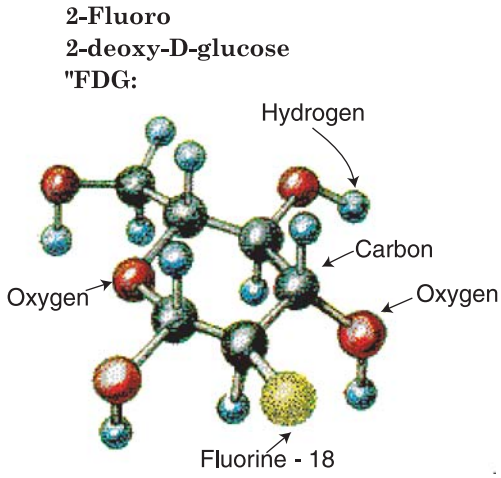

Fig.-3. *18-FDG, an analogue of glucose molecule, where an oxygen atom is replaced by a fluorine atom which is radioactive.*

Instrumental Development for Pet Imaging

The first application of positron annihilation radiation for medical imaging is well documented in the early 1950s by a simple positron scanner using two opposed sodium iodide detectors (Figure-4).

Fig.-4: *First clinical positron imaging device*

Several versions of the single pair of coincidence system were built and a hybrid scanner was developed in mid 1960s and the scanner was designed specifically for brain imaging and served that purpose for nearly a decade. Latter on, positron camera (PC-I), PC-II, PCR-I single ring and PCR-II cylinder have been developed (Figure-5).

Fig.-5: *Hybrid positron scanner.*

The recent introduction of luteum-based detectors, together with faster electronics in PET offers a further increase in sensitivity, so that examination times for whole body examination can be considerably reduced[11, 12, 13]. Using a dual or multiheaded gamma camera for PET has the obvious advantages that the same instrument can also be used for single photon imaging as well, but the performance of these systems is inferior to dedicated PET instruments. One of the major limitations of PET is lack of anatomical landmarks, particularly in the thorax, abdomen and pelvis and therefore PET images need to be interpreted in conjunction with CT or MRI anatomy for application in oncology[8].

PET-CT is the fusion of functional and anatomical information acquired almost simultaneously that lets us see the body and disease in a way that is diagnostically very useful (Figure-6).

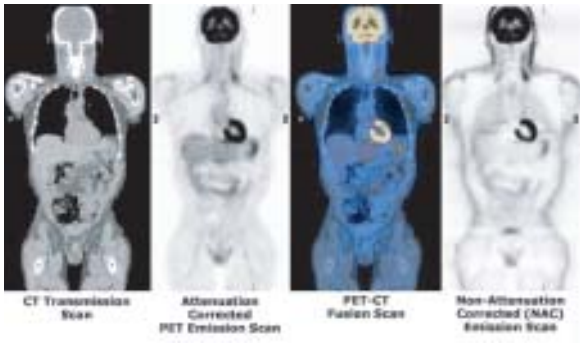

Fig.-6: *The CT scan, attenuation corrected PET emission scan, PET-CT fusion scan and Non-attenuation corrected (NAC) Emission scan.*

By combining the structural anatomic information with functional data, we are able to visualize form and function. An understanding of the normal and benign as well as the pitfalls and artifacts is essential for accurate information. The PET-CT scanner is essentially full ring coincidence detectors, the PET portion, physically mounted together with CT system of various types. Usually the CT transmission scan is acquired followed by the emission PET scan. Because the scanners are in the same gantry the patient remains on a single scanning table and in the same position for both parts of the scan. Therefore, they are intrinsically registered as seen on the fusion image. Images are presented and viewed in 3 planes (coronal, transaxial and sagittal) as well as a 3D maximum intensity projection, which can be rotated while viewing. The CT, corrected and uncorrected PET scans, as well as the fusion image can be viewed on a single page. Typically, the CT acquisition is performed first, followed by PET acquisition. The anatomical CT data can then be used to apply attenuation correction for the PET data and the resulting images can be displayed separately or fused together[4, 8].

PET Applications

Much of the early works with PET focused on brain metabolism, partly because of the smaller size of detector needed to study head. With the introduction of improved instruments allowing acquisition of whole body images in under an hour, applications in oncology, together with other areas, have developed into the major clinical use of PET.

Oncology: Over 90% of all PET scans in current practice are done in the field of oncology. Cancerous tissue has deranged glucose metabolism. Glucose uptake and glycolysis proceed about ten times faster in most solid tumors than in non-cancerous tissue. Tumor cells commonly experience hypoxia because they initially lack an extensive capillary network to supply the tumour with oxygen. PET scanning with radiotracer 18 FDG is widely used in clinical oncology. This radiotracer is a glucose analogue that is taken up by glucose-using cell and phosphorylated by hexokinase. Because the oxygen atom replaced by 18-F to generate FDG is required for the next step in glucose metabolism in all cells, no further reactions occur. This means that FDG is trapped in any cell which takes it up, since phosphorylated sugars cannot exit from the cell. This results in intense labeling of tissues with high glucose uptake, such as the brain,

the liver, and most caners. As a result FDG-PET can be used for diagnosis, staging, and monitoring treatment of cancer, particularly in Hodgkin's disease, non-Hodgkin's lymphoma, lung cancer, head and neck cancer.

