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JOURNAL OF BANGLADESH COLLEGE OF PHYSICIANS AND SURGEONS

CONTENTS

New Management Strategies of Hormone Refractory Prostate Cancer (HRPC)

Carcinoma prostate is the commonest cancer in men and recognized as the commonest killer of men. Prostate cancer incidence is increasing in Bangladesh as the detection technology and people are servings longer. Prostate cancer progression ends up at Hormone Refractory Prostate Cancer (HRPC) or stage D3 status where no endocrine manipulation is effective. The median survival at this stage of prostate cancer is usually less than 10 months. World wide life of the most of the prostate cancer patients are terminated at this stage.

Hormone Refractory Prostate Cancer (HRPC) may occur due to the fact that prostate cancer cell escape from androgen withdrawal-induced apoptosis. In this development, enhancement of growth factor stimulation has an essential role in the up regulation of survival signals and constitutive proliferation[1].

The principle of treatment for advanced prostate cancer is endocrine manipulation which includes androgen deprivation. Unfortunately, at this stage of prostate cancer most of men become resistant to hormonal manipulation, developing what is defined as hormone-refractory prostate cancer (HRPC). A decade ago, most clinicians find no answer and felt helples*ecause no Chemotherapy was considered to be ineffective and associated with unacceptable toxicity. A review of 26 chemotherapy-based trials revealed an overall response rate of 8.7% with a median survival ranging from. 6 to 10 mo[2]. For this reason, it was established that a median expected survival for patients with HRPC is 10 months. Therefore, novel therapeutic strategies that target the molecular basis of androgen resistance were required.

Role of chemotherapy in HRPC was emphasized In 2004. Two pivotal trials of Docitaxel-based chemotherapy were reported and, for the first time, a survival benefit was observed for chemotherapy in HRPC. The results from the Southwest Oncology Group (SWOG)99-16 and TAX327 studies changed the expectations of treatment outcome these patients[7,8].

Also these trials demonstrated the need for combination therapies in patients with HRPC.

The combination of Docitaxel with estramustine increases the thrombo embolic risk and necessitates a primary prophylaxis[7,8]. New combination models using Docitaxel may represent an exciting investigational field[9]. In particular, less toxic regimens, provided that the activity can be maintained, are more attractive.

Recently, Di Lorenzo et al[9] presented an interesting proposal using a combination of docetaxel, vinorelbine, and zoledronic acid as first-line treatment in patients with HRPC. Vinorelbine is a vinca alkaloid that inhibits the microtubular apparatus in malignant cells and has shown activity in HRPC[9]. The synergism of docetaxel and vinorelbine has been confirmed in preclinical studies and human trials[9]. Moreover, the use of docetaxel in a weekly schedule appears to minimize myelo suppression and has been associated with moderate toxicity[9].

Most HRPC develops bone metastases thatt are responsible for pain and morbidity. Bisphosphonates showed an inhibitory effect on prostate cancer bone metastases by blocking proteolytic activity of the matrix, cell adhesion, and possibly cancer cell growth[9]. Multicentric randomised trials of HRPC with bone metastases showed a significant reduction in skeletal related events using zoledronic acid[9].

Di Lorenzo et al[9] developed a phase 2 study to evaluate the impact of weekly docetaxel and vinorelbine and monthly zoledronic acid on PSA response, pain improvement, and toxicity profile in 40 men with HRPC. Complete and partial response (PSA reduction) were observed in 18% and 32% of cases, respectively.

The objective of this editorial is to emphasizes two possible strategies: the first, specifically targeted to the role of the neuro endocrine (NE) system in

hormone-refractory stage development, and the second, chemotherapy, not target specific and only cytotoxic.

NE activity is considered one of the factors involved in the progression from an androgendependent to an androgen-independent state and may be a possible new target therapy. In recent years a marked number of papers related to NE differentiation in prostate adenocarcinomas has published. The NE component of prostate Adenocarcinoma is androgen independent and does not produce prostate-specific antigen (PSA). The continuous use of androgen-ablation therapy may produce hyperactivation of the NE system in prostate tissue[3]. NE system products can act as immortalising factors, blocking the apoptotic process in prostate adenocarcinoma cells and then inducing androgen-independent statu5 and progression.

Several clinical trials have demonstrated impressive efficacy of somatostatin analogues for various hypersecretory disorders resistant to standard therapy. They have also proved useful for the management of symptoms caused by NE diseases. Chromogranin A (CgA) is considered the best marker of NE activity in the prostate. In different countries CgA determination started to be used and to be repeated in clinical practice for the evaluation of men with prostate adenocarcinoma. The primary effect of somatostatin analogues is not a Ikect cytotoxic effect on NE cells, but rather inhibition of the release of peptide hormones secreted by NE cells. Clinical trials on somatostatin analogues as monotherapy for prostate cancer have shownknegative results[4].The mechanism of action of these drugs may suggest their use not as monotherapy but rather as combination therapy for prostate cancer. Koutsilieris et al[5] first proposed a combination therapy with dexamethasone and somatostatin analogues in HRPC. The author combined standard luteinising hormonereleasing hormone (LHRH) analogue therapy with somatostatin analogue and dexamethasone. Median overall survival reported in this study was 12 mo, with improvement in performance status and bone pain scores. Di Silverio and Sciarra[6] analysed whether the combination of ethinyloestradiol and lanreotide can offer objective response or symptomatic improvement in patients with D3 prostate cancer. Patients with metastatic

HRPC discontinued LHRH analogue and started the combination therapy.

The rationale for this combination therapy is: (1) to inhibit the protective antiapoptotic effect of NE system on prostate adenocarcinoma cells (somatostatin analogue); (2) to use a new mechanism of castration (oestrogens); and (3) to add a direct cytotoxic effect on prostate cells (oestrogens). No major related side-effects were reported (gynaecomastia and breast pain). In this phase 2 trial, 95% of cases showed an objective clinical response as demonstrated by at least a 50% PSA decrease from baseline; in all cases the PSA response was accompanied by a significant improvement in Eastern Cooperative Oncology Group (ECOG) performance status and bone pain score; 70% of cases were without disease progression at a median of 16.5 mo of follow-up during therapy. These results suggest the need for a phase 3 trial to confirm the effectiveness of this combination therapy in HRPC.

An objective response (liver, lung, and lymph nodes) was observed in 6 of 15 patients with measurable disease. Stratifying the response in terms of Gleason score, primary treatment, and number of osseous sites, no differences were observed among these groups. No toxic death occurred and the most important grade 3 toxicities included neutropenia (25%). Pain improvement was found in 47.5% of cases. Median progression-free survival was 7 mo, with a median overall survival of 17 mo. The majority of patients received, after progression, a second line of chemotherapy. The rationale to improve docetaxel efficacy and to reduce the related toxicity using a combination with vinorelbine and zoledronic acid is of great interest.

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Serum Apoprotein (ApoA1 and ApoB) in Myocardial infarction

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Summary:

30 diagnosed cases (Male26, Female 4) of MI (myocardial infarction) with the mean age of 55.5±9.8 years (range 40-70 years) were included in a case control study to evaluate their apoprotein status. Serum apoA1 and apoB were measured and compared with those of age and sex matched healthy control subjects. Mean serum apoA1 concentration found significantly low in MI cases (91.84± 11.2 mg/dl) compared to control (123.2±10.5 mg/dl) and that of apoB found significantly high in MI cases(135.3± 23.0 mg/dl) compared to control (66.2±10.0 mg/dl).Serum apoB/apoA1 ratio of MI cases (1.49±0.3)

also found significantly higher than that of control (0.54±0.1) .Since the serum apoA1 and apoB concentration stand for relatively more comprehensive measure of antiatherogenic and atherogenic potential respectively rather than the traditional lipid profile ; measurement of this apoprotein and their ratio may be more robust and specific marker for identification of individuals at risk of MI even in individuals with normal traditional lipid profile.

Key word: ApoA1, ApoB, MI

Introduction

Coronary artery disease (CAD) is one of the leading causes of death from global point of view. The identification of subjects at risk of developing CAD is an important public health issue[1]. Atherosclerosis is the underlying cause in more than half of the patients with CAD[2]. Dyslipidemia is the corner stone of atherosclerotic process. Commonly serum total cholesterol (TC), triacylglycerol (TAG), High density lipoprotein cholesterol (HDL-C),Low density lipoprotein cholesterol (LDL-c) are used for identification of person at risk of CAD. However serum TC can not discriminate well between individuals developing CAD and those who does not; since the TC as a whole without its functional breakup to atherogenic and antiatherogenic potential is a poor indicator of the atherosclerotic scenario[3]. Traditionally serum LDL-C and HDL-C are regarded as the marker of atherogenic and antiatherogenic measure respectively, but it is not infrequent for an individual to develop CAD with traditional lipid

profile well within desired level, because LDL-C and HDL-C are not the complete representation of atherogenic and antiatherogenic lipoprotein .Important atherogenic lipoprotein are chylomicron (CM), chylomicron ramnant (CMR), very low density lipoprotein(VLDL), intermediate density lipoprotein (IDL), low density lipoprotein (LDL), and lipoprotein(a) [LP(a)]; all of which contain apoB. Although HDL is treated as antiatherogenic but the different subtypes of HDL have different degree of antiatherogenic potential; some subtype believed to be rather atherogenic and all subtypes do not containing apoA1.It is claimed that HDL contain apoA1 are antiatherogenic since apoA1 stimulate LCAT and thus help in reverse cholesterol transport (RCT) by facilitating HDL maturation. HDL containing apo-A_{II} counter act the RCT since apo-A_{II} inhibit the LCAT. So the antiatherogenecity of HDL_1 which has no apoA1 (contain only apoE) and that of other HDL subtypes with apoA_{II} is doubtful. So HDL-C cannot represent complete antiatherogenic potential of HDL[4].

With this perspective recently the major apolipoproteins like apoA1 and apoB have received attention and addressed as the major determinant of the metabolic fate of different lipoprotein[5]. The CAD has been found to be positively correlated with apolipoprotein B and inversely correlated with apolipoprotein A_1[6].

ApoA1 stimulate the reverse cholesterol transport (RCT), decrease the extent of lipid deposition and also inhibit the infiltrating monocyte/macrophages in

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aortic intima which initiate the initial stage of fatty streak formation[7]. Reduced plasma level of ApoA1 was found in AMI patient[8]. ApoA1 level can be used to predict future CAD among the young and in adult not yet manifestating the disease[9]. Although HDL considered to be rather antiatherogenic but some HDL subtype (e.g. HDL1) have recently being identified to be atherogenic and they contain no ApoA1[10]. So the individuals with normal or even raised HDL-C may be found to have CAD due probably to the predominance of HDL1 subtype or the HDL subtypes without apoA1. Therefore ApoA1 rather than HDL-C seems to be more reliable assessor of antiatherogenic potential.

Increased level of plasma apoB was shown to be a risk factor for atherosclerosis[2]. Apo B moiety of LDL seems particularly important for its atherogenicity, because lipoproteins without apo-B apparently do not produce atherosclerosis[11]. LDL are heterogenous in size and density and composed of fifteen different subtypes. Smaller and denser LDL subtypes (eg .LDL 4 ,5,6 etc) are lipid depleted particles (less cholesterol containing) but more atherogenic than larger LDL subtypes (eg LDL 1,2,3 etc) which are relatively lipid rich but all LDL subtypes plus other apo-B containing atherogenic lipoproteins contain identical & equal apo-B content irrespective of their varied cholesterol content. CAD patients are likely to have more smaller and denser LDL particle. Therefore LDL-C is an inadequate measure of LDL atherogenicity[12,13,14]. Measuring ApoB provides a direct estimate of the total number of LDL particles irrespective of their sub types[15]. So only the LDL-C measurement is a poor reflections of atherogenicity; rather ApoB stands for the complete and comprehensive picture of atherogenic risk. Because apo-B accounts all known atherogenic LP (in addition to LDL) and also the number of various LDL subtypes.

The CAD patient had significantly lower ApoA1 but higher ApoB. Both ApoA1 and B had significant discriminative power between CAD patients and normal individuals. So measurement of serum apoA1 & apoB appears to be more judicious clinically.

Materials and Methods

This case control study was carried out from july 2003 to June 2004 in the Department of Biochemistry, Dhaka Medical College, Dhaka in cooperation with the immunology Dept , BIRDEM, Dhaka. Ethical clearance was taken from Ethical committee of Dhaka Medical College. A total 50 non smoker, non-alcholic subjects free from DM, renal disease, thyroid disease, liver disease and having no history of taking antihypertensive or antihyperlipidemic drugs were studied. Fasting blood glucose, serum creatinine, TSH, serum bilirubin & ALT were measured in all study subjects to exclude DM, renal diseases, thyroid & liver diseases. Among the study subject 30 were the diagnosed MI cases collected from Cardiology ward in Dhaka Medical College and 20 were age and sex matched healthy control selected from colleagues & relatives. All study subjects were included after taking their informed written consent .MI diagnosis based on characteristic chest pain, ECG finding and rise and fall of serum cardiac marker.

5 ml fasting venous blood was collected from each subject with all aseptic precautions and allowed to clot at room temperature & centrifuged for 10-15 minutes at 2500rpm. The separated serum was stored frozen at -35^0 c until used for the measurement of apoprotein (apoA1 and apoB).

Laboratory Method Serum apoA1 & ApoB concentration was estimated by immunonephelo-metric methed with commercially available kits using BN system of Dade Behring Marburg GmbH, USA [16,17]. Results were express as their mean ± SD (Standard deviation)

Statistical Analysis: The result were analysed in SPSS by using unpaired student t-test, P< 0.05 were taken as a level of significance.

Results

Study subjects were grouped as Group -I (30 MI cases,) and Group-II (20 normal control). Group-I included 26 males (86.6%) and 4female (13.3%) of age range 40-70 years. In Group-II , 16 male (80%) and 4 female (20%) normal control were selected with age range 40-70 years. (Table -I) .

Table-II shows the serum apoA1 & apoB concentration in different Groups. In Group-I (case) mean apoA1 concentration found 91.84± 11.2 mg/dl

with the range 68.0- 105.0 and that of apo B concentration found 135.3±23.0 mg/dl with the range 106.0-187.0. In Group-II (Normal control) mean apoA1 concentration was 123.2±10.5 mg/dl with the range 105.0- 145.0 and of apoB concentration was 66.2± 10.0 mg/dl with the range 55.0-94.9 respectively. In MI cases apoB found significantly

increased and apoA1 found significantly decreased compared to control.

Table III shows the comparison of ratio of apoB/apoA1. The ratio in group1 (cases) and group II (normal control) were 1.49±0.30 and 0.54±0.10 respectively, which was found significantly elevated in case compared to normal control.

Table1

Age & sex distribution of study subjects				
Study Subject	Age (year)		Sex	
	Mean ± SD	Age range	Male	Female
MI cases (Gr-I) (n=30)	55.5 ± 9.8	40-70	26	4
Normal Control(Gr-II) (n=20)	52.6 ± **9.6**	40-70	16	4

Table II

Serum A1 and Apo B concentration of the study subjects			
Parameter Mean ± SD	Group I (cases) n=30	Group II (Control) n=20	Level of significance (p-Value)
Apo A1 (mg/dl)	91.84 ± 11.2 (68.0 – 105.0)*	123.2 ± 10.5 (105.0 – 145.0)*	0.001
Apo B (mg/dl)	135.3 ± 23.0 (106.0 – 187.0)*	66.2 ± 10.0 (55.0 – 94.9)*	0.001

P value reached by unpaired t test   * Paranthesis shows range

Table III

Comparison of the ratio of Apo B / Apo A1 between study subject.			
Parameter	Group I (cases)	Group II	Level of significance (p-Value)
Apo B / Apo A1	1.48 ± .03	0.54 ± 0.1	0.001

P value reached by unpaired t test

Discussion

In this study MI patients found to have serum apoB concentration significantly increased and apoA1 concentration significantly decreased in comparison to control. A similar phenomenon was reported in many other studies around the world.[18,19,20,21,1,22,23,24,25].

Atherogenic lipoproteins particles are heterogenous with respect to their cholesterol content but homogenous with respect to their apoB content .So serum apoB more accurately reflects the total number of circulating atherogenic particles which their total cholesterol content cannot. For example small dense LDL particles are cholesterol depleted compared to large LDL particles but all LDL subtypes contain one molecule apoB .So the number of circulating LDL particle is more accurately measured by their apo-B content rather then LDL-C. Although about 70% of plasma cholesterol is carried by LDL but apart from LDL, there are number of other highly atherogenic circulating lipoproteins, all of which contain apo-B. Therefore serum apoB is the more comprehensive and reliable marker of atherogenicity rather than the LDL-C alone[26,27,28].

HDL is regarded as an anti-atherogenic lipoprotein. Various subtypes of HDL (e.g. HDL1, HDL2, HDL3 etc.) has been described which differ from each other with respect to their apoprotein and antiatherogenicity. To be a antiatherogenic, HDL needs to contain apo-A1 which is not true for all HDL subtypes (e.g. HDL_1 contain no apo A1)[10]. Therefore it mightbe possible for an individual to present with MI having normal HDL-C but decreased serum apoA1 concentration due to predominance of HDL1 subtype or the HDL subtypes without apoA1.

Conclusion:

It can be concluded from this study that; serum ApoA1 and ApoB are more reliable tool to assess and evaluate the atherosclerotic disorders specially the CAD. Therefore if accurate precise and affordable standardized methods be come available for the measurement of apoA1 and apoB, these apoproteins measurement may be recommended as a routine laboratory test to evaluate the MI patient & to assess the risk of MI.

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Problems and Immediate Outcome of Infants of Diabetic Mothers

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Summary:

Objective:The present study was undertaken to evaluate the problems and immediate outcome of infants of diabetic mothers(IDMs) in early neonatal period and to compare the results between infants of gestational and pregestational diabetic mothers.

