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JOURNAL OF BANGLADESH COLLEGE OF PHYSICIANS AND SURGEONS

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EDITORIAL

Nutritional Iodine Deficiency in Bangladesh and Future of Thyroid Disease Management

Malnutrition, including that due to micronutrients is common in Bangladesh. Situated in an iodine deficient zone in the belt of the river Brahmaputra, Bangladesh has a vast population naturally devoid of sufficient dietary iodine. Iodinization of common salt is a recent practice in the region. As such, it is not surprising that iodine deficiency disorders including thyroid disease are the most common endocrine problems of the country. WHO estimates about one billion people to be at risk of iodine deficiency diseases and 20% of them are expected to have goitre[1]. East Pakistan nutrition survey in 1963-64 indicated 20% prevalence of goitre in the region. A current national survey in 1993 revealed the prevalence to be as high as 47% [2,3]. This not only discloses an alarming prevalence of thyroid diseases but also suggests that a large part of the newborn population is at the risk of developing neonatal hypothyroidism and therefore be intellectually deficient. 1-10 percent of the newborn population in the endemic areas remain at risk of hypothyroidism compared to only 0.015 percent in the non endemic areas. Besides, this scanty information from a national survey, data on thyroid disorder are mainly institution or region based and comes from study of small clinical samples. Nevertheless it is not difficult to compute that the problem is far greater than endemic and far beyond the cosmetic blemish of a goitre. Its effect on the national intelligence level in future is likely to be profound.

Studies have shown that the gamut of thyroid disorders are prevalent in the population but nutritional goitre is the most prevalent. It has been found that in comparison to a 47.1 % total goitre prevalence rate, 8.0% goitre are visible, 0.5% suffers from cretinism and 69% of the population is bio-chemically iodine deficient[3,4] about half of the population yet does not use salts[5]. It appears that the bulk of the disease burden is hidden and therefore not exposed to the clinicians. The bulk is likely to increase in near future if the factors contributing to the risk remain unattended. Beside the impact on the national health status, the impact of spectrum thyroid disease, as a consequence, on clinical departments are also likely to be profound. An autopsy study of thyroids in persons unsuspected of thyroid disease have found 6.6% of neoplasia including 2.33% of carcinoma with a high incidence of multicentricity[6].

As much as 50% of adenomatous goitres may harbour malignancy. The thyroid clinic of BSMMU reports a 32.67 percent prevalence of solitary nodules which may equally harbour malignancy[7].

It is therefore probable that alongside the high prevalence of endemic nutritional goiter, the prevalence of malignant thyroid disease, which also increases with rising age of the population, will increase. Similarly the prevalence of toxic disease is also likely to increase with age. With an increasing age of our population, the total burden of thyroid disease are feared to increase in near future.

Thyroid disorders have traditionally been given importance in the teaching curriculum. The recent past has observed tremendous development in the diagnosis of thyroid disorders with nuclear and Ultrasound scanning, FNAC, frozen section, antibody study, hormone estimations and

immune studies playing key role. Fortunately, Bangladesh has strategically kept pace with such recent developments. Facilities for nuclear and ultrasound scanning, FNAC, hormone estimation are now available with most medical colleges. Therefore, curriculum now demands further emphasis on thyroid disease to keep pace with the increasing disease bulk and newer modalities of diagnosis and treatment strategies. Expectedly a large percentage of the disease bulk will require surgical treatment.

Therefore surgical training also needs to be emphasised in the management of thyroid diseases. The focal point of management of thyroid disorder need further expansion from medical colleges to districts hospitals. Given this situation the clinical departments are expected to take a sight of the future and prepare for managing the incoming bulk.

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(J Bangladesh Coll Phys Surg 2002; 20 : 47-48)

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ORIGINAL ARTICLES

Management of Severe Primary Postpartum Haemorrhage: A New but Simple Suturing Technique

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Summary :

Objective : **To control severe primary postpartum haemorrhage.**

Method : **Patients having primary postpartum haemorrhage not responding to conservative therapy were the subjects of the study. 75% of the study patients had cesarean section & 25% had normal vaginal delivery. Six sutures, 3 on each sides of uterus were applied using No. 2 chromic catgut to reduce the blood supply of the uterus.**

Results : **Haemorrhage ceased immediately following application of the sutures. Follow up revealed that all the patients started menstruation without any problem.**

Conclusion : **This simple technique could be a safe, easy & effective alternative to more difficult surgery for control of severe primary post partum haemorrhage**

(J Bangladesh Coll Phys Surg 2002; 20 : 49-53)

Introduction :

Postpartum haemorrhage (PPH) is a serious obstetric problem. Primary PPH is said to occur in around 5% of deliveries. The amount of blood loss after delivery is difficult to measure and PPH may be best defined by a fall in haematocrit or by need of blood transfusion. Delay in diagnosis & or treatment may lead to life threatening situation[1].

The common causes of PPH include uterine atony (80%), lower genital tract injury, retained placenta or fragments of placenta, coagulopathy and ruptured uterus. When there is uterine atonicity, conventional managements like bimannual compression, administration of ecbolic drugs, catheterization of bladder etc is prescribed. When all these measures fail, exploration of the uterine cavity should be done quickly to remove any placental beats or blood clots to make the effective contraction of the uterus. Even sometimes intramyometrial injection of PGF_2 may be tried[2]. In most of the cases the above mentioned measure will control the bleeding but when proved inadequate & unsatisfactory, various surgical measures like ligation of the uterine artery[3,4,5], bilateral ligation of the internal iliac artery[6], ligation of the ovarian artery[7], sometimes B-Lynch suture[8] can be tried. Hysterectomy is used as a last measure to save the life of the patient. Radiographic embolization of the pelvic vessels using pieces of absorbable gelatin sponge (Gelfoam) can also control the intractable haemorrhage but it needs well-trained interventional radiologist in an institution.

In this prospective study an innovative suturing technique has been tried, which is very simple but proved to be effective to control the life threatening PPH as an alternative to more complicated surgery like bilateral ligation of internal iliac artery or hysterectomy.

Materials and Methods :

Six (6) women who had massive life threatening primary PPH, not controlled with any conventional methods - were the subjects of this study. Among them four (4) underwent lower segment cesarean section and the rest two (2) developed PPH after normal vaginal delivery. All the cesarean sections were done under spinal anaesthesia but when reopened it was performed under general anaesthesia. All patients were treated with antibiotics (Cephalosporin & Metronidazole). Average 6 bags of blood was transfused. Follow up was done either in person or over telephone.

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Technique :

Step 1 :

Under general anesthesia the patient was catheterized, abdomen was opened by an appropriate sized Pfannensteil incision or when the patient had cesarean section the same incision was used.

Step 2 :

On entering the abdomen, uterus was lifted up through the abdominal incision, and bimannual compression of the uterus was tried. Being failed uterine cavity was explored through the lower segment incision made earlier in cases with cesarean section or made newly in cases of PPH after normal vaginal delivery.

Step 3 :

Uterus was pushed away from the side to be ligated i.e. pushed to the left side when suture was decided to apply on the right side. Thus six (6) sutures, three (3) on each side were applied using No. 2 chromic catgut and a big sized curved round body needle including whole thickness of the uterine wall (both anterior & posterior wall).

Step 4 :

(a) First pair of suture was applied on either side of the lateral wall of the lower uterine segment, The needle was placed 1 cm. below the cut margin of the lower uterine segment & 2cm. medial to the lateral margin of the lower uterine segment medially and through the avuscular area of the broad ligament laterally. It obliterates the uterine artery. Similar suture was applied on the opposite side.

(b). Second pair of sutures were placed vertically over the fundus at least 3 cm away from the tubal attachment on either side to obliterate the supply of ovarian artery.

(c). A Third pair of sutures were placed on lateral wall of either side of the body of the uterus just below the level of attachment of the adnexae - thus obliterating the ovarian artery and sparing the cornue with the interstitial part of the fallopian tubes.

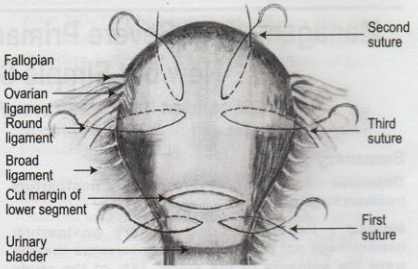

Diagram-1 : *Diagramatic representation of the anterior view of the uterus after application of the sutures.*

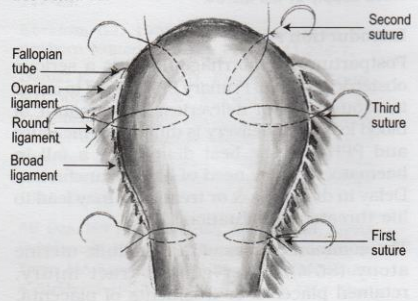

Diagram-2 : *Diagramatic representation of the appearance of the posterior view of the uterus after application of the sutures*

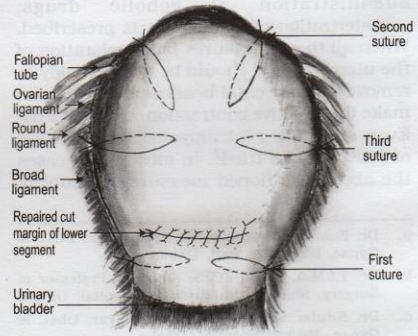

Diagram-3 : *Diagramatic representation of the anterior view of the uterus after completion of the sutures.*

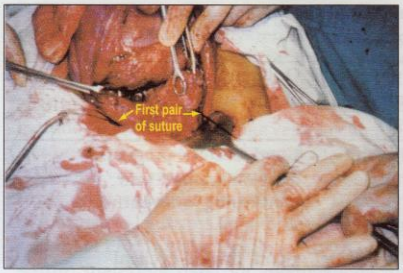

Fig.-1: *Showing first pair of suture to occlude the uterine artery with open cut margin of uterus*

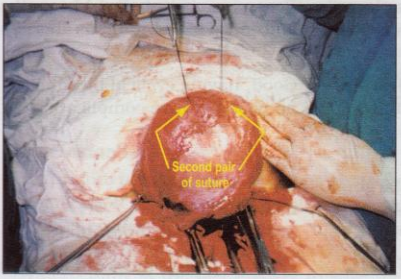

Fig.-2: *Showing second pair of suture occluding the some of the branches of ovarian artery with open cut margin of uterus.*

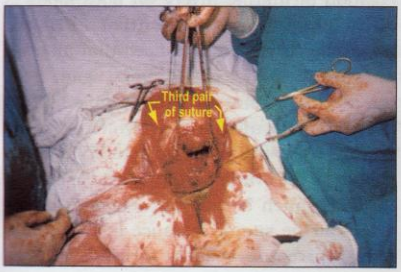

Fig.-3: *Showing third pair of suture occluding rest of the branches of ovarian artery with open cut margin of uterus.*

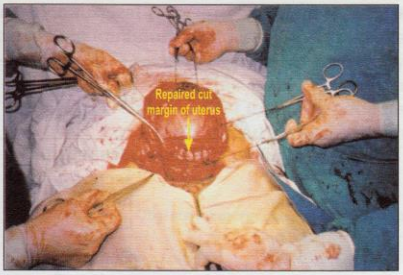

Fig.-4: *Showing complete three pairs of suture with repaired cut margin of uterus.*

Step 5 :

Bleeding was checked through the lower segment incision immediately after completion of the suture. Then cut margin of the lower segment was closed as usual in two layers.

Results:

This is a very small study of six (6) cases who developed very severe life threatening PPH. All the six (6) cases responded very quickly & effectively. Satisfactory haemostasis could be achieved immediately after completion of the suture. After opening the abdomen average time needed to complete the sutures is around 20 minutes. No patients develop any postoperative complication. All the cases required blood transfusion prior & during operation. Average six (6) bags of whole blood was transfused. All the patients were discharged in due time. During the 2 years follow-up period all the patients started menstruation timely and without any complication i.e. dysmenorrhoea, menorrhagia etc. Among these six (6) patients- 2 patients became pregnant but one ended in abortion at 2 months probably due to hyperpyrexia and second one is still continuing her pregnancy uneventfully.

Table – I
Summary of results:

Age	Parity	Weeks of gestation	Mode of delivery	Suspected cause of PPH	Outcome of operation
28	1	FTP	Cesarean section for prolonged labour	Uterine inertia;	Good, become pregnant after one & half year, continuing uneventfully.
22	1	FTP	Cesarean section for foetal distress	Uterine atony	Good, having cyclical bleeding without any complication.
32	1	36 wks.	Cesarean section for bad obstetric history	Uterine atony & placenta acreata.	Good, having cyclical menstruation. No complication. Become pregnant after 11 months and ended in spontanious abortion at 8 weeks.
30	2	FTP	History of previous cesarean section	Uterine atony	Good, having cyclical bleeding no postoperative complication
20	1	FTP	NVD	Marginal placenta previa	Good, Normally menstruating, no postoperative complication
34	3	37 wks.	NVD	Uterine atony	Good, no postoperative complication normally menstruating

Discussion:

Postpertum haemorrhage is thought to be one the major cause of maternal mortality. Statistical analysis of the published literature and unpublished hospital records reveals that PPH causes 26% of matenal death in Bangladesh. About 75-80% of primary PPH is due to uterine atony & fortunately majority of these could be controlled by the conventional methods like by manual compression, intravenous ecbolic drugs etc. Only a few percent of cases need surgical intervention like ligation of internal iliac artery or hysterectomy or other procedures. But all the above mentioned surgical procedures need experience & skill of surgeons which is not the usual expectation from the on duty residents who face such a problem at emergency.

Ligation of uterine artery on both sides is sufficient enough to control PPH but sometimes it has been noticed that after an interval of time bleeding starts again from the uterus in some patients, probably from that part of the uterine cavity which get blood supply from the ovarian artery. Isolated ligation of the ovarian artery is said to control the PPH much better[7] but isolation of the artery at the site of entrance in the uterus may injure the vessels forming a large haematoma at once or can injure the fallopian tubes which is very near to the vessels.

Due to extensive collateral circulation in the pelvis only 50% of the hysterectomy can be prevented after ligation of the internal iliac artery. It also requires high degree of skillness & the possible complications include laceration of the iliac vein, accidental ligation of the ureter & external iliac artery which are very nearby, trauma to other great veins with consequent bleeding. B-Lynch brace surgical sutures said to be effective for control of PPH but the tensile strength of the suture materials used for haemostasis for such a large sized post partum uterus might not be sufficient enough. In the present suturing technique the loop of the sutures are smaller, having much tensile strength and can be applied without shearing the catgut and no chance of slip of loop over the adnexae, thus damaging the tubes. These six sutures are sufficient enough to occlude the surface supplied by ovarian and uterine artery.

Conclusion :

Postpartum hemorrhage is a serious obstetric complication which needs urgent treatment. Various conservative & surgical procedures are practised to control the haemorrhage. Hysterectomy is the last answer to save the life. This simple suturing technique may be particularly useful because of its life saving potential, relative safety and its capacity of preserving the uterus and future fertility. Satisfactory haemostasis can be assessed immediately after completion of the procedure which occlude both uterine & ovarian artery, thus decreasing the blood supply to the uterus sparing the cornue with interstitial portion of the fallopian tubes. It is an effective & safe alternative to other major surgical procedures to control PPH. It requires minimum skillness of the surgeons and can be performed very quickly even by on duty residents. In this study the sutures were successfully applied in all the patients without any hazard and complication regarding menstruation or fertility.

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"Clinical Experience with Capecitabine as Adjuvant Therapy in Different Types of Gastrointestinal (GI) Cancers"

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Summary :

Capecitabine is a fluoropyrimidine carbamate that is formulated for oral administration. It is the first of a new class of drugs that are selectively converted to 5-FU within the tumor tissue. This study was conducted to gain clinical experience with Capecitabine as adjuvant therapy in different types of gastrointestinal tumors. A total of 36 patients were studied with 113 cycles of Capecitabine therapy being evaluated. In general, the treatment was well tolerated. Capecitabine did not produce clinically significant anaemia or jaundice, but tend to produce a decline in total count of WBC. The median overall survival was 13 months for gall bladder cancer and 10 months for pancreatic cancer. There was no incidence of grade 3-4 toxicity of the drug. From our clinical experience we suggest that Capecitabine is a convenient choice for patients, with favorable safety profile and, clinical benefit.