Most types of lymphoma show avid uptake of FDG, and is suggested that those patient with most intense uptake at presentation have the worst prognosis. When PET has been used as a staging procedure for lymphoma, it has proved to be more accurate than CT. PET is more likely to determine the presence or absence of disease in lymph nodes that are close to the normal size limits. A fall in FDG uptake which may be seen after 1-2 cycles of chemotherapy is a useful predictor of clinical response. In patient with residual mass after radiotherapy and/or chemotherapy, PET is a fairly good predictor of future recurrence. Small cell lung cancer is usually multi-focal at the time of presentation, so surgery is rarely indicated. Since systemic chemotherapy is the mainstay of treatment, precise staging is less important than in surgical cases, and the use of FDG-PET is of limited value. Non-small cell lung cancer is much more likely to be amenable to surgery, so a careful staging is needed. FDG-PET is highly accurate in staging mediastinal lymph nodes in this condition, and is at least as accurate as the combination of CT scan and bone scintigraphy for detecting metastasis in the abdomen, pelvis and skeleton. Residual soft tissue abnormality after treatment may be non-specific on CT, and in this condition a negative FDG-PET study may eliminate the need for biopsy. About one half of non-calcified, solitary pulmonary nodules which present for investigations turn out to be benign. FDG-PET offers a non-invasive method for discriminating between benign and malignant nature with sensitivity about 95% and specificity greater than 80%, so a negative PET result is more reassuring than a negative biopsy. However, because individual scans are more expensive than conventional imaging with CT and MRI, expansion of FDG-PET in cost constrained health services will depend on proper health technology assessment[5, 9,15,16,17].

Neurology: PET neuroimaging is based on an assumption that areas of high radioactivity are associated with brain activity. What is actually measured indirectly is the flow of blood to different parts of the brain, which is generally believed to be correlated, and has been measured using the tracer oxygen (^{15}O). However, because of its 2-minute half-life, ^{15}O must be piped directly from medical cyclotron for such uses, and this is difficult. In practice, the brain is normally a rapid user of glucose, and since brain pathology, such as in Alzheimer's Disease (AD), greatly decreases brain metabolism of both glucose and oxygen, standard FDG-PET of the brain which measures regional glucose use may also be successfully used to differentiate Alzheimer's disease from other dementing processes, and also to make early diagnosis of Alzheimer's disease. Several radiotracers have been developed for PET that are ligands for specific neruroreceptor subtypes (e.g. dopamine D2, serotonin 5-HT1 A, etc) or enzyme substrates (e.g. 6-FDOPA for the AADC enzyme). These agents permit the visualization of neuroreceptor pools in the context of a plurality of neuropsychiatry and neurologic illnesses. A novel probe developed at the University of Pittsburgh, USA termed Pittsburgh compound-B (PIB) permits the visualization of amyloid plaques in the brains of Alzheimer's patients. This technology could assist clinicians in making a positive clinical diagnosis of AD pre-mortem and aid in the development of novel anti-amyloidal therapies[8, 14].

Cardiology: PET imaging utilizing FDG and other perfusion tracers provides valuable diagnostic and prognostic information in patients with ischemic left ventricular dysfunction and has comparable accuracy to competing technologies for detection of viability. In clinical cardiology, FDG-PET can identify so called hibernating myocardium but its cost effectiveness in this role versus SPECT is unclear[4, 17, 18].

Neuropsychology and Psychiatry: This aspect is to examine links between specific psychological processes or disorders and brain activity. Numerous compounds that bind selectively to neruroreceptors of interest in biological psychiatry have been radio labeled with ^{11}C or ^{18}F. Radioligands that bind to dopamine receptors (mu) and other sites have been used successfully in studies with human subject including disease such as schizophrenia, substance abuse, mood disorders and other psychiatric conditions[4].

Pharmacology: In pre-clinical trials it is possible to radio label a new drug and inject it into animals. The uptake of the drug, the tissues in which it concentrates and its eventual elimination, can be monitored far more quickly and cost effectively than the older technique of killing

and dissecting the animals to discover the same information. PET scanners for rats and apes are marketed for this purpose. Drug occupancy at the purported site of action can also be inferred indirectly by competition studies between unlabeled drug and radio labeled compounds known apriori to bind with specificity to the site[4].