Design: A hospital based prospective study. Setting: The study was done in Chittagong Medical College Hospital, a tertiary hospital in Chittagong city. Method: Within one hour of delivery 52 infants of diabetic [pregastational & gestational] mothers consecutively admitted were enrolled in the study. Study period was January 2002 to August 2002.

Results: Total number of IDMs were 52.Among them 31 were gestational and 21 were of pregestational diabetic mothers.

Significant number 82.6% of IDMs were delivered by caesarean section. The mean birth weight of IDMs was significantly high(3212±563g), 21% of IDMs had birth weight>4000 g. Total 23% of the IDMs developed perinatal asphyxia .The 23% of IDMs developed hypoglycaemia.The incidence of hypoglycaemia was higher in infants of pregestational diabetic mothers as compared to that of gestational diabetic mothers(38.09% and 12.9% respectively), the difference was statistically significant(P<0.05).In majority (66%) of IDMs cases hypoglycaemia was symptomatic. Significant number

(19.2%) of IDMs had hypocalcaemia. The incidence of polycythaemia was higher in infants of gestatational diabetic mothers(GDMs) as compared to infants of pregestational diabetic mothers(25.8% and 9.5% respectively), difference was statistically significant(P<0.001). 3(5.7%) out of 52 IDMs had congenital malformation (each one in number polydactyly, cleft palate & preauricular skin tag). Total death was 3(5.7%) all of them died within 72 hours of birth. Causes of death 1 each number: perinatal asphyxia, respiratory distress syndrome and meconium aspiration syndrome. 11 IDM was macrosomic, among them 1 had birth injury(Erb's palsy), hypoglycaemia and meconium aspiration syndrome and expired within first 24 hours of life.

Conclusion:Among the important problems the present study revealed perinatal asphyxia, hypoglycaemia, hypocalcaemia, polycythaemia top the list. These babies should be delivered at hospitals where special neonatal care available for management of high risks babies to reduce the morbidity and mortality. Screening for GDMs should be performed in all pregnant women. All diabetic women should have planned pregnancy and proper antenatal care in order to maintain strict glycaemic control, to have a satisfactory outcome in infants of diabetic mothers.

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Introduction:

Diabetes mellitus is characterized by hyperglycaemia, disturbance of carbohydrate, fat and protein metabolism that are associated with absolute or relative deficiencies in insulin action and/or insulin

secretion[1]**.** Diabetes mellitus is the commonest endocrine disorder during pregnancy. In fact many prediabetics and potential diabetics may show chemical evidences of diabetes mellitus during the course of metabolic stress of pregnancy. Gestational diabetes where in glucose homeostasis returns back to nomal after delivery, also increases various risk to the fetus and newborn. The duration and severity of maternal diabetes and quality of its control during pregnancy determine the outcome of the offspring[2]

Diabetes mellitus is prevalent among 2.1% people of Bangladesh[3].Gestational diabetes mellitus (GDM) develops among 6.7% of all pregnancies in our population[4]. In western world 2 to 3% of all pregnancies are currently being diagnosed as GDM[5].

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Infant of diabetic mothers have a 47% risk of significant hypoglycaemia, 22% risk of hypocalcaemia,19% risk of hyperbilirubinemia, 34% risk of polycythaemia, 6-9% incidence of major congenital anomalies(congenital heart disease, central nervous system & vertebral anomalies)[6], 4% risk of respiratory distress syndrome, 28% risk of macrosomia & cardiomegaly (30%).

Among the various metabolic errors these infants suffer, hypoglycaemia is the commonest and most dangerous[7].Infants of diabetic mothers have hyperinsulinism at birth due to increased placental transfer of glucose and other nutrients stimulating hyperplasia of islets of Langerhans in the fetus and increased insulin secretion, raised amount of C-peptide and free insulin in cord blood. Once the maternal supply of glucose is cut-off by clamping the cord, the excess insulin circulating in the baby's system quickly rids the plasma of the remaining glucose and so blood glucose level may drop precipitously and alarmingly during the first few hours of life[8]. Hypoglycaemia is defined as a blood glucose level less then 2.6mmol/L. Symptoms of hypoglycaemia, are non specific, such as lethargy, apathy, limpness, apnea, cyanosis, weak or high pitched cry, poor feeding ,vomiting, tremors, jitteriness , irritability,seizures,coma[9]. Neonetal hypocalcaemia may be due to hypoparathyroidism, abnormal vitamin D metabolism and hyperphosphataemia. Neonatal hypocalcaemia is defined as total serum calcium concentration of less than 7 mg/dl and an ionized calcium conc. of less than 4 mg/dl[10]. Polycythaemia (haematocrit of more than 0.651) occurs in 30 to 60% of IDMs causing the neonatal hyperviscosity syndrome. The main cause of polycythaemia is chronic intrauterine hypoxaemia, which occurs as consequence of fetal hyperinsulinism and hyperglycaemia.[11].

Macrosomia (birth weight> 4000 g) may be associated with increased incidence of primary caesarean section or obstetric trauma such as fractured clavicle, Erb's palsy or phrenic nerve palsy due to shoulder dystocia [7, 9].

Hypertropic cardiomyopathy with asymmetric septal hypertrophy has been extensively documented[10].The babies may also develop small left colon syndrome, a transient delay in the development of left side of colon.[4,5].Despite improvement in diabetic care, the perinatal mortality still remains four times high than in nondiabetic women. Predominant causes of mortality are congenital anomaly, birth trauma, respiratory distress syndrome, prematurity and unexplained still birth[12].

Although in developed countries there has been significant improvement in the outcome of diabetic pregnancies largely due to better metabolic control before and during pregnancy and vigorous neonatal care, the management in our country still poses a major challenge.

Aims of this study were to find out problems of IDM during early neonatal period that threaten baby's life and with appropriate management to determine immediate outcome in hospitalized IDM. The study was designed to evaluate the problems and immediate outcome of infants of diabetic mothers in early neonatal period and to compare the results between infants of gestational and pregestational diabetic mothers in neonatal unit of Chittagong Medical College Hospital,Chittagong.

Materials and Method:

This hospital based prospective study was done in neonatal unit of Chittagong Medical College Hospital in collaboration with Department of Obstetrics and Gynecology of this hospital. Within one hour of delivery 52 infants of diabetic [pregestational & gestational] mothers consecutively admitted for observation and further management where enrolled in the study. Exclusion criterion was infants of diabetic mothers were admitted as referred case from other hospitals. Study period was January 2002 to August 2002.

 After taking the verbal consent from the attendant, the relevant information from the history, physical examination and investigation findings were recorded in a purposely prepared questionnaire. Investigations routinely underwent were capillary blood glucose at 0(cord blood), 2, 4, 6,12,24,48 and 72 hours of age by using glucostix. Peripheral blood glucose was collected with single puncture non-squeezing procedure by trained technician and level measured by Glucose oxidase method in auto analyzer at 6, 12,24,48,72 hours of age and whenever any

symptoms suggestive of hypoglycaemia developed. The glucostix(capillary blood glucose) was used for screening purpose and for prompt diagnosis and management of hypoglycaemia and estimation of peripheral venous blood glucose level was done for further confirmation of diagnosis. Serum calcium level were measured routinely at 6,24,48 hours of age and later if the baby remains hypocalcaemic or symptomatic. Hematocrit at 1hour & 24 hour of age was done routinely. Blood samples collected in each time in all cases by trained technician, results were measured by autoanalyzar and interpreted by expert person. Among other investigations: platelets count, CXR PA view, plain X ray of lumbosacral spine, Hb%, TC, DC, blood culture, ECG, echocardiography etc were done as indicated by clinical parameters, not done routinely in all cases as study population were admitted within one hour of delivery for management and further observation whether any problem developed.   Results were analyzed by analyzing software SPSS.

Results:

Total number of IDMs were 52.Among them 31(59.6%) were gestational diabetic mothers and 21(40.3%) were of pregestational diabetic mothers (Table-I).

92.3% of the IDMs were term as compared to 7.6% preterm delivery and majority of the IDMs(82.6%) were delivered by caesarean section as compared to 17.3% normal delivery (Table-II).

Macrosomia was found in 21.1 %(Table-III).

12(23%) out of 52 IDMs developed perinatal asphyxia. 25.8% of IGDMs developed perinatal asphyxia in comparison to 19% of IPGDMs, although the difference is not significant statistically(P>0.50) as shown in Table-IV. Table-V shows 23% of IDMs developed hypoglycaemia. Among the 12 infants (23%) having hypoglycaemia, only 8 were symptomatic. Lethergy & jitteriness was most commonly observed. Only 2 newborns developed seizure. The occurrence of hypoglycaemia was higher in infants of pregestational diabetic mothers as compared to that of GDM mothers(38.09% and 12.9% respectively) the difference was statistically significant (p<0.05) as in Table-VI. 10 (19.2%) of the IDMs developed hypocalcaemia.16.1% & 23.8%

infants of gestational & pregestational diabetic mothers had hypocalcaemia respectively and the difference was not statistically significant (P>0.50).Out of the 10, four had symptoms, mainly jitteriness (Table-VII).

In this study ,25.8% and 9.5% of infants of gestational and pregestational diabetic mothers developed polycythaemia respectively and the difference was statistically significant(P< 0.001) shown in Table-VIII.

In the present study, 3(5.7%) out of 52 IDMs had congenital malformation (each one in number: polydactyly, cleft palate & preauricular skin tag).In the study undertaken, 2 (3.8%) of IDMs developed RDS (respiratory distress syndrome), one of which expired and another one survived. Out of 52 IDMs one developed meconium aspiration syndrome also had birth injury (Erb's palsy) and hypoglycaemia and expired within 24 hours of birth. Another IDM had severe perinatal asphyxia and expired (Table IX).

Total survival of IDM was 49(94.2 %) and discharged within 7 days of admission.

Table-I

Distribution of neonates according to type of maternal diabetes (n=52)

Group	No. of cases	Percentage
IGDMs	31	59.61
IPGDMs	21	40.38
IDMs (n=52)		

IGDMs = Infants of gestational diabetic mothers
IPGDMs = Infants of pregestational diabetic mothers
IDMs   = Infants of diabetic mothers

Table-II

Frequency of gestational age & mode of delivery in IDMs(n=52).

Features	No.	%
Gestational age:		
Term	48	92.3
Preterm	04	7.6
Mode of delivery:		
Normal	09	17.3
Caesarian	43	82.6

Table-III

Distribution of IDMs according to birth weight (n=52)

Birth weight(grams)	No. of cases	Percentage
1500 - 2499	04	7.6
2500 - 2999	06	11.5
3000 - 3499	15	28.8
3500 - 4000	16	30.7
>4000		
	11	21.1

Mean 3212±563

Table-IV

Frequency of perinatal asphyxia in IGDMs & IPGDMs.

Group	Perinatal sphyxia Present No	%	Perinatal asphyxia absent No	%	P value
IGDMs (n=31)	8	25.80	23	74.19	P>0.50
IPGDMs (n=21)	4	19.04	17	80.95	
IDMs (n=52)	12	23.07	40	76.92	

Table -V

Frequency of hypoglycaemia in IDM: Number 12(23%)

	IGDMs n=31 No	%	IPGDMs n=21 No	%	IDMs (Total, n=52) No	%
Symptomatic	3	9.6	5	23.8	8	15.3
Asymptomatic	1	3.2	8	38.0	12	23.0
Total	4	12.9				

Table -VI

Frequency of hypoglycaemia in IGDMs & IPGDMs.

Group	Hypoglycaemia Present No	%	Hypoglycaemia absent No	%	P value
IGDMs n=31	4	12.90	27	87.09	P>0.50
IPGDMs n=21			13	61.90	
IDMs (total) n=52	8	38.09	40	76.92	
	12	23.07			

Table -VII

Frequency of hypocalcaemia in IGDMs & IPGDMs.

Group	Hypocalcaemia Present No	%	Hypocalcaemia absent No	%	P value
IGDMs n=31	5	16.12	26	83.87	P>0.50
IPGDMs n=21			16	76.19	
IDMs (total) n=52	5	23.80	42	80.76	
	10	19.23			

Table -VIII

Frequency of polycythaemia in IDMs.

Group	Polycythaemia Present No	%	Polycythaemia absent No	%	P value
IGDMs n=31	8	25.80	23	74.19	P>0.50
IPGDMs n=21	2	9.52	19	90.47	
IDMs (total) n=52	10	19.23	42	80.76	

Table – IX

Immediate outcome of IDMs in relation to problem.

Problems		Total survival=49 Number %	Total death=3 Number %	Total cases n=52 Number %
Birth weight (gm)	1500-2499	03(6.1)	01(33.3)	04(7.6)
	2500-2999	05(10.2)	01(33.3)	06(11.5)
	3000-3499	15(30.6)	——-	15(28.8)
	3500-4000	15(30.6)	——-	16(30.7)
	>4000	11(22.4)	01(33.3)	11(21.1)
Perinatal asphyxia	Yes	11(22.4)	01(33.3)	12(23.0)
	No	38(77.5)	02(66.6)	40(76.9)
Hypoglycaemia	Yes	10(20.4)	02(66.6)	12(23.0)
	No	39(79.5)	01(33.3)	40(76.9)
Hypocalcaemia	Yes	10(20.4)	——-	10(19.2)
	No	39(79.5)	03(100.0)	42(80.7)
Polycythaemia	Yes	10(20.4)	———	10(19.2)
	No	39(79.5)	03(100.0)	42(80.7)
Congenital malformations	Yes	03(6.1)	———	03(5.7)
	No	46(93.8)	03(100.0)	49(94.2)
Birth injuries	Yes	01(2.0)	01(33.3)	02(3.8)
	No	48(97.9)	02(66.6)	50(96.1)
Respiratory distress syndrome	Yes	01(2.0)	01(33.3)	02(3.8)
	No	48(97.9)	02(66.6)	50(96.1)
Meconium aspiration syndrome	Yes	00(0)	01(33.3)	01(1.9)
	No	49(100)	02(66.6)	51(98.0)

Discussion:

Diabetes mellitus is prevalent among 2.1% people of Bangladesh.[13] Among them a significant number are female. GDM (gestational diabetes mellitus) develops among 6.7% of all pregnancies in our population.[14]. In western world 2 to 3% of all pregnancies are currently being diagnosed as GDM [5]. In this study, the total number of IDMs was 52. Among them 31 were gestational diabetic mothers and 21 were pregestational diabetic mothers. Begum A [15] in a study of 105 newborns reported that 44.4% of diabetic mothers had GDM and remaining were pregestational. Begum N[16] in her study found that among 112 diabetic mothers 58.9% had GDM and 41% had pregestational diabetes mellitus. 93% of the IDMs were term as compared to 7.6% preterm delivery in the present study. IDMs may need to be delivered prematurely due to maternal or fetal problems. Ranade *et al.*[17] reported 36% of the IDMs to be preterm. Overall, 26% of the diabetic women deliver before 37 weeks gestation, compared with 10% in general population.[12]. In this study majority of the IDMs (82.6%) were delivered by caesarean section as compared to 17.3% normal delivery. Mohsin F[18] in her study found that the rate of caesarean section (80%) in IDMs. The mean birth weight was significantly high 3212 ± 563 g in the present study. Mohsin F[18] and Begum N[16] in their study found the mean birth weight of IDMs to be 3038 ± 69 g and 2970 ± 636 g respectively. Macrosomia, that is, a birth weight above the 90th percentile for gestational age or weight>4000 g. was found in 22.4% in the present study. The incidence of macrosomia in IDMs has been reported to be in the range of 20 to 32% by Gabee et al[19] and Elliot et al[20]. Perinatal asphyxia that occurs in IDMs is perhaps a result of multiple factors: maternal hypertension with resultant reduction of placental blood flow, premature labour ,fetal macrosomia and maternal hyperglycaemia within 6 to 8 hours preceding delivery ,which supposedly reduces placental blood flow[21].In the study undertaken, 12(23%) out of 52 IDMs developed perinatal asphyxia. Mohsin F[18] and Begum N [16] reported the incidence of perinatal asphyxia 12% and 20.53% respectively. In the present study, 25% of IGDMs developed perinatal asphyxia in comparison to 19% of IPGDMs, that was not significant (P>0.05). Out of 12 cases, one was severely asphyxiated and expired few hours after birth.

Among the different metabolic errors these infants suffer, hypoglycaemia is commonest and most dangerous. In this study, 12 infants (23%) having hypoglycaemia, only 8 were symptomatic. Lethergy & jitteriness was most commonly observed. Only 2 newborns developed seizure. Ranade et al[17], Hossain et al[22] and Mountain[8] reported the incidence to be 50%, 52.8% and 55.2% respectively. The occurrence of hypoglycaemia was higher in infants of pregestational diabetic mothers as compared to that of GDM mothers(38.09% and 12.9% respectively) the difference was statistically significant(p<0.05) in this study. 61% IPGDMs had hypoglycaemia in contrast to 44.2% in IGDMs as reported by Mountain[8]. Hypocalcaemia is one of the important metabolic errors the IDMs suffer, probably due to functional hypoparathyroidism[23].In this study, 10 (19.2%) of the IDMs developed hypocalcaemia.16% & 23% infants of gestational & pregestational diabetic mothers developed hypocalcaemia respectively and the difference was not statistically significant (P>0.50).Out of the 10 , four had symptoms, mainly jitteriness. Marchant et al[24],Ranade et al[17],Deorari et al[25], and Mountain[8] reported the incidence of hypocalcaemia to be 60%,14% ,13% and 25-50% respectively. In this study, total 10(19.2%) of IDMs developed polycythaemia, one case was symptomatic and needed partial exchange transfusion. Mohsin F[18] reported incidence of polycythaemia 29% in her study. 25.8% and 9.5% of infants of gestational and pregestational diabetic mothers developed polycythaemia respectively and the difference was statistically significant (P< 0.001). In the present study, congenital malformation was noticed in 3 (5.7%) IDMs (each one in number: polydactyly,cleft palate & preauricular skin tag). Congenital malformations have been reported to be 2-4 times as common in the offspring of diabetic mothers as compared to non-diabetic mothers[5, 12, 26]. Begum N[16] in her study shown the frequency of congenital malformation in IDMs was 10.7%.In the study undertaken, 2 (3.8%) of IDMs developed RDS(respiratory distress syndrome),one of which expired and another one survived. Out of 52 IDMs one developed meconium aspiration syndrome also had birth injury (Erb's palsy) and hypoglycaemia and expired within 24 hours of birth. Another IDM had severe perinatal asphyxia and expired. Despite improvement in diabetic care, the perinatal mortality still remains four times higher than in nondiabetic

women. Predominant causes of mortality are congenital anomaly, birth trauma, respiratory distress syndrome, prematurity and unexplained still birth[12]

Conclusion:

Despite the curbing of our perinatal mortality rate, the IDMs are victims of significant mortality and morbidity. Among the important problems the present study revealed perinatal asphyxia, hypoglycaemia, hypocalcaemia, polycythaemia top the list. These babies should be delivered at hospitals where special neonatal care available for management of high risks babies to reduce the morbidity and mortality. Screening for GDM should be performed in all pregnant women. All diabetic women should have planned pregnancy and proper antenatal care in order to maintain strict glycaemic control and to have a satisfactory outcome in infants of diabetic mothers.