(J Bangladesh Coll Phys Surg 2002; 20 : 54-61)

Introduction :

Gastrointestinal cancers account for a large fraction of human tumors. They are almost without exception incurable when gross metastasis exists. Of these, colorectal cancer is one of the most common cancers in the world, second only to lung cancer in men and breast cancer in women. It has been observed that colorectal cancer killed 557, 000 people world wide in 1998[1]. The incidence of other solid tumors of GI tract like gall bladder cancer and pancreatic cancer has also been rising steadily.

Cancer of the exocrine pancreas continues to be a major unresolved health problem. In the United States in 1995, pancreatic cancer was to be the fifth leading cause of adult deaths from cancer and was responsible for close to 5% of all cancer related deaths. Pancreatic cancer spreads early to regional lymph nodes, and sub-clinical liver metastases are present in the majority of patients at the time of diagnosis, even when findings from imaging studies are normal. Patient survival depends on the extent of disease and performance status at diagnosis[3]. Patients with locally advanced, nonmetastatic disease have a median survival of 6 to 10 months. Patients with metastatic disease have a short survival (3 to. 6 months)[3-6]. Survival is clearly maximized by combining surgery with either preoperative or postoperative 5-fluorouracil (5-FU) based chemotherapy and radiation therapy (chemoradiation). Knowledge of the prognosis and patterns of treatment failure associated with adenocarcinoma of the pancreas leads to the basic treatment principle of, *"the treatment must not be worse than the disease"*

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Carcinoma of the gall bladder is the most common biliary tract malignancy and the fifth most common gastrointestinal cancer[7]. The female-male ratio is 2.5:1 to 3:1. The association between gallstone and carcinoma of the gall bladder was observed by Mayo in 1903[7]. In most reports, more than 90% of patients with gall bladder cancer have coexistent chronic cholecystitis and cholelithiasis. The most effective therapy for carcinoma of the gall bladder is resection of the primary tumor and areas of local extension. Fluorinated pyrimidines have been the mainstay of treatment in adjuvant setting for cancers of the biliary tree. However, phase II trials with mitomycin C or cisplatin as singles have also reported partial responses comparable to 5-FU.

As far as colorectal cancer is concerned, surgery is the mainstay of treatment till now. There is currently no standard medical treatment for colorectal cancer. The classical "Mayo" regimen-bolus i.v 5-FU plus Leucovorin (LV)-achieves responses in about 20% of patients but most of these responses are partial and median survival time does not increase much following 5-FU/LV therapy. Furthermore, i.v 5-FU/LV bolus infusion is also associated with dose limiting adverse events, especially myelosuppression. Around 15-30% of patients requires hospitalization for the adverse events, which reduces patient quality of life and increases overall treatment costs [8, 9].

The reported trials in different types of gastrointestinal cancers had mostly been carried out in the developed world with highest degree of medical facilities available for the patients. In context of a developing country like Bangladesh, where the total sociological, economic and medical scenario for diagnosis and treatment of cancer is different from other parts of the world, the issues addressed in clinical study need to be modified from textbook protocols. Therefore, a treatment protocol containing a regimen that will address not only the length of survival, but also the quality of life along with it is a primary concern. The usually observed treatment related toxicity of conventional chemotherapeutic agents is often difficult to manage in this country where medical resources are limited. Moreover, these toxicities often are physically and psychologically distressing for the patient and their relatives, which leads to a high rate of discontinuation of treatment and drop out ultimately leading to high rate of treatment failure. These has led us to investigate a new generation of chemotherapeutic agent, Capecitabine which has now been well known for its tumor selectivity, clinical benefit response and good patient compliance. The concept of the current study was to gain clinical experience with Capecitabine in GI tumors in adjuvant setting, without compromising the principal interest of the patients.

Capecitabine is a fluoropyrimidine carbamate that is formulated for oral administration. It is the first of a new class of drugs that are converted to 5-FU within the body[10]. Capecitabine passes through the intestinal mucosal membrane as an intact molecule and is then converted to 5-FU in a sequential three-enzyme process, the final step of which is catalysed by thymidine phosphorylase (TP). This enzyme is present at significantly higher concentration in tumor tissue compared with healthy tissue. This ensures that drug levels are 3.2-fold higher in tumor tissues than in surrounding healthy tissues[11]. As TP activity is substantially elevated in solid tumors compared with normal tissues[10], it is to be expected that Capecitabine should selectively target tumor tissues and possibly even 5-FU resistant tumors. Moreover, since activity levels of TP in normal tissues are relatively low, it would be anticipated that such tumor targeting could be achieved with Capecitabine whilst keeping systemic concentrations of 5-FU relatively low, thereby limiting toxicity compared with conventional 5-FU chemotherpy. At the recommended dose of capecitabine (1250 mg/m^2 administered twice daily)[12], the amount of 5-FU delivered is 6-8 fold higher than if bolus 5-FU was used instead and 3-4-fold higher than with continuous infusions of 5-FU[10]. Thus, oral capecitabine is a convenient, patient-

oriented therapy that has demonstrated activity in patients with advanced/metastatic GI and colorectal cancer. The majority of treatment-related adverse events of capecitabine are mild or moderate in intensity, with grade 4 adverse events occurring in only 3.4% of patients. The predominant treatment-related adverse events are hand-foot syndrome, diarrhea and nausea[13].

Patients and Methods

Patient Population

This was an open-label, non-randomized, prospective study mostly concerned with obtaining clinical experience with Capecitabine as adjuvant therapy. Therefore, eligibility criteria were set up at flexible limits. Patients eligible for this study were from either sex, who had malignant tumors of gastrointestinal origin with or without metastasis. All patients required to have histologically confirmed adenocarcinoma. Eligibility criteria also included a Karnofsky performance status of at least 70, and adequate haematologic, liver and renal function. As the study treatment was intended to be at adjuvant setting, therefore all patients were required to have had first-line therapy for their primary disease. This was allowed in the form of surgery, prior chemotherapy or radiotherapy. Patients who had received any number or type of exogenous therapies, either for treatment of metastatic disease or as adjuvant therapy, were permitted to enroll onto the study. Pretreatment with 5-FU was not an exclusion criteria. Treatment with some other investigational drug within 3 months prior to study enrollment was not allowed. Patients had to recover from myelosuppressive effects of prior chemotherapy (normal blood counts for at least 3 weeks). Women of childbearing potential had a negative pregnancy test before enrollment and were advised to practice appropriate contraception while on study. Before study entry, each patient signed a written informed consent form.

Treatment regimen

This was a single center study. Capecitabine was administered orally at a dose of 1500 mg/m^2/day in two divided doses as an intermittent regimen in 3-week cycle (2weeks of treatment followed by a 1-week rest period). For practical reasons, Capecitabine doses were rounded to the nearest dose that could be administered with 500-mg tablets of the drug. Capecitabine was given approximately 12 hours apart and taken orally with water within 30 minutes after ingestion of food. The number of cycles was not limited. Treatment was continued until disease progression, unacceptable adverse effects, and withdrawal of consent by the patient or at the discretion of the investigator.

Evaluation of Response & Toxicity Assessment

Pre-treatment evaluation included a complete medical history and physical examination, a complete blood count, serum chemistry profile, carcinoembryonic antigen (CEA), CA 19.9, chest x-ray and ultrasound evaluation of whole abdomen. A complete blood count and liver function test was.performed before the start of each treatment cycle together with a serum chemistry profile, physical examination and toxicity assessment. Overall survival and performance status were considered to be the primary endpoint parameters of treatment efficacy. Overall survival was measured from the time the patient has started test drug treatment to the date of patient death/the date that this patient was last known to be alive. For performance status, Karnofsky scale was used. Toxicities were assessed according to the National Cancer Institute of Canada Common Toxicity Criteria (NCIC CTC)[14]. Hand-Foot Syndrome (palmar- erythro-dysesthesia) was classified as Grade 1 (numbness, dysesthesia, painless swelling, erythema not disrupting normal activities, Grade 2 (painful swelling disrupting daily activities), or grade 3 (moist desquamation, ulceration, blistering, severe pain, inability to work or perform daily activities).

Statistical Analysis :

Demographic data, patient characteristics and adverse reactions were summarized as incidence rates and were presented on conventional tables. All laboratory values

were calculated with exact 95% Confidence Interval (CI) at the end of study. Laboratory parameters were analyzed as continuous parameters and logistic regression trend was used to determine variations in laboratory values throughout the treatment period to assess toxicity and safety of the drug. The Kaplan-Meier product-limit method was used to estimate median survival time for each tumor type.

All analysis was based primarily on the intention-to -treat population (all patients who received at least one dose of study drug). Statistical significance was accepted at p £ 0.05.

Results :

From August 1999 through May 2002, a total of 36 patients were enrolled on to the study. The patient characteristics according to individual tumor types are listed in Table I. Overall, the study consisted of 19 male and 17 female with age ranging from 27-82 years (median 50 years). Body Surface Area (BSA) (m^2) was median 1.52 [range 1.20-1.80]. The tumor types included were carcinoma of the gall bladder (11 pts.), pancreas (7 pts.) and colorectal carcinoma (18 pts.). 8 patients (22%) had poorly differentiated adeno-carcinoma, while 25 patients (69%) and 3 patients (9%) had moderately differentiated and well differentiated tumor, respectively. 17 patients (47%) had baseline metastatic disease, while the other 19 (53%) did not have any baseline metastasis. 35 patients (94%) had no family history of malignancy. Most of the patients had stage I and II disease (according to TNM classification) at the onset of treatment (Table II).

Table-I

Patient Characteristics

Ca. Gall Bladder	Ca. Pancreas	Colorectal Ca.	Overall	
Number of Patients	11	07	18	36
Age, years				
Median	51.5	54	44	50
Range	40-70	27-82	30-73	27-82
Sex				
M/F (%)	4/7 (36/64)	6/1 (86/14)	9/9 (50/50)	19/17 (53/47)
Adenocarcinoma (%)				
Poorly Differentiated	1 (9)	1 (14)	6 (33)	8 (22)
Moderately Differentiated	10 (91)	3 (43)	12 (67)	25 (69)
Well Differentiated	0 (0)	3 (43)	0 (0)	3 (9)
Baseline Metastasis (%)				
Yes	8 (73)	2 (40)	7 (39)	17 (47)
No	3 (27)	5 (60)	11 (41)	19 (53)
Family History of Malignancy (%)				
Yes	2 (22)	0 (0)	0 (0)	2 (6)
No	9 (78)	7 (100)	18 (100)	34 (94)

Table-II

Number of patients in different stages of tumor

Stage (%)	Ca. Gall Bladder	Ca. Pancreas	Colorectal Ca	Overall
I	0 (0)	2 (28)	0 (0)	2 (6)
II	1 (9)	2 (28)	7 (39)	10 (28)
III	8 (73)	1 (16)	7 (39)	16 (44)
IV	2 (18)	2 (28)	4 (22)	8 (22)

No patient had previous radiotherapy and 5 patients (14%) had previous chemotherapy. Overall, 31 patients (86%) had been operated for their primary disease (Table III). The mean performance status of the patients at the onset of study was 74% (95% CI: 70-90) on the Karnofsky scale and 51.9% of the study population were in the range of 80-90% of the scale. A total of 113 cycles of Capecitabine therapy were assessed (median 3 cycles, minimum 1 cycle, maximum 6 cycles).

In general, the treatment was well tolerated. The baseline laboratory values (S. Bilirubin, Total Count of WBC, Haemoglobin) as well as the values in each cycle of treatment were always within the reference range. There was no incidence of clinically significant jaundice, neutropenia or anaemia. The logistic regression analysis of the laboratory blood values show that the treatment regimen did not tend to reduce haemoglobin level (Fig. 1) or elevate serum bilirubin significantly (Fig. 2), though it might have caused a decline in the total count of WBC in blood (Fig. 3). Among the study population 4 patients (11%) had diarrhoea and 6 patients (16%) had hand-foot syndrome of grade 1-2 during the course of chemotherapy. Another 8.3% of patients experienced both these side effects. Overall, there was no incidence of grade 3-4 toxicity. No patient required hospitalization for adverse events and there was no incidence of serious adverse event (SAE).

Table III

Treatment History

	Ca. Gall Bladder	Ca. Pancreas	Colorectal Ca.	Overall
Surgery (%)				
Yes	11 (100)	5 (71)	15 (83)	31 (86)
No	0 (0)	2 (29)	3 (17)	5 (14)
Previous Chemotherapy (%)				
Yes	0 (0)	3 (43)	2 (11)	5 (14)
No	11 (100)	4 (57)	16 (89)	31 (86)
Previous Radiotherapy (%)				
Yes	0 (0)	0 (0)	0 (0)	0 (0)
No	11 (100)	7 (100)	18 (100)	36 (100)

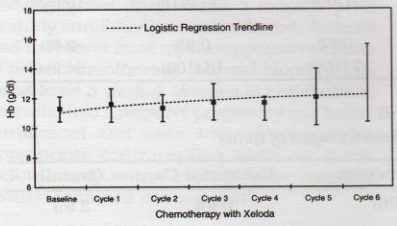

Fig. 1 : *Mean Haemoglobin levels at 3 weekly cycle of Xeloda in all patients. Error bars reflect 95% CI. (P<0.05)*

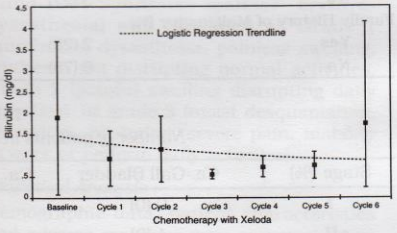

Fig. 2 : *Mean Bilirubin levels at 3 weekly cycle of Exeloda in all patients. Error bars reflect 95% CI. (p<0.05).*

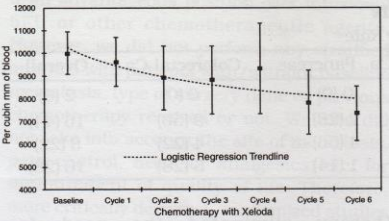

Fig. 3 : *Mean Total Count of WBC at 3 weekly cycle of Xeloda in all patients. Error bars reflect 95% CI. (p<0.05).*

The Kaplan-Meier survival analysis revealed that the median overall survival was 13 months (95% CI, 3 to 18) for gall bladder (Fig. 4), 10 months (95% CI, 2 to 15) for pancreatic cancer (Fig. 5) and a median survival for colorectal cancer has not been achieved yet (Fig.6). At the end of study 63% (n=23) of the patients achieved a performance status of 80-100% in the Karnofsky scale, the mean value being 83% (95% CI: 70-100) at the end of treatment. Overall, 44% of patients (n = 16) had no recurrence of tumor and 22% (n = 8) had stable disease at the end of treatment evaluation, while 28% patients (n = 10) developed progressive disease during study treatment (Table IV).