PET Scans Safety:

PET scanning is non-invasive, but it does involve exposure to ionizing radiation. The total dose of radiation is small, however, usually around 7 mSv (milisevdvergh, radiation dose unit). This can be compared to 2.2 mSv average annual background radiation in the UK, 0.02 mSv for a chest X-ray, up to 8 mSv for a CT scan of the chest. Because the half-life of 18F is about two hours, the prepared doses decay significantly during the working day. If the FDG is delivered to the scanning suite in the morning, the specific activity falls during the day, and a relatively larger volume of radio pharmaceutical must be injected in later patients to deliver the same radioactive dose[4].

Bangladesh Perspective:

Bangladesh, having a population of 160 million people should have several PET Scanners. Our neighboring countries like India, Pakistan, Thailand, Singapore etc. have PET Scanners running for last several years. Dhaka, being central and capital city of Bangladesh, harboring about 15 million people needs to have regular PET scanner services to ensure modern treatment in certain fields. The modern PET system consists of a cyclotron machine, PET scanner, accompanied by CT or MRI setting, usually CT scanner. The cyclotron machine produces radionuclide and is the costlier part of the system. A cyclotron machine can produce the amount of radionuclide which can be supplied to 4-6 PET-CT scanners. So, by a single cyclotron, several PET-CT scanners can run. Once the cyclotron is installed, a few more PET-CT may be installed. First PET/CT Scanner in Bangladesh has been introduced by a private multidisciplinary tertiary level hospital – United Hospital, Gulshan, Dhaka in the year 2011. United Hospital has set up the first cyclotron in its campus in Bangladesh. The cyclotron produces short-lived radioisotopes needed for medical imaging using positron emission tomography (PET). The staff of cyclotron facility includes experienced radio chemist and radio pharmacist capable of developing novel PET imaging tracers to expand the scope of imaging at United Hospital and surrounding medical institutions[19]. The Traffic jam in Dhaka city should be considered vigorously for transportation of radionuclide from cyclotron production site to the PET-CT installation centers because the half life of 18-FDG is less than 2 hours. The radionuclide (18-FDG) produced at cyclotron production site can be transported to the adjacent private and government medical institutions if they install PET/CT Scanner. The cost of PET imaging is still high (approximately Taka 65000 per scanning procedure) and should be subsidized by government.

Conclusion:

The history and evaluation of PET imaging shows continuous improvement in sensitivity and resolution. At present, PET scanning is mainly used in diagnosis, staging and monitoring of treatment of cancer as well as detection of cancer recurrence. The PET imaging system usually includes also simultaneous CT scanner in the same gantry. The PET scan demonstrates the biological function of the body tissues, while the CT scan provides information about the body's anatomy such as size, shape and location of the lesion. By combining these two technologies, physicians can more accurately diagnose and monitor diseases such as cancer, heart diseases, and certain brain disorders.The wide spread use of CT, MRI and their versions – all are concerned with analysis of structural lesions; none carrying any significant physiological data. Understanding of molecular biology and metabolism in disease states, development of suitable radiotracers, combinations of PET with other imaging modalities like CT and MRI can improve more in the diagnosis and treatment of certain diseases.

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Pulse Oximetry: The Fifth Vital Sign of Neonates

JC DAS

Summary:

When supplementation of oxygen is inappropriate there is chance of development of either hypoxia or hyperoxia. During oxygen therapy, oxygen level should be maintained within a target-able range through proper monitoring. Pulse oximetry is a useful convenient and reliable monitoring system. The principle of working of pulse oximeter is based on the fact that oxyhaemoglobin and deoxyhaemoglobin absorb light at the red end of the spectrum differently; Deoxyhaemoglobin absorbs more red than infrared and oxyhaemoglobin more infrared than red. The 'emitter' of the probe of pulse oximeter sends equal intensities of red and infrared light into the tissue. The 'sensor' detects the ratio of red to infrared that emerges. From this information the proportion of oxyhaemoglobin to deoxyhaemoglobin-that is, the percentage saturation of hemoglobin with oxygen is calculated and displayed to the monitor of the instrument. The main advantage of pulse oximeter is that it is non-invasive, less complex, does not require calibration, provides continuous measurement of hemoglobin-oxygen saturation (SpO_2), fast response time and high accuracy. Limitations of accuracy of pulse oximetry lie on poor perfusion, hypoxic events, hyperemia, severe anemia, dyshemoglobinemias, high oxygen partial pressures (P_aO_2), superficial pigments, black skin of infant, motion artifact, pressure on sensor, presence of abnormal dye, light and electrical interference. It is essential to remember the limitations of this instrument before going to pulse oximetry.

Key words: Pulse oximeter, neonate, vital signs, principals of working, limitations.