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Radioiodine (^{131}i) Therapy for Thyrotoxicosis Patients and their Outcome: Experience at Center for Nuclear Medicine & Ultrasound, Barisal

SK BISWAS[a], N JAHAN[b], KBMA RAHMAN[c]

Summary:

Radioiodine therapy appears to be an effective means in controlling thyrotoxicosis and it acts either by destroying functioning thyroid cells or by inhibiting their ability to replicate. The variable radiosensitivity of the gland means that the choice of dose is empirical. Unfortunately all attempts at dosimetry have thus far failed to reliably deliver a dose that avoids recurrence and does not ultimately lead to hypothyroidism. Ninety five patients (female 66 and male 29) with thyrotoxicosis treated with radioiodine at the Center for Nuclear Medicine & Ultrasound, Barisal and their outcome were analyzed from January 2000 to December 2004. Before radioiodine administration clinical features of the patients, palpation of the thyroid gland and ultrasonogram were performed.131_I was given as fixed dose method and the dose ranged from 8-12 mCi. Higher doses were administered for larger goiter, multinodular goiter and in relapse cases. Hyperthyroid state was controlled in 85 (89%) patients after receiving single dose of radioiodine and 13 (13.6%) patients developed hypothyroidism within 3 months of therapy. Radioiodine therapy has proved to be cheap and effective method of treatment for thyrotoxicosis.

Key words: Thyrotoxicosis, Radioiodine therapy, Hypothyroidism.

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Introduction:

Thyrotoxicosis is a clinical condition that results from high level of circulating thyroxine and triiodothyronine. These patients are usually restless, talk rapidly, and display emotional liability. Other classic signs and symptoms include sweating, heat intolerance, palpitations, insomnias, and worm, fine skin. Prominent eyes or a state may be produced by increased thyroid hormones level, but infiltrative eye signs signal the presence of Graves' disease. Graves' disease is the most common (70-85%) cause of thyrotoxicosis and occurs most frequently in young women.[1] Radioiodine therapy is a promising technique for the patients with thyrotoxicosis. The major attraction of radioiodine as a therapeutic agent for thyrotoxicosis lies in its simplicity, relatively low cost and absence of significant complications. [2] ^{131}I is administered orally as a single dose and is trapped and organified in the thyroid, the effects of its radiation is long lasting, with cumulative effects on follicular cell survival and replication. Carbimazole reduces the efficacy of ^{131}I therapy because it prevents organification of ^{131}I in the gland, and so should be avoided until 48 hrs after radio-iodine administration.[3] The majority of the patients eventually develop hypothyroidism and the incidence of hypothyroidism after radioiodine treatment varies, depending on the dose used, individual sensitivity to radioiodine and the length of follow up. The aim of the present study was to assess its effectiveness in controlling the disease as well as the incidence of hypothyroidism following radioiodine therapy.

Material and Methods:

Ninety five patients who received radioiodine therapy during a period of January 2000 through December 2004 at the Center for Nuclear Medicine & Ultrasound, Barisal were enrolled for this retrospective study. All patients were diagnosed hyperthyroidism on the basis of clinical features and thyroid hormone levels. Their total triiodothyronine (T_3) and thyroxine (T_4) level were raised with low

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thyroid stimulating hormone (TSH). Serum T_3 and T_4 were measured by radioimmunoassay (RIA) method and TSH was measured by immunoradiometric assay (IRMA). The normal range of T_3, T4 and TSH were 1.23-3.54 nmol/L, 54- 173 nmol/l and 0.3-5 mIU/L respectively in the studied laboratory.

All patients were referred by the physicians. Clinical features and body weight were recorded in a predesigned clinical proforma.Thyroid glands were palpated and ultrasonogram was performed for each individual using 5 MHz curvilinear probe. The parenchymal echotexcture and the volume of the thyroid gland were measured and noted accordingly. Radionuclide thyroid scan was performed with ^{99m}Tc pertechnate using gmma camera.

Before administering radioiodine, the nature of the treatment and its radiation risk, cost benefit ratio, the importance of precautionary measures and the necessity of subsequent follow up were explained to the patients. In case of female of reproductive age, menstrual history was taken carefully and pregnancy was excluded before radioiodine therapy and the rule of 10 days were followed.

The dose of ^{131}I was given to the patients as a fixed dose method. The dose given at first time ranged from 8-12 mCi with a mean ($\pm$ SD) of 10.6 ± 1.54 mCi. Higher dose was given for very large and multinodular goiter. Similarly lower dose was required for relatively smaller and / or diffuse goiter. Clinical features also considered carefully before estimating the dose. In case of 2nd or subsequent therapy higher doses were required. Antithyroid drugs (Crbimazole) and β blockers were given to patients who had marked features of thyrotoxicosis, very ill health, and in old age group. Antithyroid drugs were usually given for 4-6 weeks and stopped 3 days prior to radioiodine therapy. That was resumed after 3 days and advised to continue for another 4-6 weeks according to symptoms.

Patients were advised to attend the center as required or after 3 months whichever is earlier. Next follow up was performed at three months interval for first year and six monthly for subsequent years. In each follow up clinical features and thyroid hormone levels were assessed. When the 1st dose seemed to be ineffective 2nd or subsequent dosage were considered at least 6

months after the first dose. Patients who developed hypothyroidism, managed with thyroxine replacement as long as needed.

Results and observations:

Ninety five thyrotoxicosis patients treated with radioiodine (^{131}I) from January 2000 through December 2004 were available for the analysis of therapeutic outcome. Among 95 patients, female were 66 and male 29 with the age ranged from 18-75 years (Fig-1). The mean ($\pm$ SD) age of the patients was 41.65 ± 11.48 years and the female to male ratio was 2.2:1. Most of them had history of weight loss, palpitation, sweating and tremor (Fig-2), and out of ninety five, thirty six patients had exophthalmos. On ultrasonogram 90 patients (94.73 %) had diffuse
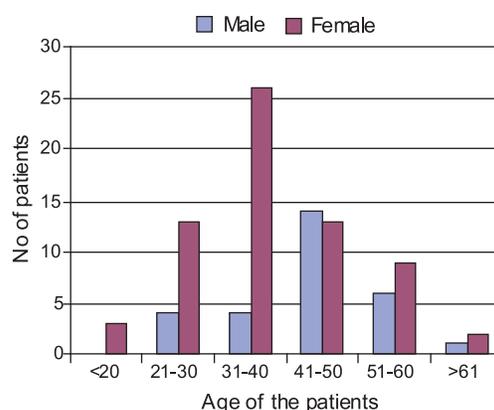

Fig.1: *Age and sex distribution of the patients with thyrotoxicosis.*
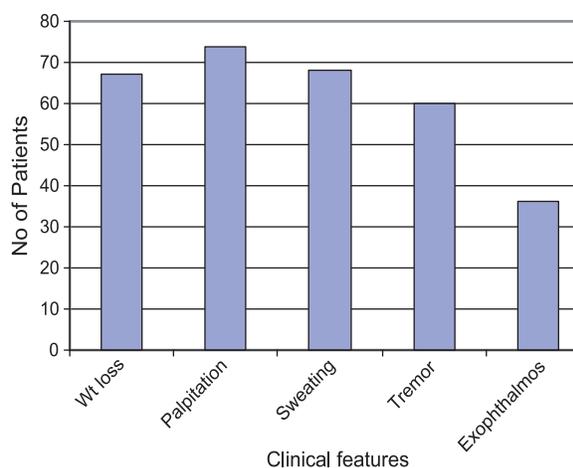
Fig.2: *Common clinical features among the patients with thyrotoxicosis.*

goiter, 3 (3.15 %) had single nodular goiter and 2 (2 %) had multinodular goiter. Their mean (± SD) T_3 level was 7.75 ± 2.85 nmol/L, mean (± SD) T_4 level was 272.75 ± 42.39 nmol/L and mean (± SD) TSH level was 0.14 ± 0.11 mIU/L.

Out of 95, follow up was possible for 60 (63%) patients and 35 (37 %) patients did not attend the center after their first follow up, probably they attended other centers for further follow up or became euthyroid. Thirty five (36.8 %) patients developed hypothyroidism following radioiodine therapy. Among the total of 95 patients,13 (13.6%) patients developed hypothyroidism within 3 months of radioiodine therapy; next 60 patients were considered for subsequent follow up and of them, 15 (25 %) patients developed hypothyroidism within 6 months, 5 (8.3 %) within 1 year, 2 (3.3 %) after 18 months. Thirty six (38 %) patients had markedly raised T_3 & T_4 and / or cardiovascular problem and they needed pretreatment with antithyroid drugs for 4 weeks prior to radioiodine therapy. Exophthalmos was present in 36 (38 %) patients and for one of them prednisolone was given, which was tapered gradually. Thyrotoxicosis was controlled (euthyroid or hypothyroid) in 85 (89 %) patients after receiving single dose of radioiodine therapy, 7 patients needed 2nd dose, 2 patients needed 3rd dose, and 4th dose was needed for 1 patient.
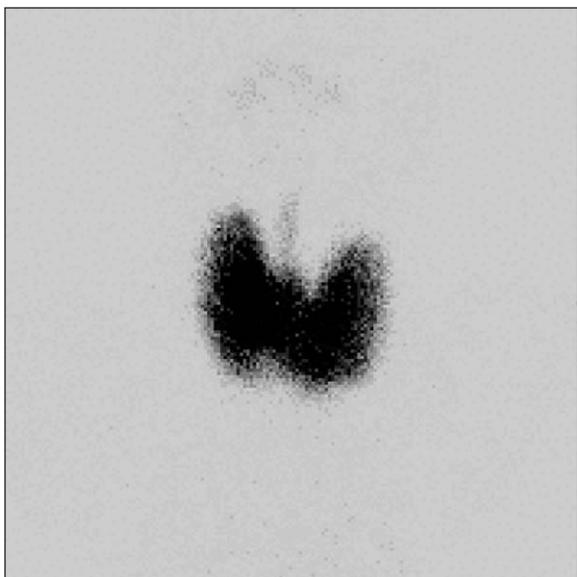
Fig.3: *Scan image of diffusely enlarged thyroid gland with intense and uniform radiotracer concentration allover.*
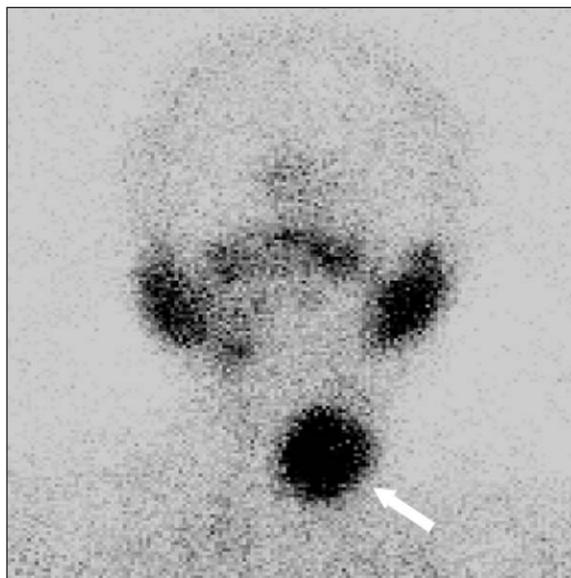
Fig.4: *Scan image of autonomously functioning toxic nodule in the left lobe*

Discussion:

Thyrotoxicosis may be managed by antithyroid drugs, surgery and radioiodine therapy.[4] Radioactive iodine is established as a simple, cheap and effective method of treating thyrotoxicosis, and in most of the cases represents the treatment of choice.[5] There is no evidence that thyroid carcinoma or leukaemia is induced by therapeutic dose of ^{131}I, or that its results in an increased frequency of congenital malformation among subsequent offspring.[6,7,8] Thyrotoxicosis may be divided into two major categories for which ^{131}I treatment may be indicated: (a) the nonautoimmune toxic nodule, including the autonomously functioning nodule and the toxic multinodular goiter; and (b) the autoimmune causes, notably Graves' disease (3).

Most patients with Graves' disease are treated with radioactive iodine ^{131}I, some early after diagnosis and others 6-12 months later. There is over 50 years of experience with use of therapeutic [131]I. Endocrinologists have become comfortable with treating patients, even children, with ^{131}I because of its high efficacy and low incidence of adverse affects. Symptomatic improvement is usually noted by 3 weeks after therapy. However, the full therapeutic effect takes 3-6 months because stored hormone must first be released and used. Some evidence suggests

that exacerbation of exophthalmos with ^{131}I therapy, so steroids are often administered.[9] In case of nodular goiter isotope is taken up selectively by the toxic nodules, which are then functionally destroyed and rest part of the gland is largely spared from the damaging effect. So the patient with toxic nodular goiter is likely to return to euthyroid state after ^{131}I therapy.[10] On the other hand in Graves' disease patient, there is relatively uniform global uptake of the ^{131}I, and ultimate progression of hypothyroidism is common.[4] Antithyroid drugs are generally ineffective for long term remission of hyperthyroidism. Harshman *et al* found that there is an early relapse or late recurrence of hyperthyroidism in about 50 % patients when treatment is stopped even after a prolonged period course of two years or more,[11] without surgical risk, still it is favored by many thyroidologists. Surgical management offers rapid resolution of hyperthyroidism, slower progression to permanent hypothyroidism, removal of large goiter causing compression and substernal extension. Indeed, isotope treatment of the nonimmune types of the hyperthyroidism would appear to be nearly ideal.[12]

Calculating the dose, based on thyroid volume and iodine uptake, it is possible to reduce the incidence of early hypothyroidism. Combining the most sophisticated ultrasonogram techniques and dosimetry, one may expect better outcome with prompt (within 3-6months) control of hyperthyroidism and delayed onset of hypothyroidism. When treatment results in hypothyroidism, the commonly observed symptoms and signs of a slowed metabolism may be accompanied by headache and generalized muscle and joint discomfort. The headache is considered to be the result of pituitary swelling; both of these symptoms clear promptly with thyroid hormone replacement.[4]

[131] I treatment causes significant reduction of thyroid volume in both toxic and nontoxic goiter.[13,14,15] The most obvious objective of radioiodine therapy is to render the patient euthyroid and off drug therapy. Routine use of antithyroid drugs prior to radioiodine therapy is not necessary. However in high risk patients with severe hyperthyroidism, associated with other complications particularly cardiovascular disease, and in old age group, it is reasonable and appropriate to bring these patients to euthyroid state with antithyroid drugs before radioiodine therapy.[16] In the present study, for 36 (38%) patients antithyroid drugs were given.

Exacerbation of symptoms may occur because of release of stored hormone from radiation thyroiditis and it may occur any time from 12 hours to 20 days after therapy, average 10-14 days. Since carbimazole blocks the organification of iodine within the thyroid, carbimazole therapy should be discontinued at least 48 hours before therapy is undertaken to ensure adequate residence of ^{131}I within the follicular cells.[17] Beta blockers which are also conventionally used for most of the patients to combat the symptoms do not affect radioiodine therapy.[18] Radioiodine therapy for hyperthyroidism has no significant complications but the major disadvantage is post treatment hypothyroidism. Chapman EM found no evidence of irradiation thyroiditis in patients administering less than 15 mCi of [131] I in a single dose.[19] Hypothyroidism is dose related; however, even with low doses, 76% patients have hypothyroidism by 11 years posttreatment. Range in first year varies between 5% and 70%. Average approximately 5.55 per month for first six months; 13% per month for second 6 months.[18] In the present study 13.6% developed hypothyroidism within 3 months of radioiodine therapy and 25 % within 6 months, which corresponds well with the previous study.