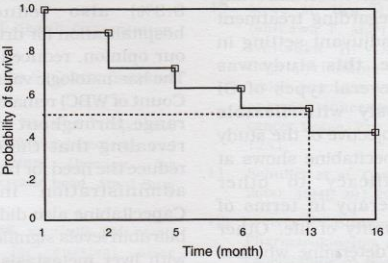

Fig. 4 : *Kaplan-Meier Survival curve for Gall Bladder cancer.*

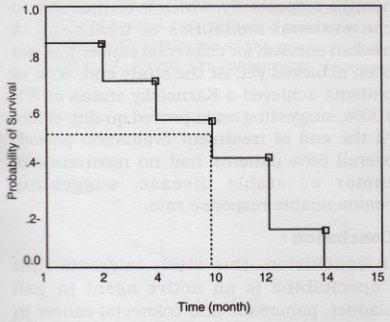

Fig.-5 : *Kaplan-Meier Survival curve for pancreatic cancer.*

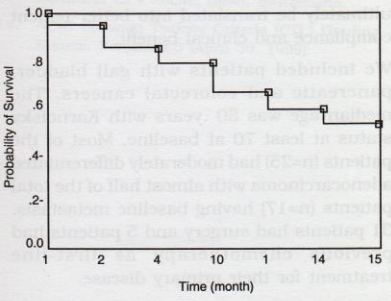

Fig.-6 : *Kaplan-Meier Survival curve for colorectal cancer.*

Table IV
Response Rate

Type of Response (%)	Ca. Gall Bladder	Ca. Pancreas	Colorectal Ca.	Overall
Partial response (PR)	2 (18)	0 (0)	0 (0)	2 (6)
No Recurrence (NR)	5 (46)	2 (28)	9 (50)	16 (44)
Stable Disease (SD)	0 (0)	4 (56)	4 (22)	8 (22)
Progressive Disease (PD)	4 (36)	1 (14)	5 (28)	10 (28)

Discussion :

We conducted a single-center, prospective, single-arm study principally concerned with gaining clinical experience with Capecitabine at adjuvant setting in GI malignancies, as no conclusive data on South Asian population clearly exists in this regard to the best of our knowledge. No formal study has been undertaken regarding treatment of GI malignancies in adjuvant setting in Bangladesh. Therefore, this study was designed to include several types of GI cancers simultaneously with flexible eligibility criteria. The objective of the study was to see whether Capecitabine shows at least comparable efficacy to other conventional chemotherapy in terms of overall survival and quality of life. Other objectives were also to determine whether Capecitabine has less incidence of chemotherapy related adverse events and its effect on blood chemistry, which can ultimately be translated into better patient compliance and clinical benefit.

We included patients with gall bladder, pancreatic and colorectal cancers. The median age was 50 .years with Karnofsky status at least 70 at baseline. Most of the patients (n=25) had moderately differentiated adenocarcinoma with almost half of the total patients (n=17) having baseline metastasis. 31 patients had surgery and 5 patients had previous chemotherapy as first-line treatment for their primary disease.

The clinical experience with Capecitabine proved to be a convenient choice for both the patient and physician. Oral, home based therapy eliminated the need for hospitalization for infusional chemotherapy, which is often unacceptable to the patient. This also gave the patients the feeling of assurance as they were taking the medicine in their familiar surroundings. Few treatment-related adverse events (diarrhoea-11%, Hand-Foot syndrome-16%, and both-8.3%) also reduced the need for hospitalization for drug toxicity and thus, in our opinion, reduced the cost of treatment. The haematologic values (Haemoglobin, Total Count of WBC) remained within the reference range throughout the treatment period, revealing that Capecitabine might also reduce the need for blood transfusion/G-CSF administration in cancer patients. Capecitabine also did not elevate the serum bilirubin levels significantly, even in patients with liver metastasis.

The median survival time for gall bladder and pancreatic cancer was 13 months and 10 months respectively, which is comparable to conventional modalities of treatment. A median survival for colorectal cancer has not been achieved yet. At the study end, 63% of patients achieved a Karnofsky status of 80-100%, suggesting an improved quality of life. At the end of treatment evaluation period, overall 66% patients had no recurrence of tumor or stable disease, suggesting commendable response rate.

Conclusion :

In conclusion, this study suggests that Capecitabine is an active agent in gall bladder, pancreatic and colorectal cancer in adjuvant setting producing clinical benefit for the patients. Its safety and tolerability gives

it an advantageous position over infusional 5FU or other chemotherapeutic agents. However, we did not perform any stratified analysis with patients with/without baseline metastasis, type of surgery done or previous chemotherapy received or not. We also did not take into account the site of metastasis, pain control, need for analgesics, etc. for measurement of quality of life. Therefore, more critically designed, randomized studies with larger sample size are needed to confirm the findings of this study.

Acknowledgements:

We gratefully acknowledge the patients and their family members who had voluntarily consented to participate in this study.

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Screening for Carcinoma - Cervix- An analysis

S KHATUN[a], S ALI[b]

Summary :

During the period January 2001 to December 2001 a total of one thousand four hundred and thirty two consecutive women underwent Pap's testing at Gynaecology out- patient department of Bangabandhu Sheikh Mujib Medical University, Dhaka Bangladesh. Inclusion criteria for the study were age more than 20 years, history of early resumption of sexual activity, excessive per vaginal discharge, post-coital or postmenopausal bleeding and history of vulval or vaginal wart.

Result of this prospective study was as follows- 70% patients were in the range of 20-40 years, 60% patients were less than para four, 60% women started sexual activity before 18 years of age. Results of Pap's testing was reported as inflammatory- 56.28%, inflammatory with squamous metaplasia- 16.41%, normal 4.82°/a, atypia- 1.05%, dyskaryosis- 42%, drop-out- 21.02%. No result was reported as cervical intraepithelial neoplasia (CIN). But among 198 suspected cases having colposcopic evaluation and directed biopsy, 20 cases were found as CIN-I, II or cervical intraepithelial neoplasia with micro-invasion. From results of papanicolaou staining, it appears that though pap's smear is widely recognized as the most cost effective cancer screening test diagnosis without further evaluation by colposcopy of CIN is likely to be missed.

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Introduction :

The incidence of preinvasive and invasive cancer cervix is increasing in the younger woman and there is an increase in the number of deaths from cervical cancer in under 35 year olds. The progression from carcinoma in situ to invasive cancer in many cases takes a shorter time than in the past. Cervical cancer remains worldwide the second most common cancer among women accounting for 15% of all female cancers. It is the most common cancer among women in many developing countries, constituting 20% to 30% of female cancers. In developed Western countries, it accounts for only 4% to 6% of female cancers[1, 2, 3, 4]. This differences largely reflects the impact of mass screening using cervical cytologic methods[5].

The limitations of traditional cytologic screening remain a source of high rate of false negative results. A meta analysis of 28 studies in which conventional cytology was evaluated for accuracy as a screening test reported a mean sensitivity and specificity of 58% and 69% respectively[6].

Epidemiological data from clinical and laboratory studies have revealed that human papilloma virus (HPV) plays an important role in 90% to 95% of Ca Cervix. Roughly half of all cervical cancers worldwide contain the oncogenic HPV 16. Other important high risk types are HPV 18, 45 and 31[7,8].

Certain types of human papilloma virus has been emerged as the most likely infectious agent causing atypical transformation of squamocolumner junction and are well established as the primary cause of cervical cancer. Several studies have shown that HPV

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testing can improve the detection rate of high grade cervical intraepithelial neoplasia (CIN), but these have been carried out primarily in younger women.[9]

Methods :

Consecutive consenting women referred with suggestive symptoms and signs to the gynaecological oncology out-patient department of Bangabandhu Sheikh Mujib Medical University Hospital by the residents and consultants of the hospital & general practitioners and consultants from other hospitals. The patients were prospectively assessed over a one year period.

A structured questionnaire was completed for each of the patients about their symptoms, obstetric history, menstrual status, personal and sexual history. To take the cervical smear, we followed the traditional method used in our country. The patient in dorsal position under good light cervix exposed with a medium sized cusco's bivalve speculum. All the discharge and blood removed by cotton ball swab. No lubricant except water used to expose the cervix. At first clinical appearance and environment of cervix was noted. Ayre's spatula inserted into the endocervix and rotated through 360 degree (Fig. 1). The sample spread on slide evenly, immersed immediately in the kofliri's jar and kept for at least 5 minutes in the jar. Slides removed,

Fig.-1 : *Ayre's spatula*

dried and sent for cytology. The results were collected and recorded in the respective document file. 198 patients requiring colposcopic evaluation was referred to the colposcopy room of the same department. All the reports of the colposcopic assessment and colposcopically directed biopsy were recorded in the same document file. Patients were managed according to colposcopy and follow-up pap's smear report. The results were analyzed according to parameter used in the study.

Results :

Bangabandhu Sheikh Mujib Medical University, the then Institute of post-graduate Medicine and Research is a referral hospital. Most of the patients seen at the GOPD of the university are nonconclusive and complicated. During the period, January 2001 to December 2001, a total 7832 gynaecological patients attended the GOPD. Among them 1432 women had cervical cytology by pap's smearing. Table I shows the incidence of pap's smear at GOPD. It was 18.28% and consistent with international figure of 20%.

Table - I

Percent of Cervical Cytology at GOPD of BSMMU

Gynecological cases	7832	81.72%
Pap's smear	1432	18.28%

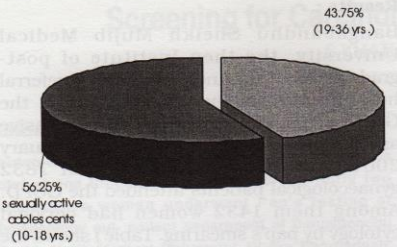
Cervical cancer is a disease of reproductive age and screening should be started at the age of onset of sexual activity. According to our inclusion criteria our patients were more than 20 years of age. 70% were at the age range of 20-40 years. Newer concept about cervical cancer does not show any direct relation with parity of the patients. 6.11: patients were nulliparous and 58.31% were of para 3. Table II shows the age and parity distribution of the patients.

Table - II

Age and Parity Distribution of the Patients

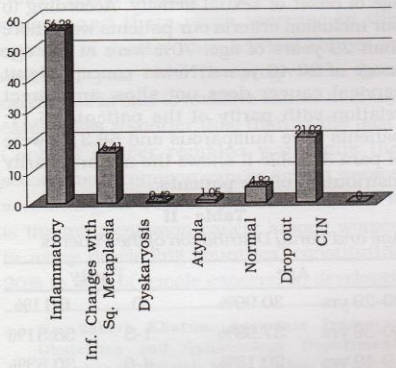
Age		Parity	
20-29 yrs	30.99%	0	6.11%
30-39 yrs	37.99%	1-3	58.31%
40-49 yrs	20.18%	4-6	30.53%
50 60 yrs	11.24%	7-9	4.15%
		10 onwards	0.90%

Early resumption of sexual activity specially at the adolescent period has direct relationship with carcinoma cervix. 56.25% of our patients having cervical cytology were sexually active since 10-18 years ago. Graph-1 shows the age of onset of sexual activity.



Graph.-1 : *Age of onset of sexual activity*

Report of the cytopathologist was not satisfactory and quite disappointing. No patient was reported as CIN. Only 1.47% patient found to be atypia or dyskaryosis. 21.02% patients did not return back with pap's report. May be these dropped-out patients reported to their own centres with abnormal reports. Graph.-2 shows 72.69% patients were reported as inflammatory or inflammatory change with squamous metaplasia.



Graph-2 : *Report of Pap's Smear*

Further evaluation of the suspicious cervices done by colposcopy and biopsy taken after application of acetic acid. Criteria of biopsy taking was acetowhiteness, penetration or abnormal vascularity. 198 patients had colposcopic assessment. 20 of them found positive.

Table III shows results of colposcopy directed histopathology report.

Table - III

Results of Further Evaluation of Suspicious Cervices by Colposcopy

Total Number of Colposcopy - 198

Positive	20	10.10%
CIN - 1	13	6.57%
CIN - 11	6	3.03%
Micro invasion	1	0.50%

Discussion :

Out of all cervical cancer cases seen in the world, only 14% are in the developed countries and about 86% occur in developing countries[10]. For primary prevention of cervical cancer we must know the etiological factors and how to remove the etiological factors. Various studies done in our country recognized the risk factors of cancer cervix as early age of onset of sexual intercourse, low socio economic status, multiple sexual partners and history of sexually transmitted diseases etc. A study was carried out at Dhaka Medical College Hospital during the period of August to June'96. From the study findings the sexual factors appeared to be important risk factor while early age of marriage had the greatest risk[11,12].

Secondary prevention of cervical cancer by eradication of preinvasive disease is very difficult in our country. Because selective cervical cancer screening which is done by traditional pap's smearing in our country does not give any clue about preinvasive disease. Almost every case needs to be evaluated by colposcopy and a colposcopy directed biopsy which is not available in many centres. Analysis of this prospective study could not found any case to be reported as cervical

carcinoma in situ or severe dysplasia. Among about one thousand and five hundred cases that has undergone pap's smearing only 6 cases were reported as dyskaryosis and 15 cases were reported as atypia. So sensitivity of pap's smearing was very low.

There are some limitations of traditional pap's smearing method. Most of the time sample is not properly taken and smearing is faulty. Due to lack of properly trained cytopathologist many a time the report is false negative. So, false negative result varies from 15-30%. We can use Aylesbury spatula instead of wooden Ayre's spatula (fig 2). Aylesbury spatula has a pointed apex which

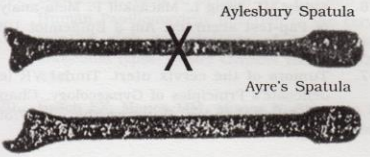


Fig.-2

can be introduced into the endocervical canal and collection of endocervical cells become easier. Also it covers wider area and collection of cells from transformation zone of a broad cervix become easier. Another alternate method is to use both cytobrush and Ayre's spatula for cervical sampling in a same patient at a time.

Various newer methods of higher technology are being used to overcome the high false negative results. 70-90% false- negative results are due to sampling and preparation error. Liquid-base thin-layered cervical cytology method is used where slide is prepared from cells in suspension. The cervical sample is taken in routine manner using conventional sampling devices. Instead of smearing the sample a glass slide the collection device is rinsed in s vial containing 20ml of a buffered alcohol liquid preservative. The vial is transferred at ambient temperature to the cytology laboratory, where a slide is prepared from the cells in suspension for papanicolaou staining and cytological screening [13].

The limitations of traditional cytologic screening remain a source of much attention and concern about false-negative results. A false-negative cytologic result occurs when the smear report does not predict the presence of any grade of cervical neoplasia. This consists of 'true' false-negative results (70%) and laboratory errors (30%)[14,15].

The main factors contributing to the false-negative rate are (a) specimen collection (b) Laboratory error and (c) deficiencies in laboratory quality assurance mechanisms.

In this study only1.47% cases were found to have cellular atypia or dyskaryosis by cytology. Where as 10.1 % cases were positive by further evaluation by colposcopy. So, false-negative rate was almost 9%. Gay et al. in 1998 documented a false-negative rate for conventional pap's smears at the Mayo Clinic of at least 20%[16].

As sexual intercourse has been established as causal factor for cervical cancer, Human Papilloma Virus (HPV) infection as sexually transmitted disease has been found to be closely associated with early cervical cancer.

A longitudinal study of the natural history of HPV infection and cervical neoplasia in women residing in a city of Brazil, conducted between November 1993 to March 1997 and involved repeated measurements of HPV and lesions with follow-up until June 2000. Main outcome was measured by papanicolaou cytology and HPV testing every 4 months in first year and twice yearly thereafter in same cervical specimens. The incidence of squamous intraepithelial lesion was. 73 per 1000 women-months (95% [Cl],.5-.9) among women free of HPV at the two initial visits and 8.68 (95% Cl, 2.3-15.1) among women with HPV type 16 or 15 infections persisting over both visits[17].

Cervical cancer has a specific and exclusive viral etiology, with the strength of the association between the chronic carrier state of hepatitis B infection and the development of hepatocellular carcinoma[18].

Human papilloma virus 16 has been universally detected with greatest frequency in high grade intraepithelial neoplasia and invasive cancers. HPV 16 is associated 50% of cervical squamous cancers[19,20,21] and over 30% of adenocarcinoma cervix[22] Cervical cancer screening that incorporate DVI (direct visual inspection) or HPV DNA testing and eliminate colposcopy may offer attractive alternatives to cytology-based screening programes in low-resource settings[23].

According to Clovel C et al. sensitivity of HPV testing for detection of histologically proven high grade squamous intraepithelial lesion (HGSIL) was 100% [24].

Various methods for Human Papilloma Virus identification has been used till now. As for example polymerase chain reaction, in-situ hybridization and Hybrid capture I and II. Among the methods Hybrid Capture II is the newest, the sensitivity of which is 95%. Falsenegative rate is also low only 4.9% and false-positive rate is 2.3%.

Colposcopy as an adjunct to cytology is not a practical means of primary screening of cervical cancer. HPV testing may be a useful adjunct to cytology and may have an important role in primary cervical cancer screening in our country.