(J Bangladesh Coll Phys Surg 2011; 29: 158-162)

Introduction:

Oxygen is commonly used throughout the world in neonatology[1]. There is chance of development of either hypoxia or hyperoxia if supplementation of oxygen is inappropriate. Hypoxia may lead to pulmonary vasoconstriction, pulmonary hypertension, neurological and other organ damage[2]. This condition may be associated with lethargy, cyanosis, hypothermia, bradycardia, metabolic acidosis or unresponsiveness to therapy[3]. Hyperoxia on the other hand produces complex physical and physiological stress[4]. It produces free radical mediated cellular damage. A number of diseases in the newborn may occur as consequences of oxygen free radicals e.g. retinopathy of prematurity, bronchopulmonary dysplasia, necrotizing enterocolitis and patent ductus arteriosus etc[3].

A good monitoring system of oxygen level is essential during its supplementation. The primary aim of monitoring of oxygen is to reduce hypoxic and hyperoxic episodes and to decrease the variability in an infant's oxygen levels through proper monitoring[5].

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There are many monitoring systems of oxygen saturation in newborn infants. In a country like ours, where facilities are constrained, a convenient, user friendly but reliable monitoring system is prioritized. Historically, the pulse and respiratory rate were the initial vital signs because their determination did not rely on any instrument. Body temperature and blood pressure recording were added as next vital parameters with simple instruments in the year of 1850 and 1900 respectively. The pulse oximeter was introduced in the early 1980_s as the 5th vital sign for accurate, precise, noninvasive measurement of arterial hemoglobin oxygen saturation. Information derived from all five reflects crucial physiological function of neonate[6].

Pulse oximeter is a good and convenient instrument that can be used even in rural areas to monitor oxygen saturation. Knowledge regarding fundamental aspects of pulse oximeter and monitoring of oxygen saturation by this instrument is prerequisite for taking reading of oxygen saturation accurately by this instrument. Scarcity of working knowledge among our physicians regarding pulse oximetry is a problem. Many studies on oxygen monitoring through pulse oximeter are conducted in different parts of the globe. But work in neonatology on our country is very limited. The review is written to orient our clinicians particularly pediatricians, regarding

some fundamental aspects of pulse oximetry so that oxygen mediated problems could be minimized.

Oxygen status in neonate:

Before going to discuss pulse oximetry, it is wise to know some basic concept of oxygen therapy. Different researchers studied oxygen levels in neonates in different parts of the world. At 5 minutes of postnatal age, the observed median SpO_2 value was 87% for infants delivered vaginally and lower value for those delivered through cesarean section. The median SpO_2 did not reach 90% until 8 minutes of age in either group[7]. Another group of researchers observed median SpO_2 at 1 minute was 63% with a gradual rise of 90% at 5 minutes[8]. The best range for SpO_2 was observed as 91% -96%[9].

Saturation within the range 85-95% largely exclude hyperoxia in preterm infants <29 weeks gestation but permit PaO_2 values far lower than those recommended in traditional guidelines[10]. Oxygen level (SpO_2) observed in Bangladeshi neonates were 95%, 94% and 92% respectively among 1st, 2nd, 3rd and 4th week of postnatal age. The normal SpO_2 value ranged from 87% to 94% in terms of normal PaO_2 (50-80 mmHg) value[11].

Principles of oxygen therapy:

In neonate the goals of oxygen therapy are (i) to maintain adequate partial pressure of oxygen in arterial blood (PaO_2), (ii) to minimize the work of breathing and (iii) to minimize the cardiac work[12].Oxygen should be administered only when indicated, given in the lowest ambient concentration and should be stopped as soon as its use is considered unnecessary[3]. A PaO_2 values of <40 mmHg and >80 mmHg is regarded as 'low' and 'high' PaO_2 values by neonatologists[13]. A PaO_2 value of 40-80 mmHg corresponds to SpO_2 values of 85-93% in majority of cases[12]. A PaO_2 of 41 mmHg may be enough to saturate 90% of hemoglobin in very low birth weight infants[14].

Strict management of oxygen therapy to minimize episodes of hyperoxia and hypoxia was associated with decreased incidences of retinopathy of prematurity (ROP) over a period of 5 years[15].In special conditions like preterm VLBW, chronic lung disease (CLD), bronchopulmonary dysplasia (BPD) oxygen therapy should be individulaised[5,12,15,16]. Generally SpO_2 is maintained at 85% -95% (85% - 92% if <29 weeks gestation) range[17]. In acute condition, the arterial oxygen saturation should be maintained between 90-95% and between 85-90% in chronic situations[3]. Oxygen can be administered through nasal prongs, nasal catheter, nasopharyngeal catheter, oxygen hood (head box), face mask and holding oxygen source close to the infant's face[18]. Oxygen may also be given through endotracheal tube connecting with self-inflating bag, continuous positive airway pressure (CPAP) or ventilator system[19].

Monitoring of oxygen:

It is useful to monitor ambient oxygen concentration by 'oxygen analyzer' in order to protect infant against oxygen toxicity. It helps in regulating the flow rate of oxygen so that desired concentration of oxygen can be delivered[3]. However, monitoring of oxygen directly on neonate is very important.