There are two ways of fixed dose administration: (a) Low dose- 3-5 mCi administered as a fixed dose. Since initial onset of hypothyroidism id dose related, has lower incidence of hypothyroidism. However, cure rate is lowered, as well. (b) High dose- 8-10mCi dose given to all patients, Success rate with one therapy using this dosage range >90%. Incidence of hypothyroidism within one or two years after treatment has a direct relationship with ^{131}I doses given to the patients [20] but delayed hypothyroidism develops at about the same rate regardless of the dose of ^{131}I used. [21,22]

All patients who have been treated with ^{131}I for hyperthyroidism must have long term follow up to detect the hypothyroidism, and motivation is very important in this respect. In the absence of any specific symptoms or signs, annual serum T_4

estimation is the best and easiest routine follow-up investigation for screening. If T_4 is below normal, hypothyroidism can be confirmed by measurement of serum TSH on the same sample. If recurrent hyperthyroidism is suspected clinically, serum T_3 should be estimated. The addition of sensitive TSH measurement to the follow up protocol improves the effectiveness of the assessment but increases the cost.[5]

Persistence of goiter along with hyperthyroidism at 3 months after treatment usually means treatment failure. However, it is still recommended to wait the additional 3 months under protection of a beta blocker and an antithyroid drug. Transient hypothyroidism may occur after several months. It is wise to delay T_4 replacement therapy until an additional 2-3 months have lapsed, allowing for the possibility that a rising TSH may raise T_4 and T_3 to normal levels. On the other hand, an enlarging goiter in a patient who is euthyroid or hypothyroid at 3 months after ^{131}I therapy may require T_4 replacement that will shrink the goiter and relieve the symptoms.[23]

In the present study 89 % patients were controlled (euthyroid/hypothyroid) receiving the single dose of radioiodine therapy which was close to that in other studies.[24,25] Recently one long term follow up study was carried out in the Institute of Nuclear Medicine and Ultrasound, Dhaka considering teenage hyperthyroidism and radioiodine therapy, which revealed that the mean administered dose of radioiodine was 10.69 ± 2.77 mCi and the mean age of the patients was 16-18 yrs. The effective control of hyperthyroidism after radioiodine treatment occurred in 60.72 % patients with a single dose, 35.71 % required a second dose and 3.57 % required more than two doses. Overall incidence rates of hypothyroidism after 1 year and 5 years of radioiodine therapy were 32.14 % and 75 % respectively and patients with Graves' disease showed a greater tendency in the evolution of early hypothyroidism.[26] Though the period of our study was not long enough to assess the outcome of radioiodine therapy for thyrotoxicosis, still follow up is continuining with the maintenance of their files.

Conclusion:

Radioiodine therapy for thyrotoxicosis is now becoming the treatment of choice due to its simplicity, relatively low cost and absence of significant complications. By measuring the exact thyroid volume and estimation of the proper dose, the incidence of hypothyroidism following therapy can be reduced. Motivation and good cooperation with the patients ensure regular follow up and ultimately better outcome of radioiodine therapy.

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Co-relation between Sepsis Score and Blood Culture Report in Neonatal Septicaemia

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Summary:

Objective: To determine the clinical profile and to co-relate the sepsis score with blood culture reports in neonatal septicaemia. Methods: Over a period of 6 months (1st week of June to 1st week of December'2005) 50 consecutive newborns with suspected septicaemia were enrolled for the study. It was a prospective study and septicaemia was suspected on the basis of clinical presentation like reluctance to feed, lethargy, fever, abdominal distension etc. Sepsis scoring was done for all of them immediately after enrollment into the study. Investigations like CBC, CRP and blood culture were sent for all the enrolled cases. Then the sepsis scores were compared with their blood culture reports to find out any correlation between them. The data analysis was done by SPSS software. Results: Among the 50 studied babies 31 were male and rest were female. Most of them were delivered by vaginal delivery (74%) but no significant difference was observed among home and institutional delivery. During delivery 24 babies experienced some problems of which 83.3% had perinatal asphyxia. About 59% of the studied babies were not exclusively breastfed. Majority of them (62%) presented with reluctance to feed and 54% were preterm low birth weight. Fever and respiratory distress were present in 19 (38%) and 18 (36%) cases respectively. Forty two percent studied babies had positive sepsis score 5 and above. Regarding correlation of blood culture and sepsis score , 70% culture positive cases had sepsis score 5 and above whereas 35% of culture negative cases had the same score. Sensitivity and specificity of sepsis score was 70 and 65 respectively with CI interval 95%. Conclusion: Sepsis score can be considered as an useful tool in the diagnosis of neonatal septicaemia specially where there is lack of investigational facilities. Before using this tool further evaluation is needed involving large sample size.

Key words: Neonatal septicaemia, sepsis score, blood culture.

Introduction

Neonatal sepsis is one of the major health problems throughout the world. Infections are a frequent and important cause of morbidity and mortality in newborn period'. As many as 2% of foetus are infected in utero and upto 10% of infants are infected in first month of life'. Data suggests that among four main causes of neonatal death, infection topped the list[2]. Every year an estimated 30 million newborns acquire infection and 1-2 million of these die[3].

Neonatal sepsis (also called septicaemia) is defined as a clinical syndrome characterized by signs of systemic infection and documented by a positive blood culture in the first four weeks of life [1,4-7] . Newborns of whole world specially those of third world countries are most vulnerable group for this illness. It is crucial to protect the newborns from infection as far as it is possible. In a poor country like ours, it is the responsibility of paediatricians (besides neonatologists) to address this serious neonatal health problems.

In developing countries the organisms causing neonatal sepsis and meningitis are different. A Bangladeshi study showed that there is considerable change in bacteriae causing neonatal sepsis and meningitis in 5 years period.(1998-2003)[8]. In that study Klebsiella pneumoniae remained the leading pathogen comprising 23% in 1998 and 23.4% in 2003 in causing neonatal sepsis. S aureus was 17% and 6% respectively and Acinatobacter 6.7% and 20.4% respectively.

A number of prepartum and intrapartum obstetric complications are associated with increased

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incidence of neonatal sepsis. Examples are: premature onset of labour (<37 weeks of gestation)[7,9], premature or prolonged rupture of membrane (>24 hours)[7,9,10], prolonged labour and excessive manipulation during labour[9°10], intrapartum maternal fever [7,9.] Pre-term and low birth weight infants are at particular high risk of infection[9]. To diagnose a newborn with neonatal sepsis a careful maternal obstetric history regarding perinatal events should be taken to identify any risk factors. Sepsis score is an useful method for early and rapid diagnosis of neonatal sepsis. It can be considered as screening test for neonatal sepsis. This is specially useful in our context where there is limited facilities for investigations. This score was developed by Tollner U in 1982[11]. It has been recommended for easy application in our situation[12].

Methodology

Type of the study: Descriptive study.

Place of the study: Neonatal care unit of ICMH.

Duration of the study: 6 months (1st week of June to 1st week of December'2005).

Sample size and sampling: Fifty (50) consecutive newborns by purposive sampling.

Inclusion criteria: suspected septicaemia on the basis of clinical presentation like reluctance to feed, lethargy, fever, abdominal distension.

Exclusion criteria: Perinatal asphyxia with features of HIE.

Sepsis score developed by Tollner U was used. Sepsis score data acquisition form includes 12 clinical and haematological parameters. Each component has some score e.g., *skin colouration* (Normal= 0, moderate change= 2, considerable change= 4), *microcirculation* (Normal=0, impaired=2, considerably impaired =3), *thrombocytopenia (No= 0,* yes= 2). Each component has been clearly explained in the form. **The interpretation of the score:** score 0-4.5 = no sepsis; score ≥ 5 = observation range and suspicion of sepsis.

Sepsis score ≥ 5 was considered as positive sepsis score in the present study. **Study procedure:** Sepsis scoring was done for all the studied babies immediately after enrollment into the study.

Investigations like CBC (Complete blood count), CRP(C-reactive protein) and blood culture were sent for all the enrolled cases. Then the sepsis scores were compared with their blood culture reports to find out any correlation between them.

The data analysis: was done by SPSS software.

Results

Among the 50 studied babies 31 were male and rest were female. Most of them were delivered by vaginal delivery (74%) but no significant difference was observed among home and institutional delivery (Table I-III). During delivery 24 babies experienced some problems, of which 83.3% had perinatal asphyxia (Table IV). About 59% of the studied babies were not exclusively breastfed (Table V). Majority of them (62%) presented with reluctance to feed and 54% were preterm low birth weight. Fever and respiratory distress were present in 19 (38%) and 18 (36%) cases respectively (Table VI). Blood culture was positive in 10 (20%) and a quite good number of patients 21 (42%) had positive sepsis score ie., 5 and above (Table VII). Regarding correlation of blood culture and sepsis score, 70% culture positive cases had sepsis score 5 and above which was statistically significant. Among the culture negative cases only 35% had sepsis score 5 and above (Table VII). Sensitivity and specificity of sepsis score was 70 and 65 respectively with CI interval 95%.

Table I

Sex distributions of studied babies (N=50)		
Sex	Number	Percent(%)
Male	31	62
Female	19	38

Table II

Mode of delivery (N=50)		
Mode	Number	Percent (%)
Vaginal	37	74
Caesarian	13	26

P value=<.001

Table III

Place of delivery (N=50)

Place	Number	Percent (%)
Home	27	54
Hospital	23	46

P value=<0.54

Table IV

Problem during delivery (N=24)

Problems	Number	Percent (%)
Perinatal asphyxia	20	83.3
Birth injury	04	16.6

Table V

Feeding pattern of studied babies (N=49)

Feeding	No	Percent (%)
Exclusive breastfeeding	20	40.8
Artificial feeding	3	6.1
Mixed feeding	6	12.2
Breastfeeding after pre-lacteal feeding	20	40.8

Discussion

Neonatal sepsis is one of the killer diseases of newborns. Specially when it occurs in the first week of life it can be a devastating neonatal problem. Male infants are more prone to develop infection[5,9]. In the present study 62% was male among the suspected neonatal sepsis babies. The resistance to infection in females is probably related to presence of mutant immunoregulatory genes located on the X chromosome[13,14]. Prolonged labour and excessive manipulation during labour may increase the incidence of neonatal sepsis [9,10]. Mode of delivery was pervaginal in 74% septic babies of present study and sepsis may be due to excessive manipulation during labour.

The frequent occurrence of foetal hypoxia and acidosis further impedes host defence mechanisms in small infants[9] which may be true for the present study, where among 24 septic babies 83% had perinatal asphyxia.

If a previously healthy baby refuses to feed or reluctant to finish food, infection should be suspected.[7,12,15,]. Reluctance to feed was the most common symptom in the present study, then was the prematurity and respiratory distress which may be the most common symptom of neonatal sepsis [7,9].

Though neonatal sepsis (also called septicaemia) is characterized by signs of systemic infection and documented by a positive blood culture [1,4-7] that is not true in 100% cases. Culture positivity may vary from less than 20% upto 70%. In some developing countries blood culture was positive in 30.8%[16] and 42%[17] respectively in otherwise proved neonatal sepsis which was 20% in the present study.

Sepsis score is an useful tool for early and rapid diagnosis of neonatal sepsis. It can be considered as screening test for neonatal sepsis. Recently a seven item weighted clinical score has been developed to diagnose late onset neonatal sepsis[18]. Culture positivity has been correlated with the sepsis score in the present study. Among the culture positive cases 70% had higher sepsis score i.e., 5 and above which was statistically significant. The sensitivity and specificity of sepsis score for the present study was 70 and 65 (with CI-95%) respectively which is quite good and acceptable for our country.

Conclusion

It can be concluded from the present study that sepsis score can be used as a tool in the diagnosis of neonatal septicaemia specially where there is lack of investigational facilities. But it needs further evaluation involving large sample size.

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Juvenile Idiopathic Arthritis
Essential Elements of Care

MR Alam

Summary:

The chronic arthritides in childhood remain a poorly understood group of conditions. Their classification has been a source of much confusion over the years with differences in terminology used by different research groups. Childhood arthritis is an important cause of short term morbidity in children and can lead to long term joint destruction and disability. Proper diagnosis and early aggressive intervention can minimize both the short and long term morbidity of the disease, thereby improving outcome during childhood as well as in adulthood. The various sub-types of JIA with their clinical features, diagnosis and differential diagnosis have been described. An outline of current management strategies and outcome of treatment are given and potential future developments are highlighted.

Introduction & Nomenclature:

Juvenile idiopathic arthritis (JlA) is a relatively rare disease affecting 1 in 1000 children in UK[1]. Important changes have occurred in the last decade regarding the course of juvenile idiopathic arthritis and resultant long-term disabilities. Published studies demonstrate that at least 50 percent of all children with JIA continue with active disease as they enter adulthood. Persistent synovitis leads to joint destruction in children much sooner than previously thought, often within 2 years of the onset of disease. The long-term impacts on the ability to function and the effects of chronic disability can be profound. Additionally, juvenile idiopathic arthritis can have detrimental effects on the physical and psychological growth of a child. There may be disruption of the family unit, divorce and other psychological stresses that affect all members of the family. The above considerations have prompted pediatric rheumatologists to treat children with juvenile idiopathic arthritis early and aggressively. The current treatment goal is resolution of disease with return to normal growth, development and activities[7]. In order to do this, patients must be accurately diagnosed as early as possible and then treated persistently until their disease resolves. It is widely thought that a comprehensive team approach is associated with a superior outcome. There has been too little awareness of the major role played by modem treatment regimen in JIA where methotrexate has transformed the outlook for most children with severe disease[4, 5].

Juvenile idiopathic arthritis is the umbrella term for a group of chronic childhood arthritis of unknown causes in children below sixteen years of age & persisting for at least six weeks[2, 19, 24]. The earliest formal description of this disease was given by Sir George Frederick Still in 1897. this work was done when he was a registrar at the hospital for sick children, Great Ormond Street, London. In this initial description of 19 patients, he identified three patterns of arthritis, one of which came to be known later as Still's Disease (now known as systemic onset JIA)[67, 68]. Subsequently different classifications were given by researchers.

According to American College Of Rheumatology it is called Juvenile rheumatoid arthritis (JRA) lasting at least six weeks with several subtypes e.g.

1. Puciarticular (1 to 4 joints involved)

2. Polyarticular (5 or more joints involved)

3. Systemic JRA

4. Spondyloarthropathies

According to European League against Rheumatic Association it is called JCA (juvenile chronic arthritis) lasting at least 3 months with following subtypes

- Puciarticutar (1 to 4 joints involved)

- Polyarticular (5 or more joints,RF negative)

- Systemic JCA

- Spondyloarthropathies

Finally the term JIA (Juvenile Idiopathic Arthritis) was first proposed in 1994 & later revised in 1997 by the International league against rheumatism as compromise for the American term JRA & the European term JCA[50,51,52]. Because the American & European classification of the disease were

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confusing, it was difficult to use the term interchangeably, in an effort to improve research and treatment, ILAR has given the name J1A.However regardless of the classification, children who develop symptoms that persist for at least six weeks before the age of sixteen years are considered to have Juvenile idiopathic arthritis. The term idiopalhic means unknown cause. This classification is gaining favour among researchers and health professionals but is not yet universally used.

JlA (Juvenile Idiopathic Arthritis) is an inflammatory disorder of connective tissue, characterized by joint swelling & pain or tenderness. It may also involve skin, heart, lungs, liver, spleen, eyes. Depending on the type the disease can occur as earty as six weeks of age, but rarely does so before the age of 6 months, peak onsets are usual between the age of one & three years and between eight & twelve years. Cause remaining unclear, but genetic factor, viral, bacterial infection, trauma and emotional stress are said to be responsible.

Difficulty arises in diagnosing cases in some of the subvarieties e.g. psoriatic arthritis, enthesitis related arthritis & systemic onset varieties.

Special problems in children:
It is important to realize that the symptoms of arthritis can vary greatly. Many children particularly young ones do not complain when they have pain in joints or may not admit it when asked. Clues that a child may be having joints problem include

- Reluctance to join in physical activities
- Unusual changes in mood
- Unwillingness to use one limb particularly
- Unusually bad behavior
- The morning journey is often difficult because of early morning stiffness
- He or she may be able to move less quickly than others between classes and sometimes teachers can play important role in recognition of the condition and improvement of quality of life

Presentation & Differential Diagnosis :
With the exception of systemic variety, children with chronic arthritis usually present with pain or swelling

of joints. In determining symptoms it must be remembered that age of the child will affect how symptoms are expressed and age appropriate assessment – must be used.

Arthralgia clearly distinguishes from arthritis, where there is objective evidence of abnormality on examination of joints.

JIA is diagnosed by presence of chronic persistent arthritis of at least 6 weeks duration on children or adolescences – who are under the age of 16 years. The diagnosis of JIA also requires exclusion of other diseases, which may present in a similar manner. As JIA is an exclusionary diagnosis, it is important to be familiar with the alternative diagnosis. The required six-week duration of arthritis is an important 1st step in excluding common conditions such as viral arthritis, trauma, Henoch-Schonlion purpura and rheumatic fever.

Orthopedic conditions such as "Legg-Calve Perthes" disease must be excluded which may have similar presentations.

Septic arthritis needs to be considered when there is monoarticular arthritis accompanied by fever, severe pain and exquisite tenderness.

Perhaps one of the most concerning aspects of diagnosis of JIA is the recognition that some childhood malignancies such as leukemia and haematoblastoma may present with musculo-skeletal pain or arthritis. Elevated 'lactate dehydrogenase' is the only test that can differentiate malignancy from JIA.

Chronic childhood rheumatic diseases like Systemic Lupus Erythomatosus; Mixed Connective Tissue Diseases; Juvenile Dermatomyosities are important differential diagnoses.

Children with growing pains have nocturnal lower extremity pain that can be relieved by comfort such as massage.

The most common subtype of JIA is oligoarthritis (1-4 joints), which may lead to polyarticular variety in course of time. One of the recognized associations of JIA is chronic frequently asymptomatic iritis. Children with involvement of 5 or more joints in the 1st 6 months are classified as polyarticular type. Generally polyarticular type tends to be symmetrical.

Systemic variety is the least common subtype. This type of arthritis is considered while fever has been present for at least 2 weeks with rash. Serositis, anemia of chronic disease, lymphadenopathy, hepatosplenomegaly all may be seen. Leucocytosis and thrombocytosis are commonly seen.

A careful history should distinguish between mechanical, inflammatory and non-organic joint pain. Examination will confirm objective evidence of join inflammation. Once a diagnosis of arthritis has been reached, the length of history and the exclusion of other causes of arthritis (e.g. infection, connective tissue disorder) will lead to a diagnosis of JIA.

Radiological and laboratory investigations are not necessary in making a diagnosis of JIA. Investigation may be useful in ruling out other pathology, determining the disease subtype and assessing disease activity in some children.

Diagnosis:
Diagnosis of JIA remains a clinical one & essentially one of exclusions in addition to pattern recognition. There are no clinical, laboratory or radiologic tests that are pathognomonic for this disease.