Acknowledgements:

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Emergency Peripartum Hysterectomy- in a Developing Country

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Summary :

The purpose of this study is to evaluate the prevalence, clinical indications and outcome of emergency peripartum hysterectomy in women delivered at Dhaka Medical College Hospital, Dhaka, Bangladesh. This is a prospective cross sectional study of all cases of emergency peripartum hysterectomy performed in the year 1999 from 1st January to 31st December. Statistical analysis were carried out with mean, standard deviation, proportion and relative risk (RR) for hysterectomy with 95% confidence intervals (CI). During the study period there were 62 cases of emergency peripartum hysterectomy (incidence of 6.63/1000 deliveries), of which 20 cases were caesarean hysterectomy. Mean age of patients was 30.28±5.93 years, median parity was 2 (range was (1 to 7) and the mean gestational age was 39.09±1.60 weeks. Indications for hysterectomy were primarily uterine rupture due to obstructed labour (66.13%, p=0.000), postpartum haemorrhage (17.74%. p=0.000). prior caesarean section with scar rupture (6.45%), uterine infection (6.45%) and placenta previa (3.23%). The relative risk of emergency hysterectomy was 68.72 (95'x, CI 49.13-96.1 1) for ruptured uterus; 10.12 (95°/, CI 5.43-1 8.85) for postpartum haemorrhage, 0.65 (95% CI 0.24-1.79) for prior caesarean delivery, 1.11 (95% CI 0.41-3.04) for uterine infection and 1.02 (95% CI 0.25-4.13) for placenta previa. Maternal death was 17.74% (n=11) and perinatal death was 79.03% (n=49). Ruptured uterus still remains an important indication for emergency peripartum hysterectomy for developing countries. Identification of patients at risk and anticipation of procedure and complications are important because peripartum hysterectomy is usually associated with considerable perioperative morbidity and mortality, though it is a necessary life saving procedure in obstetric practice.

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Introduction :

Emergency peripartum hysterectomy, although not commonly performed, remains a necessary life saving procedure in obstetric practice. Emergency peripartum hysterectomy is usually done in life threatening haemorrhage during or immediately after abdominal or vaginal deliveries. Various studies have reported the incidence of this procedure and identified the potential risk factors for peripartum hysterectomy. Caesarean deliveries, prior caesarean delivery, placenta previa and placenta accreta are the potential reproductive risk factors described in various studies of the developed countries[1,2]. Yet few studies have reported the variation in incidence and indications for developing countries[3]. Although the rising trend for caesarean birth rate increases the risk for scar rupture, placenta previa, placenta accreta etc. and these conditions in turn increase the risk of hysterectomy, most patients with uterine scar rupture do not require hysterectomy. Simple repair of the defect is all that is required. So in contemporary obstetric practice, hysterectomy has become an, uncommon operation in developed countries such as the United Kingdom, United States and Australia because the indications are few[4]. On the other hand, ruptured uterus due to obstructed labour still remains an important cause of emergency peripartum hysterectomy for developing countries like Bangladesh. Poor

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antenatal coverage, attempted home delivery by untrained personnel and delayed referral of neglected cases are still in practice.

This study was aimed to evaluate the prevalence, clinical indications, and outcome of emergency peripartum hysterectomy done in a tertiary referral center of a developing country. An attempt was made to identify the variation in incidence for developing countries by clinical indications that might predict the patients likely to rcquire this procedure.

Materials and Methods :

This is a prospective cross sectional study of all cases of emergency peripartum hysterectomy performed in the year 1999 from 1st of January to 31st of December at the obstetrics unit of Dhaka Medical College Hospital (DMCH) which is one of the important and biggest tertiary referral center located at the capital city.

Data were collected from preformed protocol for all women who had undergone emergency peripartum hysterectomy and the patients were followed up till discharge or death. The operations included in the study were performed at the time of abdominal deliveries or in the immediate 24 hours after abdominal/vaginal delivery (only one case with secondary postpartum haemorrhage was done in the early puerperium). The surgical procedures were performed by resident surgeon or the senior staff of the department. Statistical analysis were carried out with mean, standard deviation and proportion. Relative risk (RR) for hysterectomy with 95% confidence intervals (Cl) for different indications were calculated together.

Results

During the study period there were 9352 deliveries at DMCH and of this total 4334 (46.34%) were delivered vaginally and 4924 (52.65%) by caesarean section. A total of 62 (6.63/1000 birth) patients were identified who had undergone peripartum hysterectomy and all were emergency cases. Of these total 20 cases were caesarean hysterectomy, 41 cases were abdominal deliveries following rupture of gravid uterus with obstructed labour and one case was done after vaginal delivery. The mean age of the patients was 30.28±5.93 years (range 20-42), The median parity was 2 (range 0-7) 'and the mean gestational age was 39.09±1.60 weeks (Table-I).

Table-I

Patients' Characteristics

Patients Characteristics	No.	Mean	SD
Age (years)			
20-25	20		
26-30	14		
30-35	20	30.28	±5.93
36-40	7		
³40	1		
Gestational age (Weeks)		39.09	±1.60
Parity		Median	
0	6		
1	14		
2	13	2	
3	4		
4	12		
5	4		
³6	9		

Table-II listed the main indications for emergency obstetric hysterectomy and the relative risk for identified causes. The leading indication for this procedure was uterine rupture (66.13%) due to obstructed labour followed by postpartum haemorrhage (17.74%). Prior caesarean section with scar rupture and gangrenous infected uterus were the third important causes occurred in 6.45% of cases each. The relative risk of emergency hysterectomy was 68.72 (95% CI 49.13-96.11) for ruptured uterus, 10.12 (95% Cl 5.4318.85) for postpartum haemorrhage, 0.65 (95% Cl 0.24-1.19) for prior caesarean delivery, 1.11 (95% CI 0.41-3.04) for uterine infection and 1.02 (95% CI 0.25-4.13) for placenta previa.

Table-III demonstrated the details of the operative characteristics associated with the procedure. Almost all patients received transfusion either intraoperatively or postoperatively. On average 2 to 12 units of blood were transfused and 46 (74.19%) patients required massive transfusion (>4 units of blood). Mean operation time was 1.25±0.29 hours, majority (n=59) was completed within 1 to 1.5 hour, only 3 cases required more than 1.5 to 2 hours. General anaesthesia was given in 82.26% patients and 11 patients received spinal anaesthesia. Type of anaesthesia varies with clinical indication for hysterectomy. All the ruptured uterus cases due to obstructed labour received general anaesthesia.

Table-II

Indications of hysterectomy and relative risk for identified factors

Indications	Total number admitted	Hysterectomy done * no.(%)	Relative Risk (R.R)	95% Confidence Interval (CI)	P value
Ruptured Uterus (Obstructed labour)	90	41 (66.13)	68.72	49.13 - 96.11	0.00
Prior Caesarean Section (Scar rupture)	926	4 (6.45)	0.65	0.24 - 1.79	0.4012
Postpartum haemorrhage	164	11 (17.74)	10.12	5.43 - 18.85	0.00
Placenta praevia	297	2 (3.23)	1.02	0.25 - 4.13	0.7329
Uterine infection (Obstructed labour)	544	4 (f .45)	1.1.1	0.41 - 3.04	0.4949

(P 0.001 is significant); * (Figure within the bracket is the percentage among the hysterectomy patients)

Table-III

Operative Characteristics

	Unit	No %	Range	±SD
Blood Transfusion	< 4	16 (25.81)	2-12 Units	
	≤ 4	46 (74.19)		
	Hours		*Mean Time*	
Operation time	1	33 (53.23)		
	>1-1.5	26 (41.94)	1.25 hr.	±0.29 hr
	> 1.5-2	3 4.84		
Type of anaesthesia	General	51 (82.26)		
	spinal	11 17.74		

Table-IV

Maternal and Perinatal outcome

Maternal Outcome	No.	Percentage
Case Fatality	11	17.74
- Rupture uterus	3	
- Postpartum haemorrhage	7	
-Uterine infection	1	
Recovered	51	82.26
Perinatal Outcome		
- Still birth	45	72.58
- Early perinatal death	4	6.45
- Alive	13	20.97

Table-V

Complications Associated with Peripartum Hysterectomy

Complications	**No.**
Infection	
Febrile morbidity	49
Pelvic peritonitis	15
Wound infection	12
Sepsis	8
Urinary Tract Infection (UTI)	5
Burst abdomen	2
Haemorrhagic	
Massive Haemorrhage	30
Re-exploration due to haemorrhage	3
Disseminated Intravascular Coagulation (DIC)	1
Gastrointestinal	
Paralytic ileus	25
Intestinal Injury	1
Urologic	
Vesico Vaginal Fistula	2
Renal failure	1
Neurologic	
Coma	5
Stroke	1
Respiratory	
Delayed recovery from anaesthesia	
Prolonged intubation	5

Table-IV described the details of maternal and perinatal outcome. There were 11 maternal deaths (17.74%) and the reported leading cause was postpartum haemorrhage (63.63%). 62 babies delivered to 62 women and all were term babies. 49 of the babies died of which 45 were stillborn and 4 were early perinatal deaths.

Table-V listed the complications associated with peripartum hysterectomy. Maternal complications occurred in 52 patients (83.87%) either intraoperatively or postoperatively and the major complications were shown. Of these, 49 displayed febrile morbidity, 12 had wound infection, 2 had burst abdomen, 8 developed sepsis, 30 patients suffered from massive haemorrhage and one developed (disseminated intravascular coagulopathy (DIC). Urologic complications occurred postoperatively in the form of vesico vaginal fistula in 2 cases and renal failure in one patient. Respiratory complications in the form of delayed recovery from anaesthesia and prolonged intubation in intensive care unit required in 6 and 5 patients respectively.

Discussion :

The overall incidence of emergency peripartum hysterectomy at our hospital (6.63/1000 deliveries) is much greater than the rates reported previously by other institutions of other countries ranging from 0.5 to 1.5/1000 deliveries[1,2,3]. In other series reported in the recent literature, it ranged from 0.03 to 0.33 percent[4,5]. More emergency hysterectomies were performed in some African and Asian countries as compared to the United Kingdom and United States and reflected the difference of standard of obstetric care in these countries[5]. The reported increase incidence in our series is most likely linked to the relative frequency of the increasing rate of ruptured uterus with obstructed labour, which is almost non-existing in other studies of developed countries.

In different studies the common indications for emergency peripartum hysterectomy were abnormally adherent placenta, postpartum haemorrhage and uterine atony[1,2,3], ruptured uterus[1,2,6] and other such as sepsis or various sites of infection[7] and disseminated intravaseular coagulopathy[8]. Our study demonstrated the emergence of two main indications for emergency obstetric hysterectomy, namely ruptured uterus with obstructed labour and postpartum haemorrhage with uterine atony. One study using local data in Hong Kong in 1987 showed that the incidence of rupture of gravid uterus was only 0.04% with majority occurring during labour [6]. But in our hospital incidence of rupture of gravid uterus was 0.85% of total admissions. Obstructed labour with attempted home delivery by untrained personnel and delayed referral are the main aetiological factors. Peripartum hysterectomy done for uterine rupture, showed in different studies were mainly due to scar rupture. In a report from one institute, the incidence of uterine rupture in patients with prior caesarean delivery undergoing a trial of labour was 0.8 percent[9] and were similar to other studies also[10,11,12]. In this series 4 hysterectomies were performed for scar rupture with patients in labour giving an institutional incidence of hysterectomy of 6.45% for such patients. Most of our patients with prior caesarean birth are delivered by repeat caesarean section and practice of trial of labour is very limited. This is because majority are non-booked patients in labour, referred to our hospital with considerable delay, record keeping is poor and details of history of previous labour and operations are not available. Workload pattern of the hospital is also important. Moreover most patients with uterine scar rupture are usually treated by simple repair of the defect and expectant observation.

In our series 11 peripartum hysterectomies were performed for the management of postpartum haemorrhage giving an institutional incidence of 17.74% for such patients.

Other studies demonstrated more or less the same distribution varying from 21 to 28.57 percent[2,3]. From the literature review, there was a decreasing proportion of hysterectomies being done for uterine atony when compared for those performed in the past[1,2,13]. This may be due to the better pharmacological and surgical maneuvers (Pharmacological-administration of oxytocin, methergin, and prostaglandin F2 and surgical maneuver includes ligation of internal iliac arteries, B-Lynch technique, oversewing of the placental bed etc.) used in attempt to control haemorrhage [14,15]. In our series, in 8 cases, uterine atony occurred due to prolonged obstructed labour, one with abruptio placenta, one with secondary postpartum haemorrhage and one developed atony after vaginal birth.

Postpartum haemorrhage still remains a nightmare for the obstetricians. Out of 11 cases for which peripartum hysterectomy was done for the management of postparturm haemorrhage, 7 patients died contributing 63.64% of total case fatality. This figure is much higher than the case fatality due to ruptured uterus (27.27%). This indicates that although hysterectomy is done often as a life-saving procedure for the management of intractable postpartum haemorrhage and of course it is the last choice, recovery of the patients depends not only on the judicious and timely decision but also on various other factors. These factors include haenlodynamlc status of patients (reversible or irreversible shock), pre-existing anaemia, time lapse to bring the patients to the appropriate facility, time interval between the initiation of conservative management and performing hysterectomy, postoperative care and management etc.

In this series death due to PPH for which hysterectomy was done were analysed. Five patients developed PPH due to uterine atony following caesarean section for obstructed labour. Out of these 5 patients, 3 patients died between 9th to 14th post-operative days for septicaemia. Two patients died within an hour of operation due to poor recovery with irreversible shock. Each of these cases decision of hysterectomy was taken in the same sitting of caesarean section. The patient who died due to PPH following normal vaginal delivery, about 2 hours time was lapsed before operation to take the decision and for initial conservative management. Moreover patient needed relaparotomy for intraperitoneal haemorrhage and developed DIC (Disseminated Intravascular Coagulation). She expired 4 hours after operation. Another patient developed uterine atony for abruptio placenta and died 36 hours following operation due to renal failure.

From this discussion it has been revealed that timely decision, patients status, skillful operation technique, and proper postoperative management each critically determines the outcome. A definite guideline will help the practicing obstetricians to take this critical decision and further study is recommended in this field.

The association of placenta previa and prior caesarean delivery with placenta accreta and the risk of hysterectomy is well documented in the literature [16,17,18]. Neilson et al reported that the patients with placenta previa and scarred uterus has 16% risk of undergoing caesarean hysterectomy compared to 3.6% in patients with unscarred uterus[18]. Placenta accreta or pcrcreta were the leading cause of hysterectomy in many series[1,3] ranging from 38 to 64 percent. Clark et al [13] and Thonet [19] reported that 44% and 52% of cases of gravid hysterectomy, respectively had one or more prior caesarean sections and 5% to 32% of women with peripartum hysterectomy had documented placenta previa[19]. Considering that, on average placenta previa is present in 2.82% of deliveries at our hospital but contributed only 3.23% of all peripartum hysterectomies (only 2 cases-one with previous caesarean

scar and morbid adhesion and another without scar with profuse haemorrhage from placental bed). Further study is recommended to find out the risk in our population for that causal factor.

In general morbidity of emergency peripartum hysterectomy is higher than the elective one and so also the intraoperative complications, which is 4 to 5 times more common in emergency than elective cases[20]. It is associated with considerable morbidities and overall morbidity was reported in the range of 30 to 40 percent[21]. In our series there was 83.8% morbidity rate and most of them were febrile morbidity (defined as oral temperature of 38°C or more on two occasions, at least 4 hours apart, excluding the day of surgery[5]; but other serious complications were also demonstrated.

Maternal mortality rate varies from 1.4% to 26.2% in different series with a relatively high rate in some developing countries[22,23]. In our series the case fatality rate was also high (17.74%) and the commonly identified causes were massive haemorrhage with shock, septicaemia, DIC embolism and renal failure.