The objectives of oxygen monitoring is to prevent oxygen mediated complications notably reduction injury to lungs, immature retina and other tissues. In the long run the purpose of oxygen monitoring is to detect degree of hypoxia, which is likely to cause acidosis or tissue damage and hyperoxia, which may causes predominantly retinopathy of prematurity[20].

Monitoring systems:

Cyanosis may be a guide for oxygen status. But it is very much subjective and evident only when saturation is markedly low. Again, polycythemic patient may appear cyanosed despite adequate arterial oxygen tension[21]. The important monitoring systems of oxygen therapy are as follows:

1. Arterial blood gas (ABG) analysis:

Blood gas analysis provides information essential for assessment, therapeutic decision-making and prognostication of patient. The normal values of arterial blood gases are very dependent on many factors including gestational age and postnatal age of infants[22]. However, a value of 50-80 mmHg is considered as target range of partial pressure of oxygen of arterial blood (PaO_2) for newborn infants[17]. Blood sampling via umbilical artery or peripherally is preferred route. Radial or posterior tibial arteries are commonly used. Complications related to radial artery puncture include hematoma formation, arterial spasm, thrombosis, embolism, infection and inaccuracy of results[19]**.** Though such arterial blood gas analysis is considered to be the gold standard for accuracy, it provides intermittent

oxygen monitoring, is invasive, can lead to significant blood loss and erroneous results may be found if sampling is improper[23].

2. Continuous blood gas monitoring:

Continuous blood gas monitoring through an indwelling catheter has been advocated to provide rapid, real-time data and reduce the volume of blood required for repeated blood gas measurements. Recent technology has been utilized for fiber optic systems optical sensors inserted into vascular catheters already in place. Correlation with measured PaO_2 values is good but bias and precision of measurements deteriorate for PaO_2 values above 70 mm Hg[17].

3. Capillary blood gas determination:

This technique requires extensive warming of the extremity, free-flowing puncture, and strictly anaerobic condition. Under such conditions, capillary sample may be useful for determination of pH and PcO_2. Proper collection techniques are often difficult to guarantee in technical setting; however, capillary sample should not be used for determination of PaO_2[17].

4. Transcutaneous oxygen (t_cPo_2) monitoring:

Here, partial pressure of oxygen is measured from skin surface by an electrochemical sensor[19]. The sensor is affixed over the chest or upper abdomen[3]. Oxygen diffuses through a membrane into the electrode, when it is reduced, setting up an electric current[22]. The skin surface is heated to 43.5° to 44°c to maximize skin surface blood flow[17]. The electrical current is related to PaO_2 and is displayed as transcutaneous Po_2 ($tcPo_2$)[22]. This value is reliable and comparable to simultaneous PaO_2. Sensor site is to be changed every 2 hourly to avoid skin burn[3].

5. Pulse-oximetry (SpO_2):

It is very difficult to guess the state of a patient's arterial oxygenation subjectively. Introduction of pulse-oximetry in the early eighties allows reasonably accurate objective assessment of P_aO_2[24]. Its availability will help to pick up any significant change in oxygen saturation in newborn infants[25].Study has shown that using pulse-oximetry as a routine 'fifth vital sign' resulted in important changes in the treatment of a proportion of patient[26].Control of oxygenation is achieved by maintaining saturation within a target range, usually by setting alarm limits[10].

(i)Principles of working:

Oximeter makes use of the fact that oxyhaemoglobin and deoxyhaemoglobin absorb light at the red end of the spectrum differently; Deoxyhaemoglobin absorbs more red than infrared and oxyhaemoglobin more infrared than red[27]. The wavelengths of red and infrared light are 660 nm and 940 nm respectively (Fig-1)[28]. The oximeter probe consists of a 'light emitter' and a 'light sensor', which are aligned on opposite sides of a narrow part of body, such as palm or forefoot. The 'emitter' sends equal intensities of red and infrared light into the tissue. The 'sensor' detects the ratio of red to infrared that emerges. From this information the proportion of oxyhaemoglobin to deoxyhaemoglobin-that is, the percentage saturation of haemoglobin with oxygen is calculated and displayed[27].As oximeter measures the saturation of arterial blood rather than capillary or venous blood, the instrument is programmed to look only at pulsatile increases in oxyhaemoglobin concentration-hence the term 'pulse' oximetry[27]. The pulsatile signals are due to variability of arterial cross-sectional area and change in axis of erythrocytes with each cardiac cycle[24]. When light is passed through tissue some of the light is absorbed by each constituent of the tissue, but the only variable light absorption is by arterial blood (Fig-2)[29].