Laboratory investigations –
ESR: May be normal in oligoarthritis and polyarticular arthritis, but is usually very high (>60 mm/hr) in systemic onset disease. If high in patients with oligoarthritis, consider infection, underlying spondyloarthropathy (e.g., IBD, Reiter's syndrome), or malignancy.

WBC: Should be normal in oligoarthritis and polyarticular juvenile arthritis. Elevated WBC with a left shift is sometimes seen in systemic onset juvenile arthritis, including leukemoid reaction (>30,000). Remember that a normal peripheral WBC and smear cannot exclude the diagnosis of leukemia.

Platelet Count: Usually normal, except in active systemic onset juvenile arthritis, where it may be elevated (>500,000). If platelet count is low, consider malignancy).

Other investigations should be done only to exclude other diagnosis.

Ensuring the correct diagnosis is essential for further management. The misdiagnosis of non-organic joint pain as arthritis will cause immense difficulties to the child and family and may be very difficult to undo. A delay in correctly diagnosing a child with JIA will lead to a delay in the child receiving appropriate therapy that may result in long-term sequele.

Management:
Management of JIA includes multidisciplinary approach like rheumatologist, physician, pediatrician, physical medicine specialists, teachers, social workers, psychologists etc. drug treatment includes NSAIDs, DMARD, steroid. The aim of modern treatment for JIA is rapid induction of disease control to prevent joint damage, to maximize joint function & to achieve a normal joint function for patients.

Methotrexate in JIA:
Weekly methotrexate is an established treatment in pediatric rheumatology & its efficacy shown by different randomized control trials[4, 5, 7, 33]. Among DMARDs, methotrexate has transformed the outlook for children with JIA. Most of the evidences from uncontrolled clinical trails suggested that methotrexate is an effective agent for treating active JIA. A more recent randomized controlled double blind crossover multi center study by woo, et. al looked at the effectiveness and safety of orally administered methotrexate in extended oligoarticular & systemic arthritis. This study used methotrexate at dose of 15 to 20 mg/m^2/week. A significant improvement occurred in three of five variables (ESR, physicians and patient's global assessment). (The study by Giannini et al forms the basis of current use of methotrexate in pediatric rheumatological practice). This was a six month randomized, double blind controlled multi center study of 127[43, 44, 45, 46] children with resistant JIA (Mean age 10.1 years, mean disease duration 0.5-1 years). 63% of the group treated with 10mg/m^2/week improved compared with 32% of those treated with 5 mg/m^2/week & 36% of placebo group.

Mechanisms of action of methotrexate:
Methotrexate is a folate analogue with an amino (NH$_2$) & methyl (CH$_3$) group. It binds dehydrofolate (DHFR) with high affinity and inhibits synthesis of thymidylate and purine, which are essential compound of DNA.

Although the primary mechanism of action of methotrexate in JIA or adult RA is not clearly known, recent reviews suggest that the anti-inflammatory effects of methotrexate seems to be related to the extra cellular adenosine release and its interaction with specific cell surface receptor[44].

Dose & route of administration:
In general, children with JIA, methotrexate therapy started at a dose of 10 to 15 mg/m^2/week or 0.3-0.6 mg/kg/week. However children seem to tolerate much higher dose than adult and some series describe using up to 20-25 mg/m^2/week in children with refractory cases, with relative safety in the short term. At doses more than 15 mg/m^2/week the parental route may be preferred.

A recent multinational, randomized controlled study by Pediatric Rheumatology International Trials Organization (PRINTO) compared 30mg/m^2/week in children with polyarticular JIA who failed to improve with 8-12.5 mg/m^2/week. Maximum response was found with 15 mg/m^2/week and there was no added benefit of the 30mg/m^2/week dose over 15mg/m^2/week[47].

Folic acid supplementation:
A recent multi center randomized double blinded placebo controlled trail showed that 2.5-5mg folic acid supplementation 2 days after methotrexate reduced the incidence of increased liver enzyme but had no effect on the incidence of other gastrointestinal and mucosal side effects[26].

Side effects:
Nausea is infrequent and can be lessened by use of antiemetics like Ondansetron, consideration needs to be given to be psychological support of children in methotrexate, in whom habitual nausea may sometimes occur[48, 49].

Sulphasalazine:
Three recent studies have confirmed earlier reports that Sulphasalazine is effective in oligoarticular & polyarticular varieties of JIA. Usual doses are 40-50 mg/kg of body wt/day (maximum 2gm/day). In a placebo controlled study 10 of 69 patients withdrew due to side effects, which were reversible[31, 32, 33].

Leflunomide:
Leflunomide, an orally administrated inhibitor of pyrimidine synthesis has been shown to be safe and effective long term therapy for adult with rheumatoid arthritis. In a pilot open-label study of children with polyarticular course JIA, 52% of those receiving leflunomide had a response even though all patients either had no response to or were intolerant to methotrexate. To confirm this a total 48 weeks randomized control multicentre (32 centres in 12 countries from march 2002-jan 2003) study was conducted to compare leflunomide with methotrexate in children (3-17 yrs), with active polyarticular JIA. Of 94 patients, randomized response rate was 89% and 68% in methotrexate and leflunomide respectively at 16 weeks and improvement was maintained at 48 weeks. Methotrexate was used in a dose of 0.5 mg/kg/week (25 mg/week) and leflunomide 10-20 mg/day according to body wt. following a bolus dose of 100 mg/day (for l-3 days according to body wt). Methotrexate & leflunomide both resulted in high rate of improvment in JIA patient (polyarticular type) but at doses used in that study methotrexate was more effective than leflunomide[62-66].

Monitoring Methotrexate and other DMRD therapy:
Before commencing DMARD therapy baseline information regarding CBC, Liver function, renal function should be obtained. Full blood count and liver and renal function monitoring is required fortnightly until a stable dose is achieved. Thereafter monthly monitoring for 6 months, increasing to 6 weekly is the usual practice[28-30].

TNF α blocker (Etanercept):

Tumor necrosis factor was identified in synovial fluid in 45% patient of JIA & found to play a proinflammatory role in pathogenesis.

In a randomize double blind multi-centre study, TNF α blocker was found safe, effective in children with poly articular JIA who did not tolerate or had an inadequate response to methotrexate. At the end of open study 74% of patient had a 30% improvement, 64% had a 50% improvement & 36% had a 70% improvement[43].

Refractory JIA:
Refractory juvenile idiopathic arthritis should be considered when the disease does not respond to

high dose of Methotrexate (1 mg/Kg/week, subcutaneously)[23, 56]. Combination of methotrexate with other DMRDS e.g. sulphasalazine, leflunomide are required in such cases and in some JIA subtypes such as ehthesitis related and systemic onset JIA[69-73]. Eternercept as monotherapy or in combination with methotrexate resulted in signifixcant improvement in sign and symptom of JIA. More aggressive therapies like IV methylprednisolone & cyclophosphamide can be considered in some cases of refractory JIA, since the biological agents is not possible for most patients[23, 37, 39, 42].

General aspects of management:

Nutrition:
All children with chronic rheumatic disease are susceptible to both growth retardation and malnutrition[7, 8]. Fatigue, non-specific abdominal pain, or worry about poor body image may all cause anorexia, limiting dietary intake. Ensuring an adequate protein, calorie and calcium intake is important but supplements including iron, folic acid, and vitamin D may also be indicated[58-60].

Physiotherapy and splints:
Physiotherapists ensure that both passive and active exercise schedules are implemented to maintain joint movement and improve muscle function.

Compliance:
Education of children with chronic disease and their parents about the need to take medication according to prescribed regimens is essential. Parents may be wary about giving children about the multiple medications, which are often necessary. In a useful review of factors affecting compliance it was noted that between 55-95% of medication (including self-administered or by parents for younger children) is taken correctly, but adhere with physiotherapy regimens is lower at 46-86%. Where there is suspected lack of compliance with oral therapy, perhaps with adverse social factors, in association with poor disease control, the administration of methotrexate sub-cutaneously by home care team may be useful.

Written information about arthritis, treatment and support groups should be offered to children, adolescents and parents.

Remission rate or when to discontinue the therapy:
The question of when, how and by what criteria, attempt should be made to withdraw methotrexate therapy in JIA is still more a clinical art than a science. "Remission" is a controversial concept in JIA. The criteria for "remission" or "relapse" have never been operationally defined and prospectively tested in JIA. In literature on JIA, the cited criteria for remission are often subjective and have not included long-term physical and functional outcomes.

However, methotrexate withdrawal may result in disease flare in more than 50% of patients as shown by Ravelli et al, a feature also noted by others[26]. The ease with which remission is achieved when methotrexate is re-established is still unclear. Reported rates of "remission" in JIA treated with methotrexate vary from 6.9% to 45%; the average duration of methotrexate treatment until "remission" is around one year at a weekly dose 10-15 mg/m^2.

The first phase of remission is the achievement of inactive disease which is defined as: no joints with active arthritis; no fever, serositis, splenomegaly, or generalized lymphadenopathy attributable to JIA; no active uveitis; normal ESR or CRP; and a physician's global assessment of disease activity indicating no disease activity. Clinical remission on medication is defined as inactive disease on medication for a full six months, and clinical remission off medication is achieved when there is inactive disease off of medications for a full 12 months. Although many children can achieve clinical remission on medications, most will have a flare of their arthritis within three years of discontinuing medications.

Once there is complete remission, effective medications are continued for 6 to 12 months before tapering[45].

Complications of JIA:
Complication may be local or systemic, disease related or as a consequence of treatment.

Localized joint problems can be minimized by good, early control of inflammatory process. Children with inflamed joints will rapidly develop flexion deformities which may become fixed if inadequately managed. Drug treatment is combined with

physiotherapy and the judicious use of splinting to maintain correct joint position and function. Persistent inflammation in a joint may lead to bony overgrowth at that joint. This is seen particularly in children with oligoarthritis and involvement of one knee. If not controlled this may lead to overgrowth of that knee and a leg length discrepancy. Undergrowth of the mandible as a consequence of temporomandibular joint involvement may lead to significant functional and cosmetic problems.

Disturbance of overall growth is well recognized in children with JIA. Many children with JIA develop marked osteopenia. Poor diet, inactivity and steroids may contribute but other factors more directly related to disease process are clearly involved.

Anemia in severe JIA may be a significant problem and detract from the well being of child[60].

Oligoarticular arthritis is associated with chronic uveitis which is asymptomatic and may therefore go undetected for considerable time unless screened for.

Amyloidosis is well described in this condition and was previously reported to occur in around 10% of European cases[36].

Prognosis:
JIA is a chronic disease with perhaps 50% of patients will have active arthritis in adult years. JIA impacts the life style of not only the child but also the whole family. There is still very little published data to predict which patients will have a prolonged disease course & which medications are likely to be effective in which type of patients. In general those with involvement of few joints do better than those with systemic disease or RA factor positive JIA. Fifteen year follow up studies from USA & Italy of 227 patients from all subgroups of JIA show that frequently the long-term outcome is good, the worst prognostic factors were identified as the severe type of arthritis score at onset; early hand involvement & symmetrical arthritis with suggestion that ESR may have some predictive value related to quality of life[15, 16, 61].

Future developments in JIA
The aetiology of JIA remains elusive. It is hoped that an improved classification system will facilitate further research by identifying more homogeneous patient groups for study. As our understanding of these conditions improves, so the search for a 'cure' should prove more fruitful.

New developments in the field of antirheumatic therapy include biologic agents (such as anti-cytokine drugs) and new immunosuppressive agents with improved toxicity profiles. Stem cell transplantation is being increasingly used in the field of autoimmune disease and several children with severe JIA have been successfully transplanted.

Conclusion:
JIA is the most common group of rheumatic disease in childhood. Diagnosis is made on the basis of clinical criteria. The effective treatment needs multidisciplinary approach. Awareness amongst general pediatricians/ rheumatologist/ physicians, early recognition, prompt introduction of specific DMARD (e.g. methotrexate, Sulphasalazine) therapy either singly or as a combination at appropriate doses, in addition to other supportive therapies (NSAIDs, Intra articular Steroid etc.) are measures that will improve outcome and quality of life for these children. Nowadays, parents are more likely to request for newer therapies & adequate time is needed to address their concerns about the disease and the drugs.

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Approach to Subclinical Thyroid Disease

SR SUTRADHAR

Summary:
Subclinical thyroid dysfunction is defined as an abnormal serum thyroid-stimulating hormone level and free thyroxine and triiodothyronine levels within their reference ranges. The prevalence of subclinical hyperthyroidism is about 2 percent. Subclinical hypothyroidism is found in approximately 4 to 8.5 percent of the population. Most national organizations recommend against routine screening of asymptomatic patients, but screening is recommended for high risk populations. The management of subclinical thyroid dysfunction is controversial. There is good evidence that subclinical hypothyroidism is associated with progression to overt disease. Patients with a serum thyroid-stimulating hormone level greater than 10 mIU/L have a higher incidence of elevated serum low density lipoprotein cholesterol concentrations; however, evidence is lacking for other associations. There is insufficient evidence that treatment of subclinical hypothyroidism is beneficial. A serum thyroid stimulating hormone level of less than 0.1 mIU/L is associated with progression to overt hyperthyroidism, atrial fibrillation, reduced bone mineral density, and cardiac dysfunction. There is little evidence that early treatment alters the clinical course.

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Introduction:

Subclinical thyroid disease is, by its very nature, a laboratory diagnosis. Patients with subclinical disease have few or no definitive clinical signs or symptom

It is a common clinical problem. Some patients will progress to overt disease, and in some patients, the serum thyroid- stimulating hormone (TSH) concentration will remain stable over time or will spontaneously return to the reference range.[1,2]

There are many controversial issues regarding screening, evaluation and management.

In 2002, a consensus committee was formed with representatives from the American Thyroid Association, the American Association of Clinical Endocrinologists, and the Endocrine Society. The committee makes recommendations about the controversial issues.[3]

Subclinical hypothyroidism is defined as a serum TSH concentration above the statistically defined upper limit of the reference range when serum free thyroxine (FT_4) concentration is within its reference range.[4] The panel defined the reference range of normal serum TSH concentration as 0.45 to 4.5 mIU/L[3]

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Subclinical hyperthyroidism is defined as a serum TSH concentration below the statistically defined lower limit of the reference range when serum FT_4 and triiodothyronine (T_3) concentrations are within their reference ranges.[4]

Epidemiology of Subclinical Thyroid Disease:

The prevalence of subclinical hypothyroidism in the US adult population is about 4% to 8.5% in those without known thyroid disease.[5,6] The prevalence increases with age, and in women older than 60 years, subclinical hypothyroidism is present in up to 20%.[6]

Subclinical hyperthyroidism is much less common than subclinical hypothyroidism. When the lower limit of TSH is less than 0.4 mIU/L, 3.2% of the population is defined as having subclinical hyperthyroidism.[5] If patients with known thyroid disease are excluded, the prevalence decreases to 2%. Subclinical hyperthyroid disease is more common in women than men, in blacks than whites, in the elderly, and in patients with low iodine intake.[7]

Screening for Thyroid Disease:

In January 2004, the U.S. Preventive Services Task Force concludes that "the evidence is insufficient to recommend for or against routine screening for thyroid disease in adults."[1]

The 2002 consensus group's expert panel recommended against population-based screening but recommends "screening asymptomatic person for

thyroid disease should be considered, specially for those older than 60 years or with risk factors such as women with a family history of thyroid disease, prior thyroid dysfunction, symptoms suggestive of hyperthyroidism or hypothyroidism, abnormal thyroid gland on examination, type 1 diabetes, or a personal history of autoimmune disorder.[3]

The panel found insufficient evidence to recommend for or against screening pregnant women or women planning a pregnancy.[3]

The American College of Physicians (1998), recommends screening for women older than 50 years who have symptoms consistent with thyroid disease.[8]

Subclinical Hypothyroidism:

Etiology

Hashimoto's thyroiditis , protracted recovery from acute thyroiditis, early hypothalamic disorder, inadequate levothyroxine replacement therapy in a patient with known hypothyroidism.'[3]

Consequences of Untreated Subclinical Hypothyroidism:

Serum lipid levels in subclinical hypothyroidism (SCH) have been reported as either normal [9] or elevated [10] . In the Tromso study, low density lipoprotein – cholesterol (LDL-C) levels were significantly higher.[10] In Suita study, no significant association was observed between sub clinical thyroid dysfunction and lipid metabolism. The suita study reported that SCH was associated with lower fasting blood glucose (FBG).[11]

SCH patients have impaired endothelial function, normal / depressed systolic function, left ventricular diastolic dysfunction at rest, and systolic and diastolic dysfunction on effort.[12] In two studies, positive association between arterial stiffness & SCH has been reported.[12, 13] But no significant association between SCH and intima-media thickness(IMT) was observed in Suita study[11], which suggests that SCH might not be related to an increased risk of atherosclerosis.

Patient may exhibit the feature of systemic hypothyroid symptoms[6,14], neuropsychiatric symptoms[6,14] and may progress to overt, symptomatic hypothyroidism.[15]

Evaluation of Subclinical Hypothyroidism :

The TSH measurement should be repeated along with an FT_4 measurement at a minimum of 2 weeks, but no longer than 3 months, after the initial assessment.

If a high serum TSH concentration is confirmed on repeat testing and serum FT_4 is within the reference range, the patient should be evaluated for signs and symptoms of hypothyroidism, previous treatment for hypothyroidism, thyroid gland enlargement, or family history of thyroid disease. Lipid profiles should be reviewed. Women who are pregnant or hope to become pregnant in the near future deserve special consideration.

Anti-thyroid peroxidase(Anti-TPO) antibodies are to be measured because the presence of anti-TPO antibodies predicts a higher risk of developing overt hypothyroidism (4.3% per year vs 2.6% per year in antibody-negative individuals).[16]

Risks of Treating Subclinical Hypothyroidism:

The potential risks of therapy are limited to the development of subclinical hyperthyroidism, which may occur in 14% to 21% of individuals treated with levothyroxine.[17]

Treatment:

Subclinical Hypothyroidism With Serum TSH of 4.5 to 10 mIU/L.