Conclusions :

The decision to perform emergency peripartum hysterectomy is usually difficult because of obstetricians' paramount wish to preserve the uterus for future childbearing. In this series two major indications were identified for a developing country like ours - ruptured uterus and uterine atony with postpartum haemorrhage. Reported intraoperative and postoperative complications underscore the need for early and prompt intervention and critical care management. In our institute, the overall management of a patient undergoing peripartum hysterectomy often includes a collaborative approach involving obstetricians, anaesthesiologists trained in intensive care medicine. Although uterine rupture was the major cause in our series, 25'% of our patients had no such indication or prior caesarean section. Therefore the practicing obstetrician must be prepared even in a low risk settings for performing emergency peripartum hysterectomy as it remains a potentially life saving procedure in unavoidable catastrophe.

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Writing a Scientific Report

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Scientific information, facts and findings must be continuously disseminated to the scientific community for onward development of science. The best way of dissemination is through publication of results of scientific/ clinical studies in relevant journals or presenting ,the results in some clinical conference or congress. Without written documents/records, knowledge is likely to be lost as rapidly as it is gained: In fact, without publication, science is dead.

Though human beings have been able to communicate for thousands of years, but scientific communications are, relatively new. First scientific communications in a modern format were made in 1665 following the publications of two journals- "The Journal des Scavens" in France and the other "The Philosophical' transactions of the Royal Society of London, UK". Since then, journals served as the primary means of communications in science. The scientific communications at that time were not well organized and systematic. The writings were almost "descriptive". This descriptive style was appropriate for the kind of science being reported at that time, the "straight forward style". This straightforward style of scientific reporting is still used today in some cases, like "letter columns" of the editors. By the second half of the 19th century, science was beginning to move fast, following the pioneering work of Louis Pasteur who confirmed the "germ theory" of diseases and who developed "pre-culture" methods of studying microorganisms. The development of Louis Pasteur's work, in fact, led to, a great advancement in science as well as revorting science During the following years, the methodology became more important and Pasteur felt that it was necessary to describe his experiments in a methodological way so that others can easily understand and reproduce. This endeavour of Pasteur led to the development of highly structured format for writing scientific report-the "IMMRAD". This includes Introduction, Materials & Methods, Results and Discussion[1].

While writing scientific reports, this classical structured format is generally followed everywhere. To be eligible for publication in a scientific journal, a study report must be written in this defined format and fulfill certain criteria. The purpose of this article is to discuss this special structured format of writing a scientific report.

Introduction :

This is the first section in a scientific writing. The purpose of writing introduction is to introduce the research work being undertaken to the readers. It should be written with considerable care with two major objectives in view: introducing the problem in a suitable context and arousing or stimulating the reader's interest. If the introduction is dull, aimless, confusing, rambling and lacking in precision, direction and specificity, there will be little interest for the readers to continue reading. The introduction must contain a clear statement of the objectives of research, i.e. enough background information to make clear to the reader why the problem is considered worth investigating. Here other related and relevant research works should also be stated so that the present study i.e. the study being undertaken can be seen in that context. The "hypothesis" of the study, if any, and definition of the major concepts employed in the study should also be stated in the introduction. The introduction, in fact, takes the reader through the process. of reviewing the background information, existing

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lacunae, precise aims and objectives of the study being undertaken and its justification or the need of the study. The research aims and objectives are normally summarized by few sentences allowing sufficient spaces for the study design and methodology, observations and results, discussion, and valid conclusions and recommendations[2].

Now, one can question, what should be the length of the introduction? For shorter written assignments, the introduction should be written in about 2000 to 3000 words. For larger papers or thesis or dissertation, the introduction may lie in chapter length. In any case, the introduction should contain the following:

- A lucid, complete and concise statement of the problem or the general purpose of the study being undertaken.
- A rationale or justification of the study emphasizing the need and , importance of the problem being investigated.
- The "hypothesis"; if any.
- Review of other related and relevant research works pertaining to the present study. The existing lacunae of the study.
- And finally, the precise aims and objectives of the study being ' undertaken. '

It is to be remembered that there should be a good beginning to get a good ending. On the contrary, a bad beginning is likely to make a bad ending[1].

Much of the introduction should be written in present tense because one will be referring primarily to his or her problem and establishing knowledge relating to it with others' study which has relevance to the present study. However, the following four key-points are to be considered for good introduction :

- The introduction in a scientific writing should appear first with all possible clarity, nature and scope of the problem being investigated.
- It must review the pertinent literature for the orientation of the reader. Here references should carefully be chosen to provide the most important background information.
- Wherever possible, the introduction should have a predefined "hypothesis" related to the work being undertaken.
- It should have clear aims and objectives.

It is to be reemphasized that the purpose of "introduction" is to introduce the research/ study to the readers. Therefore, the above mentioned points are key elements which should be described to set a "good introduction".

Reading a scientific article is not the same as reading a detective story. The readers should not be kept in suspense, which is always found in a detective novel[1]. Here, the readers want to know from the very start about the work that has been undertaken by the investigators. Thus, the writing of the introduction should be done in such a way that the sequence of events must follow in order so that the readers can easily understand the theme of the study. Furthermore, it is likely that members of other speciality may read the research paper. Therefore, the introduction is the proper place to define any specialized terms or abbreviations, which are intended to be used in the paper.

Materials and Methods :

The methodology adopted in conducting the study must be fully explained. The scientific readers would obviously like to know in details about things like: how was the study carried out? What was its basic design? If the study was an experimental one, then what were the experimental manipulations? If the data were collected by means of questionnaire or interviews, then exactly what questions were asked? (The questionnaire or interview

schedule is usually given in an Appendix). If the measurements were based on observations, then what instruments were given to the observers?' However, this section should begin with a description of the type, place and duration of the study, the materials used in the study, the overall study design, characteristics of population and sample size, sampling technique, operational definitions, measures of outcome- variables, methods of data collection and data analysis, type of statistical tests used, etc. All these should be described in details and elaborately so that the same thing can be reproduced if repeated.

In other words, writing of this section should be self-explanatory. Most of this section should be written in past tense. For materials used, exact technical specifications and quantities, source, methods of preparation etc. should be described. Sometimes it is necessary to describe the pertinent physical and chemical properties of the chemicals and reagents used in the study. The generic or the chemical name should be used, because the generic or nonproprietary name is likely to be known throughout the world. One can also write the generic name first, followed by the trade name in brackets. Experimental animals, plants or microorganisms used in the study should be identified accurately by genus, species and strain designations. In case of clinical study where human volunteers are used, criteria for their selection and exclusion, demographic characteristics such as, age, sex, socio-economic status, occupation etc. should be described.

From ethical point of view and to comply with "Helsinki Declaration" or "Good Clinical Practice (GCP)" guidelines, informed consent, preferably in writing and other regulatory requirements described in the guidelines should be taken into consideration so that human rights are not violated, the subjects are legally protected and the results obtained are credible and accurate. Furthermore, for a method which is well established and published, there is no need to describe the methodology in details. In this case, one can refer to the publication. As for example, blood glucose was estimated according to the modified method described by Nelson and Somogyi (1952). But in case of a new and 'unpublished method, it needs to be described in greater details either in the methodology section or separately at the Appendix.

For methods, the usual order of presentation should be chronological, but the related methods should be described together. Sometimes straight chronological order cannot always be followed. For example, even if a particular assay was not done until late or advancement in research, the assay method should be described along with other assay methods not by itself in a latter part of the materials and methods. Sometimes for a method used in the study, its accuracy, specificity and sensitivity are required to know. These should also be described in the materials and method section.

The materials and methods should be described under sub-headings, as required. The sub-headings should "match" those to be used in the "result" section. The measures of outcome variables or the outcome measures both qualitative and quantitative should be described. It is to be remembered that the outcome measures or the study parameters are the key elements in obtaining the desired information from the study undertaken. Therefore, these have to he measured accurately and carefully. Finally, the methods of data collection and plan for data analysis should be described. The statistical tests used should also be mentioned here. Now a days, computerized programs for "Statistical Package for Social Science (SPSS)" are available. They can also be used.

Results :

The detail presentation of the facts, findings and figures derived from the study undertaken, i.e. data, constitute the result

section. This is in fact, the "core" of the study. The results should be presented in tables, charts, graphs or diagrams, etc. This generally constitutes the main body of the report extending over several pages. All the results should be described in past tense. No part of the method should be described here. The results, either qualitative or quantitative should be presented in a systematic way and in logical sequence. The relevant part of the results must find a place where appropriate in the report. Numerical data should be presented in appropriate tables and charts. It is always convenient to split the results into easily identifiable sections. Statistical comparisons or statistical tests to determine the level of significance should also be stated here. As already mentioned above that the "core" of the scientific study is the "data" or the "results" . Therefore, these need accurate and careful presentation.

There are usually two ingredients of the "result" section. First, some kind of overall description of the experiments or the study without describing the materials, and methods. Second, the actual data, which should be presented in a systematic way. Only the facts, findings and figures should he stated here simply and clearly, because it is the result or main outcome of the study that contributes new knowledge in the relevant field of science.

The earlier parts of the report i.e. introduction, materials and methods are designed, to tell why and how the results are obtained. The latter part i.e. "discussion" (vide infra) is designed to tell what they mean. In fact, the whole study must stand or fall absolutely on the basic of the results obtained in the study. Repetition of words or statements should be avoided. Any verbose, i.e. using more words than are needed should also be avoided[1]. Thus, it is advisable not to be verbose 'in citing figures and tables. As for example, it is not to be stated like " it is clearly shown in table-I that ciprofloxacin inhibited the growth of N. gonorrhea" Rather it should be stated like, this-" ciprofloxacin inhibited the growth of N. gonorrhea (Table-I)." There should, be an accountability of the tables, figures; charts or diagrams, etc. Tables and figures must have a legend, i.e: "title" and tables should be numbered by giving Roman letter, while figures should be given Arabic numerals. No part of the works done by others should be stated in the result section of the study being undertaken. It is important to remember that the results, which answer the questions of the purpose of the study, should be emphasized. The results, which are not relevant to the study should be excluded. Furthermore, the, results that contradict the "hypothesis" which has been formulated in the study must not be suppressed; otherwise it will be unethical. These will have to be included and discussed. The readers should freely be allowed to assess the findings of the study.

Discussion :

The "discussion" section in a scientific writing is the most difficult, harder and critical part than any other section. Many papers are either rejected or not accepted by editors of journals if the ' "discussion" is faulty or inadequate, even if the results of the study are scientifically valid and interesting. The, true meaning of the study sometimes gets completely obscured by faulty discussion and interpretation. It has been observed in reality that in many occasions, the "discussion" is either too long or too verbose: As a result, the readers lose their interests and remains in a dilemma, which should not be the case and thus, the reading of the article remains incomplete. Therefore, the "discussion" section should be written carefully, precisely and concisely.

It is to be remembered that in the "discussion" section, the authors answer the general question: "What the findings of the study really mean and how they correlate with the existing knowledge?"' A useful way to open the "discussion" is to use the end of

the "introduction" as the starting point. Before opening of the discussion it is better to review and highlight the nature and purpose of the study along with the main aims and objectives one more time so that the readers remain in the right sequence. After that the authors should discuss their study findings in a qualitative manner, i.e. the facts and findings of the study undertaken should be described in languages. No quantitative data, tables or figures, which have already been described in the result section, should be mentioned here. Then the results of the present study should be strengthened, by citing the previously published relevant studies available in the literatures. These may either agree (i.e. positive findings) or disagree (i.e. negative findings) with the present study. The possible reasons for disagreement, if any, with the present study should also be discussed. In other words, interpretations of the results of the present study both in favor and against on the gathered information obtained should carefully be discussed. It is advisable not to emphasize boldly or with great confidence" on the present findings; rather they should be discussed in an "optimistic" way.

A "discussion" is said to be good when it describes its own results and correlates the results with others, which have been published. It is important to remember that even a negative finding which goes against a proposed "hypothesis" is considered valid if it is, presented scientifically. Every scientific study is a contribution towards increasing understanding of the new knowledge or existing knowledge on a particular subject and may lead to some new clue for further research. Furthermore, any limitations, constraints, difficulties, bias or any error that have been experienced with the present study should also be discussed so that others can solve those. It is always customary that the "discussion" ends with a short summary and conclusion derived from the study. Similarly, recommendation:, if any, can also be mentioned Here. The conclusion should include a brief summary of the research problem, the methodology and the major findings obtained from the study. As already pointed out that many people lose much of interest and climax if the scientific writing is not discussed adequately. Finally, it is again reemphasized here that any verbose language and faulty technical words should be avoided.

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REVIEW ARTICLE (J Bangladesh Coll Phys Surg 2002; 20 : 81-97)

Reperfusion Strategies in Acute Myocardial Infarction-Current Status, Recommendations and New Horizons

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Coronary arterial occlusion due to thrombosis is the cause of most cases of acute myocardial infarction (AMI) accompanied by ST-segment elevation. Rapid restoration of blood flow to jeopardized myocardium limits necrosis and reduces mortality. This can be accomplished medically, with a thrombolytic agent, or mechanically, with so-called primary balloon angioplasty or stenting[1-3]. The best way to accomplish reperfusion in patients with evolving AMI continues to be debated, although there is strong agreement that very early reperfusion must be accomplished to preserve myocardium. In addition normal or nearly normal flow TIMI-3 (TIMI stands for Thrombolysis in Myocardial Infarction and is measure of epicrdial blood flow in the artery; TIMI-3 is a normal flow to the heart) must be established in the infarct related vessel to provide optimal reduction in morbidity and mortality[4]. Thrombolytic therapy is widely available and effective, but its use is sometimes associated with bleeding complications. In 10 to 15 percent of patients who receive a thrombolytic agent, clot lysis is not achieved. Only half the patients in whom antegrade coronary flow is restored have normal flow, and in a small number of these patients, occlusion recurs before discharge from hospital. Intravenous thrombolytic therapy is the standard care for patients with AMI, based upon its widespread availability and ability to reduce patient mortality well demonstrated in randomized trials. Despite its proven efficacy, thrombolytic therapy has its limitations. Many patients are ineligible for treatment with thrombolysis. Of those given thrombolytic therapy, 10 to 15 percent have persistent occlusion or reocclusion of the infarct-related artery. Consequently, primary angioplasty has been advocated as a better treatment for AMI[3]. Intravenous thrombolytic therapy, when applied in the first 1 to 2 hour after the onset of AMI, also yields good results, but despite the development of many new thrombolytic agents, there remains a relatively high incidence of intracranial haemorrhage[5].The early and long-term results of primary percutaneous transluminal coronary angioplasty (PTCA) have been demonstrated to be excellent when carried out in an experienced laboratory by expert interventionists[4-6].

No treatment has had more profound impact on the global management of patients with acute ST-segment elevation myocardial infarction than thrombolytic therapy. Recognition that acute coronary thrombosis is primary to the pathogenesis of AMI led to the consideration of plasminogen activators

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as a preferred therapeutic approach to achieve rapid thrombolysis. All of the thrombolytic agents currently available and under investigation are plasminogen activators. They all work enzymatically, directly or indirectly, to convert the single chain plasminogen molecule to the double chain plasmin which has potent intrinsic fibrinolytic activity[7]. Aside from this similarity, however, there are many differences among these agents in dose, circulating half-life, fibrin specificity, rates of coronary recanalization, risks of intracranial haemorrhage and cost. Streptokinase remains the most common thrombolytic agent used globally. It is usually used as a short-term infusion of 30 to 60 minutes in doses of 1. 5 megaunits and has a plasma elimination half-life in man of 20 minutes[6]. Within a few days, anti-SK titre rapidly rises to 50 to 100 times the preinfusion level, remaining there for many months or even years. This makes repeated administration impractical except very early after initial dosing. Anisoylated plasminogen streptokinase activator complex (APSAC) or anistreplase was the first bolus thrombolytic agent developed. Given in a dose of 30 U, its plasma half life is 90 minutes and it produces a similar fall in fibrinogen and increase in neutralizing antibody equivalent to streptokinase.