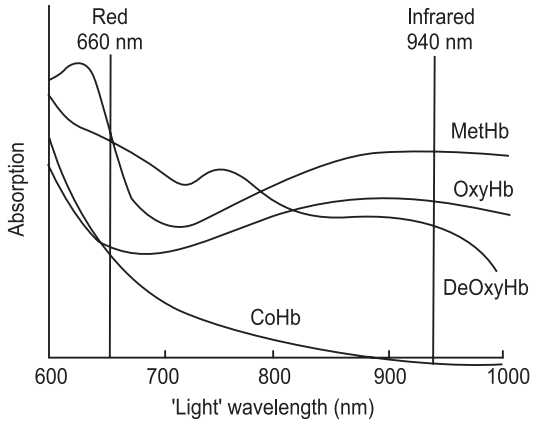

Fig.-1: *Absorption spactra of normal adult haemoglobin in saturated (OXyHb) and desaturated (DeXoyHb) states, carboxyhaemoglobin (COHb)(, and methaemoglobin (MetHb)*

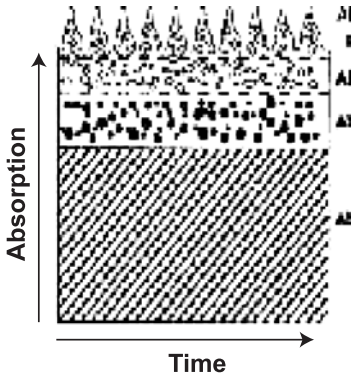

Fig-2: *Source of light absorption during pulse oximetry.*

- absorption by pulse added volume of arterial blood.
- absorption by arterial blood.
- absorption by venous blood
- absorption by tissue.

Conclusion

Oxygen therapy should be judicious. Inappropriate supplementation of oxygen may not correct hypoxia or may lead to hyperoxia. Both the conditions are injurious to neonatal health. During oxygen therapy, SpO_2 value and more precisely the PaO_2 value on neonate should be maintained within a target range. There are some monitoring systems of oxygen status in neonate. Pulse oximeter is a convenient-reliable instrument for recording oxygen saturation. Control of oxygenation may be achieved within a target-able range with this instrument. During pulse oximetry, its limitations and pitfalls should be remembered. Time-to-time PaO_2 monitoring through arterial blood gas analysis is also important.

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SHORT COMMUNICATION

Implementation of National Drug Policy in Different Countries: An Appraisal and Experience from Bangladesh

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(J Bangladesh Coll Phys Surg 2011; 29: 177-179)

Key Words: National Drug Policy, World Health Organization, Bangladesh.

In May 1975, the then director general of World Health Organization (WHO) Dr Halfdan Mahler, strongly advocated at the World Health Assembly (WHA) for the development of national pharmaceutical policies based on the affordability, quality and availability of drugs. A resolution was passed which urged the Secretariat of WHO to help Member States to formulate national pharmaceutical policies that meet the actual health needs of the people. The resolution introduced the concepts of 'essential drugs' and 'national drug policy (NDP)' so far the global public health is concerned. Bangladesh is one of those countries who responded early to that call and formulated their NDP in 1982[1]. The 1982 policy hugely benefited the pharmaceutical industry of Bangladesh and helped the entrepreneurs to develop this sector with good quality and standard. Bangladesh is now exporting drugs in more than fifty countries of the world with good reputation after completely mitigating the local demands. Not only in Bangladesh, after implementation of drug policy under WHO guidance, India now ranks 13th in world production by value and ranks 4th in the volume of pharmaceuticals produced[2]. Now there are 20 000 pharmaceutical manufacturers in India[2]. Most of the vaccines are now produced in India. Countries like Brazil, Egypt, Turkey, Indonesia etc. are now producing both active ingredients and finished products. This is a great achievement for their pharmaceutical sector[2]. By 1999, 66 countries had formulated or updated a NDP within the previous 10 years, compared with 14 countries in 1989[2]. To date approximately 156 countries have formulated their own NDP[2]. W.H.O guidelines suggest three broad objectives of drug policy: accessibility, quality, safety & efficacy of drug and finally rational use. In this appraisal the case of Bangladesh which has 27 years experience of its drug policy will be used as an example to evaluate the pitfalls of implementation of those objectives comparing some other developing countries.