● Routine levothyroxine treatment is not recommended for patients with TSH levels between 4.5 and 10 mIU/L, but thyroid function tests should be repeated at 6- to 12-month intervals to monitor for improvement or worsening in TSH level.[3] Very recently a study showed that patient with subclinical hypothyroidism with TSH > 4 mIU and FT_4 in normal range obtained improvement in their cardiovascular rick factor profile and reduced tiredness after treatment with Levothyroxine. [18] Thyroxin therapy for TSH level between 4.5- 10 mIU/L should be reserved for patients who have goitre, women that are anticipating pregnancy or are pregnant, patient with depression or dipolar disorder or TPO antibody positive. Thyroxine therapy may be considered in patients with symptoms of hypothyroidism who have TSH level between 4.5-10 mIU/L and continued only if there is clear symptomatic benefit.

Subclinical Hypothyroidism With Serum TSH Higher Than 10 mIU/L

Levothyroxine therapy is reasonable. The rate of progression is 5% in comparison with patients with lower levels of TSH. [3]

Subclinical Hypothyroidism During Pregnancy. A TSH level might be obtained in pregnant women and women who wish to become pregnant if they have a family or personal history of thyroid disease, physical findings or symptoms suggestive of goiter or hypothyroidism, type 1 diabetes mellitus, or a personal history of autoimmune disorders. Pregnant women or women of childbearing potential planning to become pregnant who are found to have elevated serum TSH should be treated with levothyroxine to restore the serum TSH concentration to the reference range. [3] The requirement for Levothyroxine in treated hypothyroid women frequently increases during pregnancy. Therefore, the serum TSH concentration should be monitored every 6 to 8 weeks during pregnancy.

Subclinical Hypothyroidism in Treated Overt Hypothyroid Individuals.

When the serum TSH is in the upper half of the reference range and levothyroxine-treated patients continue to note symptoms suggestive of hypothyroidism, it is reasonable to increase the levothyroxine dosage to bring the serum TSH into the lower portion of the reference range. Minimal TSH elevations may not require dosage adjustment in patients who feel well.

Subclinical Hyperthyroidism

Etiology

It may be transient or persistent

Persistent

- Exogenous
  - Iatrogenic- excessive thyroxine replacement
  - Intentional suppression
  - Surreptitious
- Endogenous
  - Early graves' disease
  - Toxic multi nodular goiter
  - Autonomous functioning nodules

Transient

- De Quervain's thyroiditis
- Postpartum thyroiditis

Differential diagnosis of low TSH

Hyperthyroidism

- Over
- Subclinical

Secondary

- pituitary insufficiency

Euthyroidism

- Physiological (Near end of first trimester)
- Elderly patients

Non thyroidal illness

Interpretation of Thyroid laboratory test

FT4 level	Normal TSH	Increased TSH	Decreased TSH
Normal	Normal, euthyroid sick syndrome.	Subclinical hypothyroidism	Subclinical hyperthyroidism
Increased	Early thyroitites	Hyperthyroidism (Pituitary adenoma)	Hyperthyroidism (Graves' disease, toxic nodule)
Decreased	Late thyroidites	Hypothyroidism (Primary thyroid failure)	Hypothyroidism (Primary pituitary failure)

Consequences of Untreated Subclinical Hyperthyroidism:

The potential adverse outcomes would be related to the degree of TSH suppression. Patients with serum TSH levels < 0.1 mIU / L are at higher risk than those patients with TSH levels between 0.1 & 0.45 mIU/L.[3]

Some studies noted, subclinical hyperthyroid patients have an increase in heart rate[19], increase in the frequency of atrial & ventricular premature beats[20] & an increase in left ventricular mass.[19, 21] However, a recent study noted, sub clinical hyperthyroidism was not associated with left ventricular hypertrophy.[22]

Two studies found minimal or no effect on systolic function [19, 20] and one showed slightly enhanced systolic function [23]. Biondi et al. [23] also reported a statistically significant impairment in diastolic function with decreased transmitral blood flow due to slowed left ventricular relaxation, but significant changes were not observed in two other study. [19, 20] Gussekloo et at. [24] found individuals over age 85 years with low serum TSH values had the highest rates of mortality. In contrast, two studies found no increased frequency of coronary artery disease or cardiovascular mortality. [25, 26]

Bone mineral density is lower at all sites in post menopausal women [27], in contrast, in premanopausal women it appears to be normal. [28]

In one report, the risk of vertebral fracture was elevated 4- fold and hip fracture was elevated 3- fold in women of 65 years of age or older with serum TSH values 0.1 mIU / L or less compared with control. [29]

Recently, two studies described an increase in typical hyperthyroid symptoms (Palpitation, tremor, heat sensitivity, sweating, and nervousness) in young & middle aged patients with sub clinical hypothyroidism. [19, 23]

In a community- based study of persons age 65 years & older, there were no significant differences in mood, anxiety or cognition between sub clinical hyperthyroid persons & those who were euthyroid [30].

One study showed an increased basal oxygen consumption that decreased to normal after treatment with methimazole. [31] In another study, patients with sub clinical hyperthyroidism were found to have decreased muscle strength compared with control.[32]

The risk of progression of overt hyperthyroidism varies. The etiology plays a role in this regard. Woeber[33] observed that serum TSH values normalized in five of seven patients with Graves' disease and subclinical hyperthyroidism followed for 3-19 months, whereas it remained subnormal in patients with multinodular goiters followed for 11-36 months.

Evaluation of Subclinical Hyperthyroidism :
Individuals With Serum TSH 0.1 to 0.45 mIU/L Not Treated With Levothyroxine. Measurement should be repeated by measuring FT_4 and either total T_3 or FT_3 levels. Repeat testing within 2 weeks is prudent for patient with atrial fibrillation, cardiac disease, or other serious medical conditions. Repeat testing within 3 months is recommended, when these factors are absent.[3]

If the repeat serum TSH concentration remains higher than 0.1 but lower than 0.45 mIU/L, with normal FT_4 and T_3 concentrations, and the patient has no signs or symptoms of cardiac disease, atrial fibrillation, or other arrhythmias, retesting should occur at 3- to 12- month intervals, until either serum TSH level normalizes or the clinician & patient are confident that the condition is stable. [3]

Individuals With a Serum TSH Lower Than 0.1 mIU/L. The measurement is repeated along with an FT_4 and a total T_3 or FT_3 within 4 weeks if the patient has no signs or symptoms of cardiac disease, atrial fibrillation or other arrhythmia but within a shorter interval if signs or symptoms of hyperthyroidism are present.[3]

The panel recommendts further evaluation to establish the etiology of the low serum TSH.[3]

A radio-active iodine uptake & Thyroid scan can distinguish between destructive thyroiditis & hyperthyroidism due to Graves' disease or nodular Goiter.

Risks of Treatment of Subclinical Hyperthyroidism:
The risks of treatment with antithyroid drugs are potential allergic reactions including agranulocytosis. Radioactive iodine therapy commonly causes hypothyroidism & may cause exacerbation of hyperthyroidism or Graves' eye disease.[34]

Treatment:

Exogenous Subclinical Hyperthyroidism With TSH 0.1 to 0.45 mIU/L.
The indication of thyroid hormone therapy should be reviewed. Many patients with thyroid cancer & some patients with thyroid nodules required TSH suppression and target TSH level should be reviewed by the treating physician. When prescribed for other causes the dosage of levothyroxine is decreased to allow serum TSH to increase toward the reference range.[3]

Exogenous Subclinical Hyperthyroidism With TSH Lower Than 0.1 mIU/L.

The indication for thyroid hormone therapy should be reviewed. For patients with thyroid cancer and thyroid nodules, the target serum TSH value should be reviewed by the physician. When levothyroxine is prescribed for hypothyroidism in the absence of thyroid nodules or thyroid cancer, the panel recommends decreasing the dosage of levothyroxine to allow serum TSH to increase toward the reference range.[3]

Endogenous Subclinical Hyperthyroidism (Serum TSH 0.1-0.45 mIU/L)

The panel[3] recommends against routine treatment for all patients whose TSH is mildly decreased (0.1-0.45 mIU/L). Because of a possible association with

increased cardiovascular mortality,[35] clinicians might consider treatment of elderly individuals and for those with or at increased risk for heart disease, osteopenia, or osteoporosis (including estrogen-deficient women), or for those with symptoms suggestive of hyperthyroidism, despite the absence of supportive data from intervention trials and no therapy is required for younger patient .

Endogenous Subclinical Hyperthyroidism (Serum TSH Lower Than 0.1 mIU/L)

The panel[3] recommends that treatment be considered for subclinical hyperthyroidism (TSH <0.1 mIU/L) due to Graves or nodular thyroid disease. Treatment should be considered for patients who are older than 60 years and for those with or at increased risk for heart disease, osteopenia, or osteoporosis (including estrogen-deficient women), or for those with symptoms suggestive of hyperthyroidism. Younger individuals with subclinical hyperthyroidism and serum TSH persistently (months) lower than 0.1 mIU/L may be offered therapy or follow-up depending on individual considerations.

Conclusions:

There are many controversies regarding the management of subclinical thyroid disease.Until data of well conceived and executed intervention trials are available, following may be recommended: If TSH > 10 mIU/L, thyroxine therapy is to be given. If TSH 4.5- 10 mIU/L, thyroxine therapy may be given for goitrous patients, women who are pregnant or anticipating pregnancy, or patient with depression or TPO antibody positive. Postmenopausal women or patient older then 60 years or with heart disease or osteoporosis or symptoms of hyperthyroidism should be treated if TSH <0.1 mIU/L and considered for treatment if TSH 0.1 to 0.45 mIU/L. Premenopausal women or patient <60 years, or no heart disease or osteoporosis or symptoms of hyperthyroidism therapy is optional if TSH <0.1 mIU/L and no therapy is required if TSH 0.1 to 4.5 mIU/L

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Gonadoblastoma: Primary Amenorrhoea with Gonadal Dysgenesis

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Summary:

A seventeen year old unmarried girl presented with no development of breasts and non establishment of menstruation till then. She was with average height & weight, chromosome analysis was 46XY (Swyer Syndrome). Laparoscopy followed by laparotomy showed irregular surfaced gonads with rudimentary uterus. Gonadectomy done & histopathology revealed features of gonadoblastoma. She had under gone 6 cycles of combination chemotherapy and hormone replacement therapy and showed excellent response.

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Introduction:

Gonadoblastoma is a rare and always a benign form of cancer. It is exclusively found in patients with an underlying gonadal disorder. It accounts for two-third of gonadal tumour in women with an abnormal karyotype [1,2,3]. Most of the cases, it is highly associated with abnormal development of the reproductive system [3,4]. The neoplastic nature of gonadoblastoma has been questioned because some lesions are small & may undergo complete regression by hyalinization & calcification [4]. In 1953, gonadoblastoma was first detected in details by Scully as a gonadal tumour composed of germ cell & sex cord derivatives [1,2]. Gonadoblastoma occurs almost always in patients with pure gonadal dysgenesis with 46XY karyotype (Swyer Syndrome) [7]. Some times it occurs in mixed gonadal dysgenesis or in male pseudohermaphrodites [7,8]. Dysgerminoma occurs in 50% of patients & it may be associated with more malignant germ cell tumours [6,7].

Case Report:

A 17 year old unmarried girl was admitted in gynaecology & obstetrics department of BSMMU on 12th June, 2006 with non establishment of menstruation and absence of development of breasts till then. She gave no history of periodic lower abdominal pain, dysuria, frequency or retention of urine. She had no heat or cold intolerance, constipation and no significant weight loss, visual disturbance, trauma or tuberculosis. Her mother gave no history of relevant drug intake during pregnancy and she had no history of difficult labor during her birth or encephalitis in childhood. There was no family history of primary amenorrhea, tuberculosis or diabetes. She gave no significant drug, medical or surgical history.

She was examined thoroughly and general parameters were found normal. Her height was 5' 3'', weight 52 kg, & had masculine type body built. She was depressed but co-operative. Her scalp hair was long, axillary & pubic hair was well developed with female distribution. Her visual field was normal with normal color vision. She gave no history of anosmia & had no bony abnormality. Her thyroid gland was not enlarged & other lymph nodes were not palpable. Her breasts were not developed & had widely spaced nipples. She had no stigmata of chromosomal or other endocrine diseases.

Her per abdominal examination revealed no palpable mass or abnormality. Pubic hair was well developed & female type in distribution. Vulva including labia majora, minora & clitoris was well developed. No swelling was found in the inguinal region. Vaginal introitus was narrow & per vaginal examination could not be done. Per rectal examination was done & a nodular firm cord like structure was found in the midline at the apex of the examining finger.

All the relevant investigations were done. Her karyotype was 46XY with no structural or numerical

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abnormality of autosome. Her ultrasonography report showed no abnormality of the internal genital organs except that the uterus was smaller in size (24mm X 12mm X 24mm). Her general biochemical investigation report showed no abnormality. Hormone assays were done which showed low level of oestrogen & testosterone & high level of FSH & LH. The value of oestrogen & testosterone were 21.1 pg/ml & 44 ng/ml respectively.On the other hand the value of FSH & LH were 87.40 IU/L & 32.63 IU/L respectively. Her clinical diagnosis of primary amenorrhoea with gonadal dysgenesis was confirmed by these investigation reports. She was then properly counseled and Examination Under Anesthesia (EUA) & laparoscopy was done on 25th July, 2006. Laparoscopic examination revealed uterus smaller in size, mobile, anteverted. Cervix & vaginal canal present & normal. Both sided gonads were present, size of which were 2cm × 1 cm × .5cm, surface irregular. Then laparotomy & bilateral gonadectomy were done. Histopathology of the gonads showed a tumor composed of biphasic population of germ cells & stromal cells, arranged in nests, areas of hyalinization and calcification present.

So, finally she was diagnosed as a case of primary amenorrhoea due to gonadal dysgenesis with gonadoblastoma. She was then referred to medical oncology department of the university where she received 6 cycles of combination chemotherapy as Bleomycin, Etioposite & Cisplatin. Simultaneously she received hormone replacement therapy by conjugated equine oestrogen. Oestrogen was given in the dose of .625mg daily for 21 days. In the last week of the cycle, progesterone was added in the dose of 5mg daily. She had withdrawal bleeding regularly & start development of breasts after 3-6 months of hormone therapy. Her hormone therapy will be continued for at least 1 year to 3 years.

Discussion:
Primary amenorrhoea is defined as non establishment of menstruation. The case of primary amenorrhoea should be investigated by the age of 16 in presence of secondary sex characteristics & by the age of 14 when there is no secondary sex characteristic [5]. For establishment of menstruation, 5 criteria must be fulfilled: i) she must be chromosomally competent female. ie 46XX karyotype. ii) hypothalamo pituitary

ovary axis must be intact & well functioning. iii) must have responsive endometrium. iv) must have patent outflow tract. v) active support from thyroid & adrenal gland [13].

Menstruation is the final result of a series of events which results in sexual maturity [5]. Maturation of the hypothalamo pituitary ovary through several years of late childhood begins a cascade of events which finally result in establishment of normal menstrual cycle & menstruation. Amenorrhoea will result when there is defect or failure of function in any one of the organs involved in this cascade [5].

Gonadoblastoma is a gonadal tumour & is composed of combination of germ cells and sex cord stromal cells. This tumour occurs in sexually abnormal individuals, most commonly affected by gonadal dysgenesis and carrying the Y chromosome (i.e. XY gonadal dysgenesis or XO-XY mosaicism) [4,7]. Sometimes gonadoblastoma occurs in both phenotypically & chromosomally normal females, even those with normal pregnancies [8,9].

3 cases of gonadoblastoma were reported from a study, done in department of pathology, Tehran University in 1992. All were presented with primary Amenorrhoea.

24 year old patient with complete female phenotype with 46 XY Karyotyping & small uterus & fibrotic ovaries (Swyer Syndrome). Bilateral gonadectomy revealed features of gonadoblastoma.

19 years old girl with female phenotype with uterine agenesis with 85% 46 XY & 15% 46 XO pattern. Bilateral small ovaries (8mm) removed and showed gonadoblastoma.

19 years old girl with female phenotype with small infantile uterus (3cm × 2cm × 5cm), 46 XY karyotype. Bilateral gonadectomy revealed gonadoblastoma overgrown by dysgerminoma.

So all patients with gonadoblastoma showed abnormal karyotype. It is bilateral in one-third cases [7]. Hence all patients with primary amenorrhoea ē 46XY karyotype must be carefully counseled about the malignant potential of gonads (30%). Gonadectomy must be done at a time when counseling is completed. Patients & her guardians must be informed about the karyotyping & nature of gonad [5].

Conclusion:

The exact incidence of gonadoblastoma is not known as poorer section of the community present to doctors for proper diagnosis & management. It needs a lot of sophisticated investigations like karyotype, ultrasonography, hormone profile, sometimes laparoscopy, directed biopsy and histopathology. They need treatment by chemotherapy. All these investigations & treatment are costly. So, for proper management, there should be cost effectiveness facilities in specialized centre at least in tertiary level hospitals.

Patients with pure gonadoblastoma have excellent prognosis provided both gonads have excised as gonadoblastoma have never been detected with metastatic lesion & never occur outside the gonads [4,5]. The prognosis of patients with gonadoblastoma associated with dysgerminoma is also good provided course of chemotherapy has strictly followed.

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Henoch-Schonlein Purpura in an Elderly Women Presenting with Severe GI Bleeding: A case report

MAJ CHOWDHURY[a], SM ARAFAT[b], ABED HUSSAIN[c]

Summary:

A 65–year-old lady presented with recent onset of purpuric rash over the lower limbs, polyarthritis, severe colicky abdominal pain associated with bloody diarrhea following a short episode of upper respiratory tract infection. Henoch-Schonlein purpura (HSP) was diagnosed on the basis of normal platelet count, normal serum complement, leucocytoclastic vasculitis on skin biopsy and negative search for rheumatoid factor (RF), antinuclear antibody (ANA), hepatitis B and C virus markers and other infective causes.