Urokinase is a naturally occurring 2-polypeptide chain plasminogen activator derived from human urine and human kidney cells in culture. It produces extensive fibrinolysis, is nonimmunogenic, and has achieved coronary patency rates approximating that of streptokinase[6]. Streptokinase and urokinase are approved for intracoronary use, but this route of administration for AMI is now virtually obsolete[8]. rt-PA (alteplase), a fibrin specific plasminogen activator has high affinity for plasminogen in the presence of fibrin. The recommended dose of rt-PA for the treatment of AMI is 100 mg administered "front loaded" starting with a bolus of 15 mg followed by 50 mg in the next 30 minutes and the remaining 35 mg in the following hour[6]. The GUSTO (Global Utilization of Streptokinase and TPA for Occluded Arteries) trial conclusively demonstrated that rt-PA, a fibrin selective molecule, was superior to streptokinase, a non-fibrin selective agent, for both early and 1-year mortality reduction[9]. The angiographic substudy of GUSTO also demonstrated an important relationship between the establishment of early coronary patency and survival[9]. Recently Gulba et al demonstrated that a 60-minute rt-PA infusion in an open-labeled, nonrandomized study yielded an 81% TIMI 3 patency at 90 minutes[10]. Another significant tPA variant is the triple-substitution mutant tenecteplase (TNK-tPA). 30 to 50 mg of weight adjusted TNK-tPA was compared with accelerated rt-PA and revealed virtually identical 30 day (6. 18% for TNK-tPA; 6.15% for rt-PA) and 1-year mortalities[11]. Although there were fewer systemic bleeding complications and reduced requirement for blood transfusion with TNK-tPA, intracranial haemorrhage rates remained higher than desirable in both treatment arms, i.e, 0. 93% for TNK-tPA and 0. 94% for rt-PA[11]. Lanoteplase, a novel plasminogen activator (nPA) is a deletion mutant of rt PA. In TIME-2 trial 120 kU/kg dose was compared with accelerated rt-PA. Although the 30-day mortality rates for nPA (6. 77%) and rt-PA (6. 60%) were similar, there was an unacceptable excess of intracranial haemorrhage with nPA (1.13% versus 0. 62%) and an increase in the composite of mild to moderate bleeding with nPA (22% versus 17%) [12]. Staphylokinase (SAK) is a protein produced by selected strains of staphylococcus aureus, is known to have fibrinolytic properties. Promising TIMI 3 patency ie >60% at 90 minutes with a bolus and 30-minute infusion of SAK, has been observed without systemic fibrinolysis[13,14].

Comparative Thrombolytic Efficacy

The primary goal of thrombolysis is rapid, complete and sustained restoration of blood flow through the infarct related artery to salvage left ventricular muscle tissue, limits the size of the infarct and improves the chances of survival. Patients presenting with either ST elevation or new-onset left bundle branch block within 12 hours of the onset of ischaemic symptoms should receive reperfusion therapy by means of thrombolytic therapy or percutaneous revascularization[15]. Since publication of the first guidelines for the early management of patients with AMI results of important trials comparing thrombolytic regimens directly have been published, evaluating relative rates of coronary patency, functional benefit and survival. In two large mortality trials GISSI-2 (Gruppo Italiano per lo Studio della Soprayvivenza nell'Infarto Miocardico) and ISIS-3 (Third International Study of Infarct Survival), mortality rates at 4 to 5 weeks were similar (GISSI-2 :TPA =8.9%, streptokinase=8. 5%;ISIS-3: alteplase=10. 3%, streptokinase=10. 6%, anistreplase=10. 5%)[16,17].The GUSTO trials subsequently tested four thrombolytic regimens among 41,021 patients. Alteplase was given in an accelerated dose regimen to further improve early patency and concomitant heparin administered intravenously to maintain patency. Other regimens included streptokinase with subcutaneous or intravenous heparin and a combination of alteplase and streptokinase. Thirty-day mortality was lower with alteplase (6.3%) than streptokinase and subcutaneous heparin (7.2%), streptokinase and intravenous heparin (7.4%) and combined streptokinase and alteplase plus intravenous heparin therapies (7.0%). There was a significant excess of haemorrhagic stroke for accelerated alteplase and the combination strategy compared with streptokinase only. However, net benefit was still achieved with alteplase compared with streptokinase, with 9 fewer deaths per 1000 patients treated[18].The mechanism of improved benefit with alteplase was assessed in the GUSTO angiographic substudy, which found differences in early (90-minute) patency among regimens (81%, 56%, 61%, 73%) for alteplase, streptokinse-subcutaneous heparin, streptokinase-intravenous heparin and combinations regimens, respectively[19].

The Food and Drug Administration has approved the thrombolytic agent reteplase for use. Reteplase, a mutant of wild-type tPA, has a longer half-life than its parent molecule and has been compared with alteplase in a large clinical trial. An angiographic trial found that 60 and 90 minute TIMI grade flow and coronary patency rates were higher with reteplase than with the accelerated infusion of alteplase. When compared with an accelerated infusion of alteplase, reteplase did not provide any additional survival benefit. The mortality rate at 30 days was 7. 5% for reteplase and 7. 2% for alteplase; and the rates of the combined end point, death or nonfatal MI, disabling stroke were 7.98% and 7.91% respectively[20]. In addition to alteplase and reteplase, newer agents have been developed (eg, TNK-tPA and lanetoplase).Recent trials with alteplase have used an accelerated regimen given over 90 minutes. The accelerated regimen leads to the highest patency rate without an increase in intracranial haemorrhage and has become the preferred method of administration. The advantage of reteplase is that it can be given by bolus, which is convenient[21].

Current use rates of Thrombolytic agents

National Registry of Myocardial Infarction (NRMI-2) tracks the use of thrombolytic therapy in the United States and has enrolled 330,928 patients treated at 1470 US hospitals.Barron at al recently reported an analysis of this database, attempting to determine what proportion of patients with an AMI who are eligible for reperfusion

Table-I

Contraindications and cautions for Thrombolytic use in AMI

Contraindications:

Previous haemorrhagic stroke at any time, other strokes or cerebrovascular events within 1 year.
Known intracranial neoplasm
Active internal bleeding (does not include menses)
Suspected aortic dissection

Caution/relative contraindications:

Severe uncontrolled hypertension on presentation (blood pressure >180/110 mm of Hg)
History of prior cerebrovascular accident or known intracerebral pathology not covered in contraindications.
Current use of anticoagulants in therapeutic doses (INR >2)
Known bleeding diathesis
Recent trauma (within 2-4 weeks) including head trauma or traumatic or prolonged (>10 min) CPR or major surgery (3 weeks).
Noncompressible vascular punctures
Recent (within 2 to 4 weeks) internal bleeding
For streptokinase/anistreplase:prior exposure (especially within 5 days-2 years) or prior allergic reaction
Pregnancy
Active peptic ulcer
History of chronic severe hypertension.

(From J Am Coll Cardiol 2001; 37(8) : 2230)

therapy do not receive this proven treatment. Baron used a conservative definition of thrombolytic eligibility (diagnostic changes on ECG or LBBB <6 hours after onset of symptoms and no contraindication to thrombolytic therapy indicated) Investigators found that 31% of their cohort were eligible for reperfusion therapy; 5% had nondiagnostic initial ECGs; 41% presented >6 hours from onset of symptoms and 3% had contraindications to thrombolytic therapy (22).Of those who were eligible for thrombolytic therapy, 24% did not receive any form of reperfusion therapy (7.5% of all patients).Multivariate analysis revealed that the independent predictors for eligible patients not being given reperfusion therapy were the presence of LBBB, the disappearance of chest pain at the time of presentation, age>75 years, female gender and various pre-existing cardiovascular conditions. Perhaps most disconcerting was the finding that patients with the highest risk of death from AMI were the least likely to receive reperfusion therapy (patients with a history of congestive heart failure or the presence of LBBB).Both groups had an in-hospital mortality rate of 20%,well above the mortality rate of 7.9%, yet the presence of LBBB made it 78% less likely that a patient would receive reperfusion therapy than patients who presented with ST-segment elevation[22].

In patients younger than 65 years, overall usage of thrombolytic therapy ranges between 40% and 50%.In those older than 65 years, the overall use rate is below 20% and should be higher. Some increase in the use rates probably can be achieved but contraindications prohibit a vast increase in use rates[23].

Considerations in Selecting Thrombolytic Regimens

The weight of data from the large randomized trials indicate that it is more important to decide whether to give thrombolytic agents than which agent to give.Although GUSTO suggests that accelerated rt-PA offers a small survival benefit over streptokinase (SK), SK is 20 fold less expensive. The cost effectiveness of routinely using rt-PA therefore remains an issue[24-26]. That is why streptokinase is the most widely used thrombolytic agent worldwide.

GUSTO-1 and GUSTO-III and other recent studies suggest that accelerated alteplase and reteplase with intravenous heparin are currently the most effective therapies for achieving early coronary reperfusion but both are substantially more expensive and carry a slightly greater risk of intracranial haemorrhage than SK[21].

Thrombolysis –Prehospital issues

Several studies have reported results of trials of thrombolytic therapy initiated before hospital admission. Most have been designated to evaluate time savings, resulting left ventricular function, infarct size and mortality differences in patients treated in the prehospital setting as compared with in-hospital treatment. The largest trial, the European Myocardial Infarction Project (EMIP), was carried out in 15 European countries and Canada. Anistreplase was given as a bolus in the prehospital setting to 2,750 patients and their outcomes were compard with those of 2,719 patients treated in the hospital. Total mortality was reduced by 12% and cardiac mortality by 16% in prehospital treated versus hospital treated patients[27]. These issues were also evaluated in The Grampian Region Early Anistreplase Trial (GREAT) and in The Myocardial Infarction Triage and Intervention trial (MITI). In the meta-analysis of the three major trials, there was a significant reduction in the mortality among patients randomized to prehospital therapy. It was estimated that the benefit-time gradient at 35 days was 21 lives saved per thousand patients treated[27]. These trials have suggested that when long delays of 60 to 90 min or greater are routine, then prehospital initiation of thrombolytic agent should be considered.

In CAPTIM study (Comparison of Angioplasty and Prehospital thrombolysis in Acute Myocardial Infarction) whether primary angioplasty is better than prehospital

Table-II

Pharmacology of the Thrombolytic agents for treatment of AMI

Property	Alteplase	Saruplase	Reteplase	-tPA	Lanoteplase	SAK
Dose	100 mg/90 min	80 mg/60 min 30 min apart	2X10 IU bolus bolus	0.5 mg/kg	120 IU/kg bolus	5mg bolus
Fibrin Specificty	++	+/-	+	+++	+	+++(+)
Antigenicity	—	—	—	—	—	+
90-min patency	+++	+++	++++	+++(+?)	++++	+++(+?)
Mortality reduction	++	+(+)	++	++	?	?
Haemorrhagic stroke	++	++(+)	++	++	+++	?
Clinical development	Established Standard	Not approved	Approved for general use	FDA approved Likely to replase rt - PA	Not further developed	Phase 2 ongoing

+ signs is proportional to efficacy,extent or frequency

From Armstrong PW.Circulation 2001;103:2863.

thrombolysis was evaluated[28].The median delay between onset of symptoms and treatment was 130 min in the prehospital-thrombolysis group and 190 min (time to first balloon inflation) in the primary angioplasty group.The rate of the primary end points (death,non-fatal reinfarction and non-fatal disabling stroke at 30 day) was 8.2% in the prehospital thrombolysis group and 6.2% in the primary angioplasty group[28].The ER-TIMI-19 (The Early Retavase-Thrombolysis In Myocardial Infarction) trial was designed to test the feasibility of prehospital initiation of the bolus-thrombolytic reteplase (rPA) and to evaluate the time saved by prehospital administration of rPA. By 30 minutes after first medical contact,49% of study patients had received the first bolus of thrombolytic agent compared with only 5% of controls.Prehospital administration of rPA appears to be a feasible approach for accelerating reperfusion in patients with AMI.Valuable time savings can be achieved in the settings of contemporary transport and door to drug times and may translate into an improvement in clinical outcomes[29].

Given the critical relationship between the time to successful reperfusion and outcomes in the treatment of patients with AMI, the potential advantages of prehospital administration of thrombolytic therapy have a sound theoretical basis. However, despite consistent evidence that prehospital thrombolysis reduces time to treatment and meta analysis of results from randomized trials that suggests improved survival,a number of barriers have hindered the widespread development of prehospital thrombolysis program.The complexity of administering thrombolytic agents those require weight adjusted continious infusions may have limited their use in the field[30,31].

Thrombolytic resistance-Role of Glycoprotein IIb/IIIa inhibitors

Although thrombolytic therapy is a mainstay of treatment for AMI it has well documented limitations.With current thrombolytic regimens,patency is restored in 60% to 85% of patients with AMI and only 54% to 60% of patients achieve full myocardial reperfusion,angiographically defined as TIMI-3 flow in the infarct related artery[32]. In addition reocclusion or reinfarction or both occurs in roughly 30% of patients by three months which is associated with increased mortality.Finally thrombolytic therapy is associated with increased risk of bleeding complications,including intracranial haemorrhage which ranges from 0.5% to 0.9% in major randomized trials[32].

To address these limitations,newer thrombolytic agents have been developed that result in higher rates of early coronary artery patency and lower rates of bleeding complications. In addition reduced dose of thrombolytic agent in combination with the administration of a potent antiplatelet agent (glycoprotein IIb/IIIa inhibitors) restores antegrade flow as effectively as full-dose thrombolytic therapy but associated with lower rates of reocclusion and reinfarction .

The results of GUSTO V, TMI-14, SPEED (Strategies for Patency Enhancement in the Emergency Department) and ASSENT-3 (The Assessment of the Safety and Efficacy of a New Thrombolytic Regimen) suggests that low dose thrombolytic agents along with standard dose of glycoprotein (GP) IIb/IIIa inhibitors enhances reperfusion after AMI[33-36].

In GUSTO-V Trial 16588 patients with evolving AMI were randomly assigned for standard dose of reteplase or half-dose reteplase and full dose abciximab. The primary endpoint was 30 day mortality and secondary endpoints included various complications of MI. At 30 day 5.9% patients in the reteplase group had died compared with 5.6% in the combined reteplase and abciximab group[33]. Although combined reteplase and abciximab was not superior to standard reteplase in reduction of overall mortality,combination therapy led to a

Table-III

Mortality rate in AMI : Thrombolysis versus PCI (Results from a meta analysis)

Variable	Primary PCI	Thrombolysis
Anterior Infarct	8%	15%
Age >70 years	13%	24%
Previous MI	10%	23%
Diabetes	9%	19%

From Hutter AM et al. J Am Coll Cardiol 2000; 35 : 852

consistent reduction in key secondary complications of AMI including reinfarction. 346 patients with AMI were enrolled in TIMI-14 trial. The patients were treated with either tPA alone or abciximab plus reduced dose tPA (combination therapy). Patients receiving combination therapy had a 59% rate of complete ST resolution at 90 minutes versus 37% in those treated with tPA alone[34]. SPEED trial documented low dose reteplase with standard dose abciximab enhances reperfusion 90 minutes after AMI compared to reteplase alone[35].

One of the main concerns in considering combination therapy of a thrombolytic agent and a potent antiplatelet agent is bleeding in particular intracranial bleeding. A meta analysis of three randomized trial showed that GP IIb/IIIa inhibitors produce no increase in intracranial bleeding[32]. Accumulated experience with GPIIb/IIIa receptor inhibitors has shown a very low associated incidence of intracranial bleeding from 0.09% to 0.2%[32]. There is strong rationale, both clinical and physiologic, for combining the potent GPIIb/IIIa receptor inhibitors with thrombolytic agents in AMI[32,37].

Low molecular weight heparin in AMI with thrombolysis

Low molecular weight heparin is also actively being studied in the setting of AMI with or without thrombolytic therapy. One study documented that following thrombolytic therapy,a 4 day course of enoxaparin led to a significant reduction in the rate of death,myocardial infarction or readmission from acute coronary syndrome compared with unfractionated heparin. The rate of the composite end-points at 3 month was 36.4% for heparin vs 25.5% for enoxaparin[38]. With regard to early reperfusion one study found a slight improvement in early TIMI grade 3 flow with enoxaparin following t-PA, 53% vs 48% for unfractionated heparin,but a greater effect on reducing reocclusion 5.9% vs 9.8%[39]. In streptokinase treated patient TIMI-3 flow tended to be higher in patients treated with dalteparin 68% vs 51% and number of ischaemic episodes on continuous ECG monitoring was lower 16% vs 38%[40] .