Accessibility: The main objective of the Bangladesh NDP was to ensure that every people can get the essential and necessary drugs easily with affordable price. With this end in view 150 'essential drugs' were identified in the drug policy (1982) of Bangladesh with controlled pricing[3]. This list has been reduced to 117 in the year 1993[3]. The maximum retail price of the essential drugs was fixed by the drug administration authority though the real scenario is different. Prices of essential medicines are not consistent with each other. There is wide variation of the price of same medicine within different brands. For example the price of each 'Ciprofloxacin (500mg)' tablet ranges from taka 5 to taka 15(US$ 0.7-0.22)[2]. It is said that the production cost of this drug is less than 2.5 taka per tablet[3]. So some companies are making an astonishing profit of Tk.12 (US$ 0.17) per table. In Malaysian drug policy, the Government relies on market forces to decide the price of the 'essential drug', rather than controlling it. But this policy is now showing some discomfort too among mass people and public perception is now rising

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towards control of drug prices in Malaysia though it seems unsuccessful in Bangladesh.[4] Price of medicine directly related to the accessibility. In Cameroon, a course of treatment for peptic ulcer costs almost twice the monthly wages of a government employee which is clearly unaffordable[2]. A study carried out in Ghana and Cambodia also highlights the huge gap between prices of generic and brand medicines[2]. A good number of countries do not even attempt to control medicine prices.[2] Over 40% countries have no regulation of medicine prices which is a mandatory part of WHO proposed effective NDP. This is really painful as drug is not like other commercial commodities rather it has got humanitarian value. Pharmaceutical business should be more humanitarian oriented. Pharmaceutical companies should keep in mind that medicines produced by them have direct impact on public health. They must not tag inordinate high price to their products which will in turn adversely affect the public health. Poor people naturally refrain themselves from buying very costly medicines. So, the companies must adopt a humanitarian approach in setting their profit margin. Over-pricing causes inadequate access to needed medicines in developing nations. To enhance the accessibility of drugs, companies should work hand in hand with the governments.

Quality, safety and efficacy of Drugs: At present more than 16000 different brands of drugs are available in the market of Bangladesh and these are produced by as many as 300 pharmaceutical companies.[1] Only 4000 brands are tested for quality and 12 thousands are entering in the market without any test for lack of technical support and trained manpower[1]. Financial solvency is an important factor in this regard. This is a burning issue in many developing countries too. The drug control authority of these countries should give permission very cautiously for licensing a new drug. Moreover in many cases these drugs may be useless or ineffective and of similar nature. This also creates a favourable environment for fake, spurious, adulterated and harmful smuggled medicine to come in to the market. In 2004, Bangladesh drug testing laboratory tested 5000 samples and detected 300 drugs which are either counterfeit or of very low quality[1]. In 1998 it was 260 out of 5920[1]. 'No medicine without prescription' is strictly followed in almost all developed countries but unfortunately this practice is absent in the developing world. As a result misuse of valuable drugs including antibiotics is very common. In drug policy of every developing country, there should be clear rules and provision of a definite list of drug to be prescribed by the traditional village quacks or non-graduate practitioners to minimize the misuse of medicine. A recent WHO report on medicine stated that an estimated two-thirds of global antibiotic sales occur without any prescription, and studies in Indonesia, Pakistan and India showed that over 70% of patients were prescribed antibiotics without valid reason and among them the great majority (up to 90%) of injections are estimated to be unnecessary[2]. Adverse drug reaction (ADR) and resistance to antibiotics are another two points of concern. Even in United States ADR rank among the top 10 causes of death and are estimated to cost between US$ 30 and US$ 130 billion each year[2]. For the treatment of malaria, chloroquine resistance is now established in 81 of the 92 endemic countries.[2] Resistance to common antibiotics also established against gonorrhea, pneumonia and bacterial meningitis. These drug resistances not only put the individual at much greater risk of poor treatment outcomes but also put tremendous pressure over the national economy of a country. At present there are 67 000 licensed drug stores in Bangladesh but practically it exceeds 0.2 million.[1] There are no trained personnel in these drug shop and they do not hesitate to sell adulterated and low quality drugs for exorbitant profit.[5] This malpractice is rampant in the rural areas Bangladesh where illiterate poor people are adversely affected. This is a common scenario for many developing countries too. Recently Malaysia took decisive steps to improve the consciousness of drug use among mass people by launching different motivation and awareness program which turn out to be effective. They also improve post-marketing surveillance and monitoring.

Rational Use of Drug: Irrational and inappropriate use of medicine is a global problem. Recently in Bangladesh many pharmaceutical companies launched a group of multi vitamin- multi mineral tablets for removing deficiency without consideration of local need and socio-economic condition of the country[1]. Bangladesh drug market is now flooded with different vitamins and herbal products imported by various distributor companies which are completely unnecessary and illegal to be marketed[6,7]. Physicians have to play vital role and

responsibilities in this regard. They should be more cautious and judicious in prescribing drugs. For example, Oman have got improvement in prescribing patterns when the government established a directorate of rational use of drugs in 2000, besides national drug control authority.[8] Recently in Iran, government thinking for a drug prescription control committee in each province, with a computer link to a national committee, which will evaluate all prescriptions and send an annual report to all respected physicians[9]. Iranian government recently finished an experimental pilot project in two provinces and found it very effective. They are expecting to reduce the total drug cost around 10% annually by this way[9].