(J Bangladesh Coll Phys Surg 2008; 26: 100-102)

Introduction

Henoch-Schonlein purpura (HSP) is a non thrombocytopenic purpura and systemic vasculitis of childhood, [1] that occurs twice as often in males then in females. Heberden and William first described Henoch-Schonlein purpura in the early 19th century.[2] This mainly affects children between 4 and 11 years.[3] Annual incidence is 14 cases per 100,000 people and occurs more frequently in the spring and fall.[3,4] It may present as a triad of symptoms: palpable purpuric rash especially on the lower extremities, abdominal pain or renal involvement and arthritis.

There are only few reported cases of HSP in adults. In this citation an elderly lady who presented with severe GI bleeding and extensive erythematous skin rash in addition to joint and abdominal pain but with minimal renal involvement is reported.

Case History

A 65-year-old Bangladeshi woman, well controlled hypertensive for seven years, presented with 5 days history of painful swelling of multiple joints and erythematous rashes coalescing together giving rise to large blotchy patches on her lower extremities which gradually involved the whole body. This was followed by colicky abdominal pain with post prandial exacerbation and passage of profuse bloody

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stool. She had two episodes of haemoptysis within three days of her illness.

On clinical examination she was afebrile, anxious and uncomfortable with abdominal and joint pain. Skin was marked by tender palpable erythematous maculopapular rashes all over the body which were non-blanching and non-itchy. Both ankle and knee joints were swollen, tender, warm with mild effusion. Abdomen was diffusely tender without any organomegaly.Bowel sound was present. Neither lymphadenopathy nor bony tenderness was present. Examination of other systems was unrevealing. Funduscopy revealed no abnormality.

Laboratory investigation showed raised WBC count of 16700 with 90% neutrophill. Except raised serum IgA other laboratory profile including ESR, platelet count, liver function test, renal function test, coagulation profile were normal. ANA, antinuclear cytoplasmic antibody (ANCA), RF, HBV and HCV markers were negative. Routine urine examination revealed mild proteinuria, few red blood cells and pus cells but no cast. Twenty four hours urinary total volume (UTV), urinary total protein (UTP) and creatinine clearance rate (CCr) were within normal range. Stool examination showed plenty RBC per high power field (HPF). Colonoscopy showed patchy ulceration with normal appearing intervening mucosa (Fig. 1). Abdominal ultrasound was unremarkable. Skin biopsy showed granular deposition of IgA and C3 along the dermal capillary wall but no deposition of IgG, IgM or fibrin. With these clinical and laboratory scenarios this patient was diagnosed as a case HSP and was initially treated with intravenous methyl prednisolone 1 gm daily for three consecutive days. There was marked improvement of abdominal and joint pain; skin lesions gradually faded away and

GI bleeding was stopped. Oral prednisolone was started 3 days after IV steroid but unfortunately quick tapering of steroid resulted in reappearance of abdominal pain, skin lesions and passage of fresh per rectal bleeding. At this stage parenteral hydrocortisone was started and continued for 4 days followed by oral prednisolone. With this her condition was improved dramatically. Repeat colonoscopy revealed no more evidence of colitis (Fig. 2). She was discharged with gradual tapering of prednisolone and he is being monitored for development of any possible complications especially of renal origin.
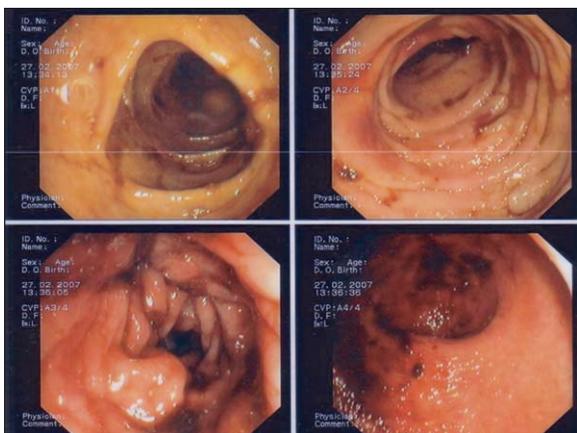
Fig.-1: *Colonoscopic findings of vasculitic colitis in HSP*
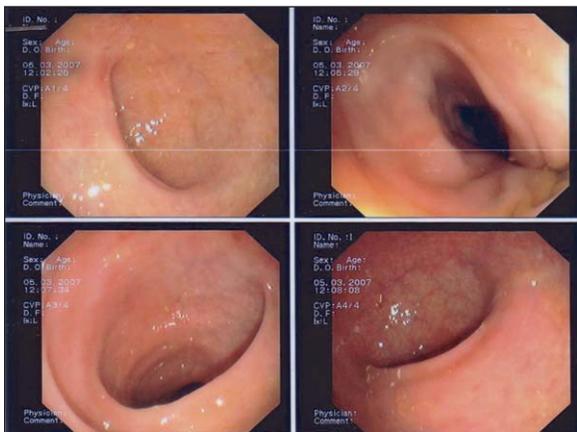
Fig.-2: *Colonoscopic findings after treatment with steroid*

Discussion

HSP is a vasculitis syndrome comprising of characteristic skin rash, abdominal colic, joint pain and renal involvement. Previously it was known as

anaphylactoid purpura [4], purpura rheumatica and peliosis rheumatica.[5]

The syndrome is mainly a disease of early childhood with most cases present around 10 years of age.[6] It is infrequent in adults over the age of 20, though HSP in a lady of 81 years old has been documented.[7] Males are affected as twice as females [5]. HSP in elderly women at the age of her 65 is a rare entity worth reporting. Recent history of respiratory tract infection was reported in 90 % of cases as is in our case.[6] Any of the four major components of the syndrome may present in advance of the other but renal disease usually presents late.[5]

Classical vasculitis rash appears over the extensor surfaces of arms and legs and over the buttocks and elbows. However it had been reported that abdominal and chest wall involvement occurred in 54% of cases.[8] Individual lesions are mostly less than 1 cm in diameter but they may coalesce to form large discolored patches and disappearing over two weeks. In more severe cases, hemorrhagic, pupuric or necrotic lesions may be prominent. It becomes then mandatory to differentiate these lesions from those of meningococcal septicemia, or other septic emboli or toxic vasculitides, such as seen with drug reactions.[9]

Joint involvement occurs in 60- 84% of cases [10] and generally affects ankles and knees. It is the most incapacitating part of the illness though may be transient and leave no permanent deformity.[11]Children usually had large joint involvement but in adults involvement of the small joints is common.[8]

Gastrointestinal disease occurs in up to 70% of patients [10] varying from colicky abdominal pain, nausea and vomiting to intestinal hemorrhage, intussusceptions, pancreatitis and hydrops of gall bladder. More than 30% of patients experienced diffuse abdominal pain as described as bowel angina typically occurring after meal and accompanied by bloody diarrhea. Occasionally, the abdominal symptoms may mimic an acute surgical abdomen. Though adult HSP is said to be characterized by lower frequency of abdominal pain but extensive bowl infarction has been reported.[12] The extensive lower GI hemorrhage due to colitis associated with vasculitis in the reported case is an uncommon presentation of HSP in a woman of this age group. There is increased risk of renal disease in those patients with bloody stools.[13]

The reported incidence of renal disease ranges from 20-100%.[14] Renal involvement is often more

common and more severe in adult.[15] In 80 % of those with renal involvement, it becomes apparent within the first four weeks of illness. The remainder predominantly occurs over the next two months although a few are further delayed.[16] Haematuria with or without protienuria is the most common symptom. Acute nephritic syndrome may be associated with renal insufficiency, Nephrotic syndrome or both. The case in vignette had minimal renal impairment indicating good prognosis.[12]

Direct immunofluroscence in case of HSP shows IgA dominant immune deposit affecting small vessels and differentiates vasculitis of HSP from microscopic polyangitis or hypersensitivity vasculitis which may also present as palpable purpura. The presence of IgA deposits should be interpreted only in combination with clinical criteria since the former are not unique to HSP and can be seen in a variety of clinical situation in different inflammatory and neoplastic process.

There is no specific treatment for HSP. Bed rest and supportive care such as adequate hydration, are helpful .[7] NSAID can relieve joint and soft tissue discomfort although there are some controversy as it may affect the renal function. Corticosteroids have some use in severe cases especially for patients with severe abdominal pain. However corticosteroids are not routinely recommended for treatment of rash, joint pain and renal disease alone. Corticosteroids administered during acute phase help to ameliorate the symptoms of severe abdominal pain, arthralgia, and may prevent progression of renal disease in some cases. It is important to recognize the parvovirus B-19 related cases as the treatment is intravenous IgG and IFN alpha but not the immunosuppressive therapy. In the absence of renal and central nervous system involvement the prognosis for patients with HSP are excellent. One half of the patients experience recurrence. A long term follow up is necessary for patients with renal disease as long term renal complication occurs in 5% of patients.[17] Though adult HSP represents a more severe clinical syndrome with worse outcome,[18] the reported case responded well to intravenous methyl prednisolone and hydrocortisone.

Conclusion:

Henoch-Schonlein Purpura is a vasculitis syndrome that can present with extensive skin lesions and profuse lower GI bleeding even in the very elderly women and responds well to intravenous steroid therapy.

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Malignant Melanoma of the Vagina - A Case Report

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Summary:

A 52 yrs old post menopausal lady was admitted in-the Gynae department of SSMC & Mitford Hospital with a small mass in the lower vagina, foul smelling discharge and occasional itching at that site for 1 year. Examination revealed a small, irregular, firm, partially necrosed, non tender growth with foul smelling brownish discharge 2cm below the external urethral meatus, uterus atrophied, cervix flashed, fornicesfree but few small, black, flat nodules scattered in the posterior vaginal wall. She had no history of exposure to any radiation or sunlight to that area or surgery but only received antitubercular drugs for six month for pulmonary tuberculosis. After conservative treatment excision biopsy was taken and histopathology revealed Malignant Melanoma. She was referred to cancer Institute for adjuvent radiotherapy .

(J Bangladesh Coll Phys Surg 2008; 26: 103-105)

Introduction :

Melanoma of the vagina is rare and carries a poor prognosis five year survival rate is seven percent depending upon the depth of the epithelial invasion. Its clinical feature and treatment are similar to those of the squamous cell carcinoma of the vagina.[1] The anterior surface and lower half of the vagina are the most common sites. Grossly, the tumour are exophytic and described as polypoid or pedunculated with secondary necrosis.[2] Therapeutic irradiation may be a factor in the development of this type of lesion in non-sun exposure area like genital tract.[3] Though it is very rare, but its diagnosis is usually easy if a melanine pigment is present.[4] The natural history of the vaginal malignant melanoma differs from that of the skin with a more aggressive behaviour as it metastasizes early through the blood stream. Primary treatment should be wide local excision of the tumour, however treatment is ineffective if it is deeply invasive. It does not response to chemotherapy.[1,5]

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Case report

A 52 years old post menopausal widow was admitted in Gynaecology department of Sir Salimullah Medical College & Mitford Hospital for a growth in the lower vagina with foul smelling brownish per vaginal discharge for one year. According to her statement she was menopausal for three years and for one year she felt a small, soft, blackish swelling just below the external urethral meatus with occasional itching but no pain.

After that, the growth gradually increased in size with continuos brown and occasional blood stain discharge which became foul smelling. She also complained a single episode of vaginal bleeding three months back. Initially the growth was soft but gradually it became firm in consistency.

On admission, physical examination disclosed an essentially healthy appearance and normal vital signs. Pelvic examination disclosed that there was foul smelling brownish discharge from the growth which was irregular, firm, partially necrosed, non-tender, not bleeds on touch and about 4 cm x 3 cm in size arising 2 cm below the external urethral meatus in the lower part of the vagina. Uterus was atrophied, cervix flashed with the vagina, fornices were free. There was also few small, black, flat surface nodule scattered in the upper part of the posterior vaginal wall . She had no history of surgery or radiation else where in the body. Her skin did not demonstrate any suspicious melanotic lesion. Upon further questioning, the patient denied having had any appreciable sun exposure to the thigh and pelvic areas. Her past medical history only revealed that she was treated for pulmonary tuberculosis with anti tubercular drugs for

6 months. All necessary investigation including USG of whole abdomen was done. All reports were found within normal limit except ESR which was 52 mm during 1st hour and provisional diagnosis of vaginal carcinoma was made.

Initially a short course of conservative treatment to control secondary infection was given with ciprofloxacin, metronidazole and antifungal drugs. After subsidence of local infection a biopsy was taken from the growth and other black sport, and histopathological report revealed malignant melanoma. Then patient was finally treated by wide local excision of the growth with ·5 cm of surrounding apparently normal tissue. The histopathology of all excised tissue finally conclude the malignant melanoma. The patient made an uneventful immediate post operative recovery and she was referred to cancer institute for adjuvant radiotherapy.

Discussion

Malignant melanoma is a virulent disease characterized by steadily rising incidence and mortality rates.[6] In 1996 an estimated 38.300 new invasive cases are expected in the United states resulting 7300 deaths.[7] The incidence of malignant melanoma of the vagina in the united states has been estimated to be 0.026 per 100,000 per year, with a five year survival rate of 19%.[8] Epidemiologic and case control studies suggest that sunlight is the most important environmental factor in the pathogenesis of the melanoma, with radiation in the ultraviolet B range proposed to be the critical component. Furthermore melanoma arising from non sun exposed area such as the genital tract are uncommon and its origin is disputed. Some consider that a vaginal tumour of this type is always secondary to a lesion else where. Other postulate a primary development as a result of metaplasia or misplacement of mesodermal and epithelial tissue, fewer than 140 primary case was reported.[1,9] About 5% of the vulval carcinoma are malignant melanoma. Since 0.1% of all nevi in the women are on vulvar skin and most commonly arise in the region of labia minora and clitoris, and there is a tendency to superficial spread towards the urethra and vagina.[2] Neovaginal malignant melanoma of a 71 years old caucacian lady following surgery and radiation for vulval squamous cell careinoma also reported by a case report.[3] CobellisL, et al reported,

twenty patient affected by vaginal malignant melanoma, 15 of which were evaluable for outcome, were observed from 1969 to 1993. All patients died of their disease and median overall survival rate was 19 months.[5] A review of the literature revealed 22 long term survivals after treatment of malignant melanoma of the vagina and only four surviving more than 10 year.[10] With cytodiagnosis however it is difficult to differentiate amelanomic melanoma or scantily pigmented melanoma from other conditions. Monoclonal antibody HMB-45, the efficacy of which has been established in histological studies was used in the cytodiagnosis of amelanotic melanoma in the vagina, particularly because it obviated the need for tissue invasion.[4] The sentinel node biopsy has been established as standard procedure in many types of cancer. Nokogawa-s et al reported successful detection of the sentinel node using a radiopharmaceutical directed mapping technique in malignant melanoma of the vagina.[11] Metastatic ovarian malignant melanoma are more common than primary ovarian malignant melanoma; to date, about 73 cases of malignant melanoma metastatic to ovary, compared to only about 20 cases of primary ovarian melanoma have been reported in the world literature.[12]

Conclusion

Nevi rarely occur in the vagina, therefore any pigmented lesion of the vagina should be excised or biopsied. Melanomas of the vagina metastasize like epidermoid cancer, although liver and pulmonary metastasis are more common. In general the prognosis in women with these malignancy is poor regardless of type of surgery. Depth of the infiltration seems to be the only important prognostic factors influencing the survival. With wide local excision intracavitary irradiation may be given as adjuvant therapy.