The role of enoxaparin as an adjunct to thrombolytic therapy was evaluated in ASSENT-3 trial.6095 patients with AMI were randomly assigned to one of three regimens:full dose tenecteplase and enoxaparin for a maximum of 7 days, half dose tenecteplase with weight adjusted low dose unfractionated heparin and 12 hour infusion of abciximab or full dose tenecteplase with weight adjusted unfractionated heparin for 48 hours. There were significantly fewer efficacy endpoints in the enoxaparin and abciximab group. Both new antithrombotic regimens showed a reduction in the combined end points of 30-day death, myocardial infarction,recurrent ischaemia or major bleeding (17.0% unfractionated hepain,13.7% enoxapain and 14.2% abcixima b).Although the rates of intracranial bleeding were the same for each group, there was a higher rate of major bleeding with

Table-IV

Efficacy of Enoxaparin in the treatment of Acute Myocardial Infarction

Reperfusion strategy	Outcome- triple end points (death, reinfarction, angina) at 30 days
Tenecteplase + Heparin	15. 4%
Tenecteplase + Enoxaparin	11. 4%
Streptokinase + placebo	21%
Streptokinase + Enoxaparin	13. 4%

From Eur Heart J 2002; 23 : 1285 and Lancet 2001;358:608.

abciximab. Thus, the most simple regimen appeared to have the best efficacy and safety profile-tenecteplase plus enoxaparin[36].

In AMI-SK study (Acute Myocardial Infarction –Streptokinase) showed that enoxparin and streptokinase restored normal coronary blood flow in the blocked artery by a relative increase of 22% vs streptokinase with placebo[41]. The study documented 36% relative risk reduction in the triple end points (death, reinfarction and recurrent angina) with enoxaparin.Overall,these results showed that the enoxaparin and streptokinase combination improves early reperfusion and late patency at day 5-10 over streptokinase with placebo. The triple clinical end-point of death, reinfarction and recurrent angina at 30 days was reduced with enoxaparin (13% vs 21%). In addition the combination group had fewer clinical events suggesting less reoccluion. Streptokinase and enoxaparin combination do not produce excess bleeding compared to streptokinase alone[41,42]. This is an important therapeutic advance because streptokinase is the most widely used thrombolytic agent worldwide. Current thrombolytic agents fail to achieve optimum reperfusion in many patients.Low molecular weight heparins and GPIIb/IIIa inhibitors have shown the potential to improve pharmacological reperfusion therapy.

Thrombolysis in elderly patients

The efficacy of thrombolytic therapy in elderly patients has not been evaluated to the same extent as it has been done in younger patients. Pooled data from the large clinical trials showed that the 35-day mortality of patients 75 year of age and older was 24.3% for those treated with thrombolytic therapy and 25.3% for the placebo group[43]. Recent analysis of the FTT (Fibrinolytic Therapy Trialists) data for the 3300 patients>75 years of age presenting within 12 hours with only ST elevation or Left bundle branch block reveals a mortality risk reduction from 29.4% to 26.0%[44].

Alternative to current thrombolytic therapy

One of the most animated debates in contemporary cardiovascular medicine relates to the relative merits of primary mechanical intervention as opposed to thrombolytic therapy for the management of AMI.Primary PCI (Percutaneous Coronary Intervention) has been considered in the American College of Cardiology/American Heart Association (ACC/AHA) guidelines in 1999 to be an alternative to thrombolysis. Since then 21 trials randomized more than 6800 patients,all of which show clear benefit of PCI over thrombolysis[45-50]). A meta analysis of the randomized trials carried out showed a clear reduction in mortality, recurrent MI, stroke,and intracranial haemorrhage. Mortality was reduced by 34% (6.5% for thrombolysis vs 4.4% for primary PCI),suggesting that 20 lives would be saved for every 1000 patients treated with primary PCI instead of thrombolytic therapy[50]. Non

fatal reinfarction was reduced nearly 50% (5.3% for thrombolysis and 2.9% for PCI) and intracranial haemorrhage was essentially eliminated (1.1% with thrombolysis and 0.1% with PCI). A more recent registry data show a benefit of primary PCI over thrombolysis. A study of more than 62000 thrombolytic eligible patients in the National Registry of Myocardial Infarction compared patients treated with primary PCI with those treated with thrombolysis[51]. Because hospital volume is an important marker of overall skill, experience and outcomes in performing primary PCI, patients were stratified into groups reflecting low, intermediate and high volume centers, based on primary PCI volume of the hospitals at which they were treated. At high volume centers in-hospital mortality was lower among patients treated with primary PCI (3.4%) than with thrombolysis (5.4%)-ie, 20 lives saved for every 1000 patients treated with primary PCI (52).Mortality at intermediate-volume hospitals was also lower for patients who received PCI than for those who received thrombolysis (4.5% vs 5.9%).At low volume hospitals, mortality was similar between thrombolytic treated and primary PCI treated patients (52,53). However across all hospitals, primary PCI had a safety advntage, with nonfatal stroke occurring in 0.4% vs 1.1% (52).A recently published meta analysis demonstrated that for every 1000 patients treated with primary PCI rather than thrombolysis, an additional 20 lives are saved, 43 reinfarctions are prevented,10 less strokes occur and 13 intracranial hemorrhage are avoided[45]. Recently, primary PCI has been shown to reduce the composite rates of death, reinfarction or stroke compared with tissue plasminogen activator even if patients must be transferred by ambulance for up to 3 hours to reach an intervention center[54].

Moreover, whereas the efficacy of pharmacological reperfusion has reached a plateau, the introduction of new devices, including coronary stents and the optimization of drug regimens during the angioplasty procedure has significantly improved the early safety profile and long term results of PCI in AMI (45,55).The primary PCI at experienced centers, is superior method of reperfusion for evolving AMI. This conclusion now stands on firm evidence despite the unavoidable delays from presentation to angioplasty inherent with mobilizing the team required for angiography and angioplasty, which averages nearly 2 hour in the USA (60-90 minutes in Europe)[53].

Primary PCI versus thrombolytic therapy wars:Results of current megatrials

C-PORT[56]

C-PORT (Cardiovascular Patient Outcomes Research Team) study, a randomized controlled trial compared primary PCI and thrombolytic therapy for treatment of AMI. Four hundred fifty one thrombolytic eligible patients with AMI of less than 12 hours duration associated with ST elevation were enrolled in the trial to determine whether treatment of AMI with PCI is superior to thrombolysis. The incidence of the composite end points was reduced in the primary PCI group at 6 weeks 10.7% versus 17.7% and at 6 months 12.4% versus 19.9%.Six-months rates for individual outcomes were 6.2% vs 7.1% for death,5.3% vs 10.6% for recurrent MI and 2.2% vs 4.0% for stroke for primary PCI vs thrombolytic therapy respectively. Median length of stay was also reduced in the primary PCI group (4.5 vs 6.0 days).

C-PORT trial concluded that compared to thrombolytic therapy, treatment of patients with primary PCI at hospitals without on-site surgery is associated with better clinical outcomes for 6 months after index AMI and a shorter hospital stay.

MITRA and MIR[57]

The clinical outcome of primary PCI and thrombolysis for treatment of AMI were investigated in MITRA (Maximal Individual

Table-V

Primary Angioplasty (PCI) versus Thrombolytic therapy in AMI : Analysis from 23 randomised Trials

Variable	Primary PCI	Thrombolysis
Death	7%	9%
Non fatal reinfarction	3%	7%
Stroke	1%	2%
Combined endpoint of death, non-fatal reinfarction and stroke	8%	14%

From Keeley EC et al. Lancet 2003;361:13

Therapy in Acute Myocardial Infarction) trial and from MIR (Myocardial Infarction Registry) .Of 10,118 lytic eligible patients with AMI,1385 (13.7%) were treated with primary PCI and 8,733 (86.3%) received intravenous thrombolysis. Hospital mortality decreased significantly in the primary PCI group compared to thrombolysis.

CADILLAC[58]

2082 patients with AMI were assigned to undergo percutaneous transluminal coronary angioplasty (PTCA) alone (518 patients), PTCA plus abciximab therapy (528), stenting alone with the Multilink stent (512) or stenting plus abciximab therapy (524).Normal flow was restored in the target vessel in 96.9% to 98.5% of patients and did not vary according to the reperfusion strategy.At six months,the primary end points- a composite of death,reinfarction,disabling stroke and ischamia driven revascularization of the target vessel had occurred in 20% of patients after PTCA,16.5% after PTCA plus abciximab,11.5% after stenting and 10.2% after stenting plus abciximab.At experienced centers,stent implantation with or without abciximab should be considered the routine reperfusion therapy for AMI.

Air PAMI[59]

Patients with high risk AMI who were eligible for thrombolytic therapy were randomized to either transfer for primary PTCA or on-site thrombolysis in The Air Primary Angioplasty in Myocardial Infarction (PAMI) trial. .One hundred thirty eight patients were randomized before the study ended (71 to transfer for PTCA and 67 to thrombolysis).The time from arrival to treatment was delayed in the transfer group (155 vs 51 minute). At 30 days, a 38% reduction in major adverse cardiac events was observed for transfer group. This study concludes that patients with high risk AMI at hospitals without a catheterization laboratory may have an improved outcome when transferred for primary PTCA versus on-site thrombolysis.

DANAMI-2[60]

In The Danish Multicenter Randomized Trial of Thrombolytic Therapy Versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2) a total of 1572 patients were randomized to treatment with front-loaded tPA, alteplase,up to 100 mg, given at the presenting center without transport or early transfer for primary PCI with stenting. The primary end points was a composite of mortality/ reinfarction / disabling stroke at 30 days. The primary point rates were 14.2% for the thrombolytic therapy group and 8.5% for the primary PCI group. The DANAMI-2 trial showed a relative risk reduction exceeding 40% for primary PCI versus front-loaded tPA over 30 days. The trial therefore confirms previous trials indicating that primary PCI is superior to thrombolytic therapy whether

or not the PCI-treated patients required transport to a PCI center as long as transfer time does not exceed 3 hour.

PRAGUE[61]

The PRAGUE study (Primary Angioplasty in patients transferred from General community hospitals to specialized PTCA Units with or without Emergency thrombolysis) compared three reperfusion strategies in patients with AMI, presenting within 6 hours of symptom onset at community hospitals without a catheterization laboratory: group A - thrombolytic therapy in community hospitals (n-99), group B – thrombolytic therapy during transportation to angioplasty (n-100), group C – immediate transportation for pimary angioplasty without pre-treatment with thrombolysis. The combind primary end-points (death/reinfarction/stroke at 30 days) was less frequent in group C (8%)compared to groups B (15%) and A (23%).The incidence of reinfarction was markedly reduced by transport to primary angioplasty (1% in group C vs 7% in group B vs 10% in group A). PRAGUE trial documented that transferring patients from community hospitals to a tertiary angioplasty center in the acute phase of AMI is feasible and safe. This strategy is associated with a significant reduction in the incidence of reinfarction and the combined clinical end-point of death/ reinfarction / stroke at 30 days when compared to standard thrombolytic therapy in the community hospital

Thrombolysis versus primary PCI

Based on the results of these mega trials primary PCI is considered a superior strategy both from efficacy and safety. The caveats to this conclusion were that these excellent results were obtained in the setting of clinical trials with experienced interventionists. Could these benefits be accomplished in the real world ? initial data from 2 registries actually suggested otherwise, with no difference in outcomes between patients treated with primary PCI vs thrombolysis[51].

However, interventional cardiology has advanced dramatically during the last decade with the advent of sirolimus-eluting stents and GP IIb/IIIa inhibitors, which have appeared to make a difference in outcomes in patients treated with an invasive strategy[62,63]. For the patient with AMI both primary PCI and intravenous thrombolytic therapy are effective in restoring antegrade coronary blood flow, improving left ventricular systolic function and reducing mortality. Primary PTCA is effective when performed quickly by experienced operators. It is the preferred therapy in the patient a) with a contraindication to thrombolytic therapy b) aged 70 years or older and c) in whom thrombolytic therapy is likely to be ineffective (i.e the patient with cardiogenic shock).Thrombolytic therapy is widely available and can be given quickly and easily. As a result, it remains the treatment of choice for most patients with AMI. The goal of therapy for the patient with AMI is the rapid and sustained restoration of coronary blood flow. For the individual patient, the better therapy-primary PCI or thrombolytic therapy-is the one that can be given more safely and expeditiously[64].

ACC/AHA recommendations for PCI in AMI[63]

Class I indication (Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective)

1. As an alternative to thrombolytic therapy in patients with AMI and ST segment elevation or new or presumed new left bundle branch block who can undergo angioplasty of the infarct artery <12 hour from the onset of ischaemic symptoms or >12 hours if symptoms persist, if performed in a timely fashion by individuals skilled in the procedure in an appropriate laboratory environment.
2. In patients who are within 36 hours of an acute ST elevation/Q-wave or new left bundle branch block who develop

cardiogenic shock, are <75 years of age and revascularization can be performed within 18 hour of the onset of shock by individuals skilled in the procedure and supported by experienced personnel in an appropriate laboratory environment

Class IIa indication (Conditions for which there is conflicting evidence and /or a divergence of opinion about the usefulness/ efficacy of a procedure or treatment) As a reperfusion strategy in candidates who have a contraindication to thrombolytic therapy.

Class- III indication (Conditions for which there is evidence and /or general agreement that the procedure/treatment is not useful/ effective, and in some cases may be harmful).

1. Elective PCI of a non-infarct related artery at the time of AMI.
2. In patients with AMI who:

a. have received thrombolytic therapy within 12 hours and have no symptoms of myocardial

ischaemia.

b. are eligible for thrombolytic therapy and are undergoing primary angioplasty by an inexperienced operator.

c. are beyond 12 hours after onset of symptoms and have no evidence of myocardial ischaemia

ACC/AHA recommended performance standard for PCI in AMI[63]

1. balloon inflation within 90 (+/— 30) minutes of hospital admission.
2. Individuals who perform >75 PCI procedures per year.
3. Centers that perform >200 PCI procedures per year and have cardiac surgical capability.

Rescue PCI in AMI

Rescue (also known as salvage) PCI defined as PCI after failed thrombolysis for patients with continuing or recurrent myocardial ischaemia. Rescue PCI has resulted in higher rates of early infarct-artery patency,improved regional infarct zone wall motion and greater freedom from adverse in-hospital clinical events compared to a deffered PCI strategy (63). Prompt restoration of TMI-3 flow improves survival in patients with AMI.Thrombolytic therapy fails to restore TIMI 3 flow within 90 minutes in 40 to 50% of patients.Rescue PCI versus conservative therapy after thrombolytic therapy trial (RESCUE I,RESCUE II) enrolled 1456 patients with AMI.PCI after failed thrombolysis appears to reduce early severe heart failure (3.8% vs 11.7%) and improve survival over one year in patients with moderate to large MI (92% vs 87%) and possibly reduces early repeat MI (4.3% vs 11.3%).These data suggest a probable benefit of rescue PCI after failed thrombolysis[64].

CABG in AMI

Coronary artery Bypass graft operation (CABG) can be performed on patients with AMI with acceptable operative mortality as a strategy for reperfusion. Recently analysis of SHOCK (Should we emergently revascularize Occluded Coronaries for cardiogenic shocK) trial registry demonstrated that the combination of thrombolytic therapy, intraaortic balloon counterpulsation, CABG and PCI decreased the mortality of this high risk group of patients by 46.9%[65]. Patients with high risk AMI should be sent directly to the cardiac laboratory for emergency coronary angiography. After careful reviewing the angiogram, most patients will be treated with PCI . Nevertheless, patients with severe left main disease, left main equivalent or three proximal obstructions should be sent for CABG[66,67]. Both PCI and CABG can work together for the benefit of patients during the early days after AMI. In patients with multivessel disease, PCI and stenting can be done first at the culprit lesion. A few days later, when the enzymes come down to normal levels,multiple CABGs can be performed without increasing the operative risk. This

double step procedure has been applied safely[66].