Implementation of a national drug policy has not been paid required attention by the governments of most developing countries. Notwithstanding the fact, Bangladesh as a developing country has registered several significant progress in the field of public sector. Especially the national drug policy 1982 is a commendable step from the part of Bangladesh Government. However, still there is huge scope to make the drug policies of developing countries more effective. This paper has pointed out several aspects of implementation process of a national drug policy. Drugs regulators in developing countries should consider these aspects in implementing their drug policies. Only in this way, public health in developing countries will be ensured to a great extent.

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LETTER TO THE EDITOR

(J Bangladesh Coll Phys Surg 2011; 29: 180-181)

To
Editor in Chief
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At first I would like to thank to the editor for publishing the time demanding review on Treatment of Gout and Hyperuricemia (April Vol 29, No2,2011 Page 85-95). Both specialist and non- specialist should know the recent update about hyperuricemia and gout .As we are adopting western life style day by day , the incidence of metabolic syndrome including gout may increase in future.

I have gone through the article and have certain observations. The content and illustration of the articles were very nice and informative. A systematic review with Pubmed, embase or Cochrane collaboration for specific duration of time would have been more informative in review process. The article reviewed a number of papers but did not mention the mesh or key wards used for generating the search. The review almost covers everything regarding gout but recent update of treatment was not included. I would like to draw your attention to the new advancement that have taken place in the field of treatment of gout in recent past.

Genetic advances with the identification of the urate anion transportor (URAT-1) and genetic variation in SLC 2A9 as a key regulator of urate homoeostasis, have given us deeper understanding of the pathophysiology of gout, and also allow for more targeted treatments[1,2]. Hopefully, new and emerging therapeutic options will reduce treatment-resistant gout in patients who are unresponsive or unable to take traditional urate lowering therapy. In 1996, rasburicase was developed by recombinant DNA technique from a genetically modified strain of Saccharomyces cerevisiae. Rasburicase is given IV at a dose of 0.20 mg/kg for 5–7 days to treat tumour lysis syndrome (TLS)[3]. Rasburicase is successfully used in gout with renal transplant patients and patients intolerant to allopurinol.[4,5] PEG–uricase is another potentially powerful agent for treating refractory gout in those who are unable to tolerate other treatments. PEG–uricase is effective in resolving tophi[6] and could have a role in 'debulking' tophi in advanced gout before switching to another agent for maintenance treatment[4]. Losartan, an angiotensin II receptor antagonist used for hypertension, and fenofibrate, a fibric acid derivative used in hyperlipidaemia, both have uricosuric actions and reduce Serum uric acid(sUA)[7]. This effect of losartan and fenofibrate on sUA is particularly beneficial, given the frequent co-existence of hypertension and hyperlipidaemia with gout.

Anakinra, an IL-1 receptor antagonist, is a new treatment in development. an open-labelled pilot study have shown subcutaneous injections of anakinra 100 mg daily to be a safe and efficacious treatment of flares.[8] In addition to anakinra, other IL-1 inhibitors are in development such as rilonacept, which is currently undergoing Phase III trials .Novel therapies including febuxotat, Anakirna and PEG- uricase offer hope to patient groups previously difficult to treat.

Traditionally, gout was viewed as a disease of the privileged, but is now increasingly prevalent among the lower socio-economic classes who have high rates of obesity and diabetes. More is known about which life style factors protect or cause gout. However, despite significant advances in understanding and exciting developments of new treatments, the management of gout remains sub-optimal in primary and secondary care. So, treatment of gout is necessary to learn by every physician in this respect.

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Authors Reply

We feel pleasure to get a feedback about the review on 'Treatment of hyperuricemia and gout'. Its really appreciating that Dr. Aparna Das has read the article thoroughly and between the lines. She has rightly mentioned the key words were not used and we deliberately omitted it is not practiced in BCPS journal. Regarding the option of drugs, if we would include all, the article would be more voluminour and divert the attention of the the readers from the most relevant one, therefore we tried to pick up the most pertinent one, although we talked on IL-1 antagonist in out abstract and we also talked on uricsse especially pegluticase. Drugs like ascorbic acid also now considered to be an adjunct in treatment of Gout.

Finally, we would like to thank the reader again for the suggestions in this article and keen interest in the field of rheumatology.

Warm regards

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DESK FROM EDITOR

Dear Fellow,

You will be glad to know that the July, 2011 issue of the BCPS Journal has been published. It was only possible due to the sincere effort of the editorial board and the fellows alike. We have a huge backlog of articles waiting to be published and we are trying to find out means to cut short the list. In future we would also like to improve the quality of the journal with an aim at international recognition. The process of enlisting BCPS Journal as a Pub Med indexed journal has been started. Though it is a time consuming procedure, with heartiest effort of all our fellows we shall try to achieve this target as early as possible Inshallah.

I once again would like to thank you all for your kind support.

Professor H.A.M. Nazmul Ahasan
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