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COLLEGE NEWS

Examination News:

Result of FCPS Part-I, FCPS Part-II and MCPS Examinations held in January, 2008 are given below:

3905 candidates appeared in FCPS Part-I Examination held in January, 2008, of which 571 candidates came out successful, Subject- wise results are as follows:

FCPS Part-I Examination:

SL No.	Name of the Speciality	No. of Candidates Appered	No. of Candidates Passed	Fail	% of Pass
1	Medicine	1272	291	923	22.88
2	Surgery	641	60	554	9.36
3	Paediatrics	397	42	335	10.58
4	Obst and Gynae	923	93	789	10.08
5	Otolaryngology	64	1	62	1.56
6	Opthalmology	109	21	82	19.27
7	Psychiatry	13	3	10	23.08
8	Anaesthesiology	44	7	35	15.91
9	Radiology	60	4	52	6.67
10	Radiotherapy	25	2	22	8.00
11	Dermatology and Venerelogy	92	11	78	11.96
12	Physical Medicine & Rehabiliation	22	2	18	9.09
13	Dentistry	183	21	156	11.48
14	Family Medicine	4	1	3	25.00
15	Haematology	24	10	13	41.67
16	Biochemistry	5	1	4	20.00
17	Microbiology	11	0	11	0.00
18	Histopathology	13	1	11	7.69
19	Transfusion Medicine	3	0	2	0.00
	Grand Total	3905	571	3160	14.62

760 candidates appeared in FCPS Part-II Examination in Different subjects, List of candidates who satisfied the board of examiners is as follows:

Roll No.	Name of candidate	From where Graduated	Speciality
072-7017	Dr. Md. Rafiqul Hassan Khan	Mymensingh Medical College, Mymensingh	Anaesthesiology
072-7031	Dr. Sabbir Muhammad Shawkat	Dhaka Medical College, Dhaka	Dermatology & Venereology
072-7041	Dr. Mousumi Ahmed	MAG Osmani Medical College, Sylhet	Histopathology
072-7075	Dr. Syeda Adib Sultana	Chittagong Medical College, Chittagong	Medicine
072-7078	Dr. Aparna Das	Chittagong Medical College, Chittagong	Medicine
072-7081	Dr. Dilip Kumar Ghosh	Mymensingh Medical College, Mymensingh	Medicine
072-7094	Dr. Md. Sirajul Islam	Dhaka Medical College, Dhaka	Medicine
072-7107	Dr. A.S.M. Ahsannul Karim	Institute of Applied Health Science Under USTC, Chittagong	Medicine

Roll No.	Name of candidate	From where Graduated	Speciality
072-7113	Dr. Mohammad shahid Ullah	Chittagong Medical College, Chittagong	Medicine
072-7114	Dr. Mohd Azharul Haque	Rajshahi Medical College, Rajshahi	Medicine
072-7122	Dr. Abu Syed Mohammad Salimullah	Mymensingh Medical College, Mymensingh	Medicine
072-7124	Dr. Md. Zahirul Haque	Dhaka Medical College, Dhaka	Medicine
072-7125	Dr. Saki Md. Jakiul Alam	Dhaka Medical College, Dhaka	Medicine
072-7131	Dr. Md. Wali-ur Rahman	Rangpur Medical College, Rangpur	Medicine
072-7133	Dr. Rowsan Ara	Chittagong Medical College, Chittagong	Medicine
072-7138	Dr. Syed- Zakir-Hossain	MAG Osmani Medical College, Sylhet	Medicine
072-7140	Dr. Ayesha Rafiq Chowdhury	MAG Osmani Medical College, Sylhet	Medicine
072-7147	Dr. Mohammed Nurul Alam	Dhaka Medical College, Dhaka	Medicine
072-7163	Dr. Provat Kumar Podder	Sir Salimullah Medical College, Dhaka.	Medicine
072-7176	Dr. Mohammed Zafarullah	Sir Salimullah Medical College, Dhaka.	Medicine
072-7179	Dr. Md. Royes Uddin	Dhaka Medical College, Dhaka	Medicine
072-7187	Dr. Syeda Aleya Sultana	Dhaka Medical College, Dhaka	Medicine
072-7191	Dr. Maruf Bin Habib	Chittagong Medical College, Chittagong	Medicine
072-7206	Dr. Md. Aminul Islam	Dhaka Medical College, Dhaka	Medicine
072-7208	Dr. Shah Md. Sarwer Jahan	Rangpur Medical College, Rangpur	Medicine
072-7223	Dr. Mushtaque Ahmed Rana	Dhaka Medical College, Dhaka	Medicine
072-7230	Dr. Kaniz Fatema	Sher-e-Bangla Medical College, Barisal	Medicine
072-7236	Dr. Md. Shadiqul Hoque	Dhaka Medical College, Dhaka	Medicine
072-7241	Dr. Quazi Arif Ahmed	Dhaka Medical College, Dhaka	Medicine
072-7243	Dr. Md. Abu Shahin	Rajshahi Medical College, Rajshahi	Medicine
072-7249	Dr. Md. Nure Alom Siddiqui	Rajshahi Medical College, Rajshahi	Medicine
072-7255	Dr. Sofia Andalib Safiullah	Sir Salimullah Medical College, Dhaka.	Microbiology
072-7256	Dr. Chandan Kumar Roy	MAG Osmani Medical College, Sylhet	Microbiology
072-7260	Dr. Jakeya Rashid	Dhaka Medical College, Dhaka	Obst & Gynae
072-7261	Dr. Asma Habib	Dhaka Medical College, Dhaka	Obst & Gynae
072-7264	Dr. Afroza Akther Mazumder	Mymensingh Medical College, Mymensingh	Obst & Gynae
072-7267	Dr. Salma Yasmin	MAG Osmani Medical College, Sylhet	Obst & Gynae
072-7295	Dr. Mohammed Kamal Hossain	Dhaka Medical College, Dhaka	Obst & Gynae
072-7298	Dr. Dalia Rahman	Dhaka Medical College, Dhaka	Obst & Gynae
072-7303	Dr. Ismat Ara	Mymensingh Medical College, Mymensingh	Obst & Gynae
072-7309	Dr. Bilkis Begum	Mymensingh Medical College, Mymensingh	Obst & Gynae
072-7316	Dr. Shahnaz Sigma	Rajshahi Medical College, Rajshahi	Obst & Gynae
072-7324	Dr. Jannath Parvin	MAG Osmani Medical College, Sylhet	Obst & Gynae
072-7328	Dr. Hosna Akter	MAG Osmani Medical College, Sylhet	Obst & Gynae
072-7332	Dr. Khodeza Khatun	Sher-E-Bangla Medical College, Barisal	Obst & Gynae
072-7344	Dr. Parvin Akter	Sir Salimullah Medical College, Dhaka.	Obst & Gynae
072-7363	Dr. Kamrun Nahar	MAG Osmani Medical College, Sylhet	Obst & Gynae
072-7366	Dr. Farzana Rabee Choudhury	MAG Osmani Medical College, Sylhet	Obst & Gynae
072-7371	Dr. Nahid Sultana	Rangpur Medical College, Rangpur	Obst & Gynae
072-7378	Dr. Mosammat Bilkis Parvin	Rajshahi Medical College, Rajshahi	Obst & Gynae
072-7401	Dr. Afroza Begum	Rangpur Medical College, Rangpur	Obst & Gynae

Roll No.	Name of candidate	From where Graduated	Speciality
072-7403	Dr. Rehana Begum	Rangpur Medical College, Rangpur	Obst & Gynae
072-7414	Dr. Shahana Begum	Rajshahi Medical College, Rajshahi	Obst & Gynae
072-7425	Dr. Afroza Ferdous	Sir Salimullah Medical College, Dhaka.	Obst & Gynae
072-7429	Dr. Rokshana Rahman	Mymensingh Medical College, Mymensingh	Obst & Gynae
072-7436	Dr. Md. Sanwar Hossain	Rajshahi Medical College, Rajshahi	Opthalmology
072-7443	Dr. Md. Mahmud-Ul-Huda	Rangpur Medical College, Rangpur	Opthalmology
072-7451	Dr. A.K.M Mozammel Hoque	Mymensingh Medical College, Mymensingh	Opthalmology
072-7458	Dr. Salma Parveen	Mymensingh Medical College, Mymensingh	Opthalmology
072-7462	Dr. Mohammad Muklesur Rahman	Dhaka Dental College, Dhaka	Orthodontics & Dentofacial Orthopaedics
072-7470	Dr. Kazi Shameemus Salam	Sir Salimullah Medical College, Dhaka.	Otolaryngology
072-7471	Dr. Mohammad Tawhidul Islam	Sir Salimullah Medical College, Dhaka	Otolaryngology
072-7475	Dr. Md. Abdur Rahman	Sir Salimullah Medical College, Dhaka	Otolaryngology
072-7476	Dr. Md. Mostafizur Rahman	Sir Salimullah Medical College, Dhaka	Otolaryngology
072-7478	Dr. Ashok Kumar Dey	MAG Osmani Medical College, Sylhet	Otolaryngology
072-7479	Dr. Debesh Chandra Talukder	Dhaka Medical College, Dhaka	Otolaryngology
072-7480	Dr. Md. Sailful Islam	Dhaka Medical College, Dhaka	Otolaryngology
072-7485	Dr. Md. Rafiqul Islam	Dhaka Medical College, Dhaka	Otolaryngology
072-7486	Dr. Bithi Bhowmik	Rajshahi Medical College, Rajshahi	Otolaryngology
072-7493	Dr. Kazi Shah Alam	Sir Salimullah Medical College, Dhaka	Otolaryngology
072-7506	Dr. Md. Mostafizur Rahman	Dhaka Medical College, Dhaka	Paediatrics
072-7507	Dr. Sukhendu Shekhar Sen	Dhaka Medical College, Dhaka	Paediatrics
072-7509	Dr. Santosh Kumar Saha	Mymensingh Medical College, Mymensingh	Paediatrics
072-7533	Dr. Md. Ibrahim Khalil	MAG Osmani Medical College, Sylhet	Paediatrics
072-7550	Dr. Nobo Krishna Ghosh	Rajshahi Medical College, Rajshahi	Paediatrics
072-7561	Dr. Ujjal Mitra	Dhaka Medical College, Dhaka	Paediatrics
072-7568	Dr. Ananda Kishore Ghosh	Chittagong Medical College, Chittagong	Paediatrics
072-7593	Dr. Naheed Nabi	Mymensingh Medical College, Mymensingh	Paediatrics
072-7598	Dr. Mohammad Kamrul Hassan	Dinajpur Medical College, Dinajpur	Paediatrics
072-7603	Dr. Ehsanul Haque Khan	Mymensingh Medical College, Mymensingh	Physical Medicine & Rehabilitation
072-7606	Dr. S. Abdullah-Al-Farooq	Sir Salimullah Medical College, Dhaka	Psychiatry
072-7613	Dr. Kamrun Nahar	Chittagong Medical College, Chittagong	Radiology & Imaging
072-7649	Dr. Mohammad Shahidur Rahman	Sir Salimullah Medical College, Dhaka	Surgery
072-7670	Dr. Major Md Neazul Islam	Chittagong Medical College, Chittagong	Surgery
072-7675	Dr. Md. Nabir Hossain	Dhaka Medical College, Dhaka	Surgery
072-7686	Dr. Kishore Kumar Das	Dhaka Medical College, Dhaka	Surgery
072-7706	Dr. A.k.M. Ahsan Ullah	Sher-e-Bangla Medical College, Barisal	Surgery
006-8019	Dr. Mohammed Zahir Uddin	Dhaka Medical College, Dhaka	Preli-Paediatrics
006-8028	Dr. Mst. Masuma Sarker	Dhaka Medical College, Dhaka	Preli-Surgery
006-8034	Dr. Md. Abdul Mannan	Sir Salimullah Medical College, Dhaka	Preli-Surgery
011-8502	Dr. Md. Delwar Hossain	Dhaka Medical College, Dhaka	Gastroenterology

245 candidates appeared in MCPS Examination in different subjects. List of candidates who satisfied the board of examiners is as follows:

Roll No.	Name of candidate	From where Graduated	Speciality
072-9002	Dr. Md. Wakely Mandal	Rangpur Medical College, Rangpur	Anaesthesiology
072-9005	Dr. K.M. Baki Billah	Sher-e-Bangla Medical College, Barisal	Anaesthesiology
072-9008	Dr. Tayeba Haque	Rajshahi Medical College, Rajshahi	Anaesthesiology
072-9019	Dr. Md. Sarul Alam Hafiz	Rajshahi Medical College, Rajshahi	Clinical Pathology
072-9021	Dr. Rezina Jasmine	Rajshahi Medical College, Rajshahi	Clinical Pathology
072-9023	Dr. Md. Emdadul Hoque	Dhaka Dental College, Dhaka	Dental Surgery
072-9123	Dr. Mst Nasima Begum	Rangpur Medical College, Rangpur	Obst & Gynae
072-9124	Dr. Fatheha Ferdous	Comilla Medical College, Comilla	Obst & Gynae
072-9125	Dr. Nurun Nahar	Sher-e-Bangla Medical College, Barisal	Obst & Gynae
072-9127	Dr. Mohammad Abdul Ali	Dhaka Medical College, Dhaka	Obst & Gynae
072-9131	Dr. Rubana Gulshan	Mymensingh Medical College,Mymensingh	Obst & Gynae
072-9142	Dr. Tohura Taj Laizu	Shahid Ziaur Rahman Medical College, Bogra	Obst & Gynae
072-9146	Dr. Nargis Sultana	Chittagong Medical College, Chittagong	Obst & Gynae
072-9149	Dr. Mohammed Shahadat Hossen	MAG Osmani Medical College, Sylhet	Obst & Gynae
072-9150	Dr. Sayeda Fatema Khatun	Sir Salimullah Medical College, Dhaka	Obst & Gynae
072-9161	Dr. Tahminaafreendaise	Sir Salimullah Medical College, Dhaka	Obst & Gynae
072-9176	Dr. Begum Shaira Sharifa	Sher-e-Bangla Medical College, Barisal	Obst & Gynae
072-9182	Dr. Enamul Karim	Rajshahi Medical College, Rajshahi	Opthalmology
072-9184	Dr. Md. Harunur Rashid	MAG Osmani Medical College, Sylhet	Opthalmology
072-9185	Dr. Tanuja Tanzin	Chittagong Medical College, Chittagong	Opthalmology
072-9186	Dr. Taslima Mazid	Mymensingh Medical College,Mymensingh	Opthalmology
072-9194	Dr. Md. Kamal Hossain	Jahurul Islam Medical College, Bajitpur	Otolaryngology
072-9200	Dr. Swapan Kumar Sarkar	Sher-e-Bangla Medical College, Barisal	Paediatrics
072-9208	Dr. Probir Kumar Sarkar	Dinajpur Medical College, Dinajpur	Paediatrics
072-9209	Dr. Md. Jahirul Islam	Dhaka Medical College, Dhaka	Paediatrics
072-9213	Dr. Shah Muhammad Mustaquim Billah	Comilla Medical College, Comilla	Radiology & Imaging
072-9215	Dr. Towhida Khan	Mymensingh Medical College,Mymensingh	Radiology & Imaging
072-9216	Dr. Zebun Nahar	MAG Osmani Medical College, Sylhet	Radiology & Imaging
072-9217	Dr. A.F.M. Nurullah	Sher-e-Bangla Medical College, Barisal	Radiology & Imaging
072-9220	Dr. Syed Monirul Islam	Chittagong Medical College, Chittagong	Surgery

45 candidates appeared in Priliminary FCPS- II Examination in different subjects. List of candidates who satisfied the board of examiners is as follows:

Roll No.	Name of candidate	From where Graduated	Speciality
006-8019	Dr. Mohammad Zahir Uddin	Dhaka Medical College, Dhaka	Preli-Paediatrics
006-8028	Dr. Mst. Masuma Sarker	Dhaka Medical College, Dhaka	Preli-Surgery
006-8034	Dr. Md. Abdul Mannan	Sir Salimullah Medical College, Dhaka	Preli-Surgery

Continuing Professionals Development Lectures

Date	Time	Topic	Speaker	Chairperson / Moderator
04-03-08 Tuesday	11-00am to 11-50am	" An Update on Oral Contraceptive Pill."	Dr. Neaz Tahera Parveen B-21 Arambagh Eastern Housing Mirpur, Dhaka-1221.	Prof. Ameena Majid (Chairperson) Dr. Fatema Begum (Chairperson) Dr. Anwara Begum (Moderator) Gynae
	11-50 am to 12-10pm	TEA		
	12-10 pm to 1-00 pm	"Hospital Emergency Incident Command System (Heics) and its role in disaster"	Dr. Dewan Ali Hassan Chowdhury Assistant Professor of Surgery Sylhet MAG Osmani Medical College	Prof. Abu Ahmed Ashraf Ali (Chairperson) (Surgery) Dr. Md. Kamruzzaman Khan (Chairperson) (Surgery) Dr. A.F.M. Anwar Hossain (Moderator) (Surgery)
11-03-08 Tuesday	11-00 am to 11-50 am	" Gene Therapy."	Major Mah Jabeen Ara Classified Specialist in Pathology Armed Forces Institute of Pathology Dhaka Cantt, Dhaka.	Prof. Ruhul Amin Miah (Chairperson) (Pathology) Prof. F.M. Siddiqui (Chairperson) (Medicine) Dr. Md. Ayub Al Mamun (Moderator) (Medicine)
	11-50 am to 12-10 pm	TEA		
	12-10 pm to 1-00 pm	" Endometriosis- Current update".	Dr. Laila Parveen Banu Assistant Prof. Obst. & Gynae Faculty Institute of Child & Mother Health (ICMH) Matuail, Dhaka-1362.	Prof. Hosne Ara Begum (Chairperson) (Gynae) Dr. Suraiya Begum (Chairperson) (Gynae) Dr. Kishwar Sultana (Moderator)

Date	Time	Topic	Speaker	Chairperson / Moderator
18-03-08 Tuesday	11-00am to 11-50 am	"1. HPV vaccines in prevention of cervical cancer" and

2. " The first Breastfeed | Prof. Sameena Chowdhury Prof & head of Department Obst. & Gynae Faculty Institute of Child & Mother Health (ICMH) | Prof. Mahmuda Khatun (Chairperson) (Gynae)

Prof. Nasima Begum (Chairperson) (Gynae) |
| | 11-50 am to 12-10 pm | TEA | | Prof. Rashida Khatun (Moderator) |
| | 12-10 pm to 1-00 pm | "Current trend in the management of Glaucoma- Bangladesh Perspective" | Dr. Md. Nazrul Islam Associate Professor of Ophthalmology BIRDEM Hospital, Shahbag, Dhaka. | Prof. Brig. Gen. Nazrul Islam (Chairperson) (Ophthalmology)

Dr. Md. Shafiqul Islam (Chairperson) (Ophthalmology)

Dr. Shamima Islam (Moderator) |
| 25-03-08 Tuesday | 11-00am to 11-50 am | "Meibomian Gland Dysfunction (MGD)- A common eyelid disorder and usually missed by ophthalmologist in their clinical practice." | Dr. Md. Abdul Quader House# 12, Road # 11 Nikunja # 2, Badda, Dhaka. | Professor Ava Hossain (Chairperson) (Ophthalmology)

Dr. Md. Hazrat Ali (Chairperson) (Ophthalmology) |
| | 11-50 am to 12-10 pm | TEA | | Dr. Md. Musharaf Hossain (Moderator) (Ophthalmology) |
| | 12-10 pm to 1-00 pm | " Aged Population Sceneries in Bangladesh and their rehabilitation Concepts" | Dr. Md. Shahidur Rahman Dept. of Physical Medicine BSMMU, Shahbag, Dhaka. | Prof. Birendra Nath Bhattacharjee (Chair.P.) (Physical Medicine)

Dr. Shamsun Nahar (Chairperson) (Physical Medicine)

Dr. Md. Ahsan Ullah (Moderator) (Physical Medicine) |