Reperfusion strategies in Cardiogenic shock

Cardiogenic shock is still the commonest cause of death in patients with AMI.In the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO –I) trial, cardiogenic shock occurred in 7.4% of patients treated with thrombolytic therapy, accounting for 58% of death within 30 days. In the GUSTO-III shock occurred in 5.4% of patients[68]. Characterized by hypotension and organ hypoperfusion, cardiogenic shock has an estimated mortality of 60 to 80 percent[68-70]. Many non randomized studies have reported that mortality from cardiogenic shock was lower in patients treated with revascularization procedures than in those managed medically[68]. The Swiss Multicenter Evaluation of Early Angioplasty for Shock Following Myocardial Infarction (SMASH Trial) randomized patients developing cardiogenic shock with 48 hours after AMI. 69% of patients randomized to PCI and 78% of the patients randomized to medical therapy died within 30 days[71]. In SHOCK Trial patients with cardiogenic shock due to AMI were randomly assigned to emergency revascularization or initial medical stabilization.Revascularization was accomplished by either CABG or PCI. Overall mortality at 30 day were 46.7% in the revascularization group and 56% in medically treated group. Six month mortality was significantly lower in the revascularization group than in the medically treated group (50.3% vs 63.1%). The totality of evidence suggest that early revascularization tends to reduce the frightfully high mortality associated with cardiogenic shock,particularly in patients younger than 75 years[72,73]. Early revascularization should be strongly considered for patients with AMI complicated by cardiogenic shock following AMI if proper facilities are available according to ACC/AHA guidelines.

The advent of primary PCI provided an alternative method for the emergent recanalisation of an occluded infarct related artery. Proponents of this direct or primary PCI approach to reperfusion therapy argued that compared with thrombolytic therapy, PCI results in higher rates of patency and TIMI-3 flow. In addition avoiding thrombolytic administration virtually eliminates the approximate 1% risk of intracranial haemorrhage inherent with systemic thrombolysis[74,75]. Depending upon the results of recently conducted randomized trials, primary PCI is considered a superior strategy both for efficacy and safety. The caveats to this conclusion were that,these excellent results were obtained in the setting of clinical trials with experienced interventionists in the catheterization laboratories of world standard cardiac centers. Could these benefits be accomplished in the real world ? Many researchers still believe that primary PCI resulted in excessive delays to treatment compared with thrombolytic therapy, was never proven beneficial in most of the trials and was only available in a few hospitals. Intravenous thrombolytic is still the standard care for patients with AMI, based upon its widespread availability and ability to reduce patient mortality well demonstrated in randomized trials.

The best way to accomplish reperfusion in patients with evolving AMI continues to be debated,although there is strong agreement that very early reperfuion must be accomplished to preserve myocardium. In addition normal or nearly normal flow (TIMI-3 flow) must be established in the infarct related artery to provide optimal reduction in mortality and morbidity.The early and long-term results of primary PCI have been demonstrated to be excellent. Intrvenous thrombolytic thrapy,when applied in the first 1 to 2 hours after the onset of AMI, also yields good results along with aspirin, clopidogrel and enoxaparin.It now appears that a combination of platelet GPIIb/IIIa inhibitors

and a lower dose of thrombolytic agent may be superior to any of the pharmacologic revascularization strategies currently in use. There is now at least a reasonable hope that in the near future pharmacologic therapy that is the equal of primary PCI will be available in every community hospital.

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Simple Liver Cyst with Portal Hypertension & Obstructive Jaundice - Report of a Case

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JA CHOWDHURY, MBBS[b], M RAHMAN, FRCS, FACS[c]

Summary :

About 2 percent peoples have some form of liver cyst during their lifetime. Most of them are asymptomatic. Only few percentages of cysts become symptomatic because of the infection, pressure effect to surrounding structures or sequelae of rupture of the cyst. We have encountered a case of huge liver cyst that obstructed the portal vein and bile duct causing portal hypertension and obstructive jaundice. Review of the literature revealed that there had been very few case reports of such combination. We report the case highlighting its clinical presentation diagnosis and management and discuss the case in the light of published literature.

(J Bangladesh Coll Phys Surg 2002; 20 : 98-101)

Case History :

A 53-year-old diabetic man was admitted to BIRDEM hospital with recurrent episodes of upper abdominal pain for 8 months, jaundice for 3 months and swelling of abdomen & lower limbs for 2 months. Physical examination revealed that the patient had jaundice, moderate ascites and leg edema. Liver was palpable, about 9 cm from the costal margin. Biochemical profiles were compatible with the features of obstructive jaundice (S Bilirubin was 5.05 mg/dl, Alkaline phosphatase 727 IU/1). Ultra sonogram revealed a large cyst in the right lobe of the liver, dilated intrahepatic biliary tree, enlargement of the left lobe and moderate ascites. CT scan revealed a large cyst in the right lobe. It compressed the bifurcation of the portal vein and bile duct at their confluence (Fig.1). The right and left branch of the portal vein and bile duct were grossly displaced by the compression of the cyst. The left lobe of the liver was hypertrophied. Grade-I gastric fundal varices were noted in the upper gastrointestinal endoscopy. ERCP revealed compression of the bile duct with dilatation of proximal biliary tree (Fig.-2). Endoprosthesis could not be inserted because of the fear of perforation of the cyst. Serological tests for hydatid cyst were negative. Tumor markers (CEA, CA19-9) were within normal range. Based on the above-mentioned findings, the patient was diagnosed as large simple cyst of the right lobe of the liver with obstructed portal vein and bile duct.

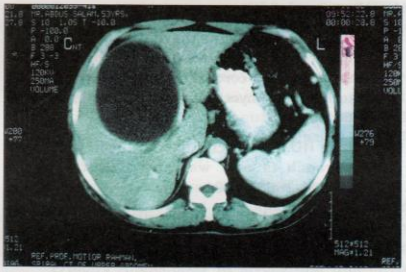

Fig.-1 : *Large simple cyst with compression of Rt. & Lt. Branch of Portal Vein*

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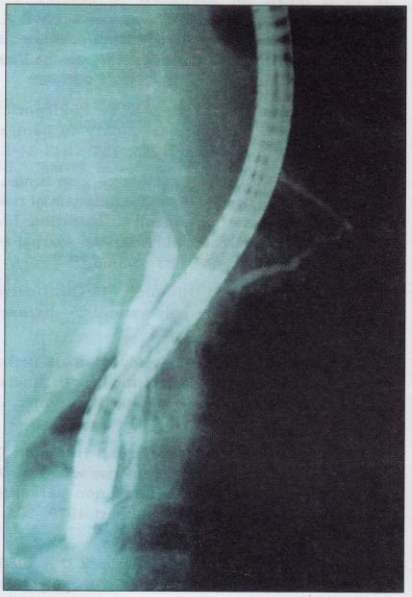

Fig.-2 : *Large simple cyst with compression & occlusion of Bile Duct*

Laparotomy was performed through right subcostal incision. The liver was mobilized by dividing the falciform ligament. A large tense cyst was noted in the right lobe. It compressed the confluence of the portal vein. The main portal vein was dilated and tortuous. The bile duct was also compressed at the hepatic hilum and downward. The cyst content was aspirated, it revealed straw colored fluid. The right hepatic vein was seen from inside the cyst cavity passing through the wall of the cyst. The left lobe was grossly hypertrophied and healthy. Partial pericystectomy was performed. The portal vein and bile duct was relieved from the compression after excision of the cyst. Bile leaked from two sites of the medial aspect of the interior of the cyst, these were closed with suture. Omentoplasty was done. The divided falciform ligament was resutured to prevent the rotation of the hypertrophied left lobe to the right side. Liver biopsy was taken to exclude any chronic changes in the liver.

Histopathologically the cyst was of simple type. Liver biopsy revealed mild cholestasis. Cytology of cyst fluid was negative for malignancy. His postoperative course was uneventful and discharged on the 13th postoperative day. Repeat endoscopy after 6 weeks revealed disappearance of fundal varices. The patient is well with normal liver profile.

Discussion :

Although simple cysts are found in about 1 % of the necropsies in adults, very few become large, and even fewer causes symptom. In general, the cysts in symptomatic cases are larger than those in asymptomatic[1,2]. Symptomatic simple liver cysts mostly present with upper abdominal pain, abdominal discomfort and abdominal distension. The presentation of simple liver cyst with the features of portal obstruction[3] and obstructive jaundice[4-7] is very rare. Arie et al.[8] reported a large series of liver cyst treated in a tertiary center. They treated 78 patients with symptomatic liver cyst during a 15-year period; of them (73.1 %) patients were simple cyst. None of them was with the features of portal obstruction and obstructive jaundice in Arie's series. We have treated 145 cases of hepatobiliary cyst in BIRDEM and other hospitals of Dhaka city during the last 70 months. Of the 145, 70 (48.27%) were simple cysts. The present case is the only patient of the series who presented with the features of obstruction of both bile duct and portal vein. Large cyst of the liver may produce the symptoms in different ways. It may erode or compress the adjacent intra or extra hepatic structures: biliary tree, portal vein, hepatic vein or inferior vena cava[9]. Portal hypertension caused by cystic lesions are more common in polycystic liver diseases [10,11] but very rare in case with simple liver cyst.

Abdominal ultrasonography is the principal diagnostic tool for uncomplicated simple liver cyst [12-14]. Contrast enhanced CT is essential for complicated hepatic cyst.

Several therapeutic approaches have been described for simple liver cyst. It includes simple aspiration, with or without injection of Sclerosing agent[15-16], Laparoscopic unroofing[17-19], internal drainage of cyst with cystojejunostomy[20], and wide deroofing [21, 22]. Atypical or typical liver resections also needed in some complex conditions[23]. Simple aspiration of the cyst is obsolete because cyst recurs frequently[24]. Injection of sclerosing agent into the cyst cavity is sometime dangerous, because chemical cholangitis may develop if biliary canaliculi remain open[25]. Laparoscopic approaches have limitations in large and complicated hepatic cysts. Wide deroofing is the treatment of choice for simple liver cyst. We performed partial pericystectomy, which is the synonym of wide deroofing. Remaining cyst wall was examined carefully and bile-leaking points were closed. Omentoplasty was done, to prevent any secretion from the remaining surface of the cyst- The patient is followed up for last three years and he is free from illness.

In summary. large simple cyst may present with the features of obstructive jaundice and portal vein obstruction, which is a very rare condition. Careful evaluation, preoperative work up and judicious surgical intervention are necessary to diagnose and manage such case successfully.

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Chemodectoma - A Relatively Rare Neoplasm of Neck

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Summary :

A twenty six years old unmarried male was admitted into Khalispur clinic of Khulna with a history of slowly enlarging right sided neck mass of five years duration. Systemic examination revealed a palpable, painless, pulsating and 'firm right sided neck mass. During surgical exploration of neck an ovoid gray to pink firm rubbery apparently encapsulated mass was removed. Histopathological examination of the specimen revealed chemodectoma.

(J Bangladesh Coll Phys Surg 2002; 20 : 102-105)

Introduction :

Chemodectoma is the name suggested by Mulligan[1] for a neoplasm consisting of chemoreceptor tissues such as occur in the carotid and aortic bodies, the glomus jugularis and in groups of similar cells associated with the ganglion nodosum of the vagus, the ciliary ganglion in the orbit and even the lung. The chemoreceptor tissue in this locations is identical microscopically, as are the tumours which arise from the various sites, and differentiation depends on the anatomic site of origin. Those arising at the bifurcation of common carotid artery are termed carotid body tumours (CBT)/ chemodectomas and those presumably arising from glomus intravagale are termed vagal body tumours (VBT), and also glomus Jugulare tumour (GJT) is used arbitraily to include all chemodectomas arising in the vicinity of the middle ear. Microscopically chemoreceptor tissues are consisting of nests or clusters of "chief cells" which are large epithelioid cells containing a large amount of finely granular cytoplasm. The chief cells are arranged in cell nests or "zellballen" surrounded by fibrous stroma rich in capillaries. This chief /epithelioid cells are richly supplied with nerve endings-which may be specialized to receive chemical stimuli[2]. However stimulation of chemoreceptor tissue of the carotid body produces an action potential in the glossopharyngeal nerve and an increase in the rate, depth, and minute volume of respiration. On the other hand an increase in sympathetic nervous system activity as shown by increased pulse rate, elevated arterial blood pressure, increased vasoconstrictor tone, and liberation of adrenaline and also increased cerebral cortical activity.

Pearse[3] has shown that the chief cells of the avian carotid body is of neural crest origin and tumours developing from this cell are included in his list of APUD tumours[4]. The hormonal product of the carotid body and other related branchiometric paraganglia is presumed to be one or more of the biogenic amines instead of polypeptides and some paragangliomas have been associated with symptoms related to catecholamine secretion[5]. Chemodectomas (Carotid body tumours) constitute the most common and important group of extra-adrenal paragangliomas[6]. They are located at the bifurcation of common carotid artery and become closely adherent to it. This firm adherence is often misinterpreted by the surgeon as sign of malignancy. The other preoperative differential diagnostic possibilities include enlarged neck node, salivary gland tumour, branchial cleft cyst, neurofibroma, and carotid artery aneurysm. Pre-operative selective arteriography demonstrates chemodectomas particularly well because of their rich vascularity. Most chemodectomas, follow a benign clinical

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course. The quoted incidence of malignancy is in the range of 10% - simillar to that of adrenal pheochromocytomas[7].

Details of chemodectomas (Carotid body tumours) perhaps have not yet been reported previously in our country. Here a rare benign tumour-chemodectoma of carotid body which was diagnosed clinically as tuberculous lymphadenitis or malignant neoplasm is reported.

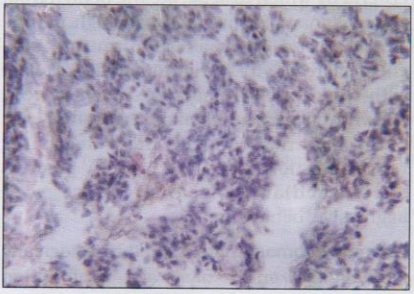

Fig.-1 : *Sections show well defined nests of polyhedral cells/cuboidal cells ("zellballen") separated by highly vascularised fibrous stroma. (H & E X 375).*

Case report :

A twenty six years old unmarried male was admitted into Khalispur clinic of Khulna on 23rd February '2002 with the complaints of slowly enlarging right sided neck mass, local discomfort, headache and dizziness. The patient came of an average socio-economic background and his general condition was good. Systemic examination revealed a palpable, painless, pulsating and firm right sided neck mass which was variable in size.

Haematological investigation showed the following: haemoglobin-12.6 Gm/dl, total leukocyte count-$7.5X10^9$/L and ESR-12 mm after first hour (Westergren method).

Ultrasonography showed a solid homogenous mass in right neck region particularly at the bifurcation of common carotid artery. Fine needle aspiration cytology revealed inconclusive report.

Selective angiography was not done because of lack of facility. Surgical resection on neck was done on 25th February 2002. With all aseptic precaution, under general anaesthesia carotid sheath was explored. Ipsilateral carotid artery was temporarily ligated. Tumour was identified at bifurcation of common carotid artery. It was carefully dissected free and enucleation - excision was done. Per-operatively carotid artery was not injured. Wound was closed after proper haemostasis. Grossly the tumour mass was ovoid to round in shape, firm rubbery in consistency and gray to pink in colour and apparantly encapsulated. Foci of haemorrhage were seen. The resected tumour mass was sent for histopathological examination.

Morphological findings:

Gross appearance: Specimen consisted of a gray to pink ovoid tumour mass resected at the bifurcation of common carotid artery measuring about 3X2X1.5 cm. It was firm rubbery in consistency and partly encapsulated. Foci of haemorrhage were seen and tan on cut section. Two blocks were made for paraffin embedding.

Microscopic appearance: Haematoxylene and eosin stained slide prepared from tumour mass showed a benign tumour consisting of well defined nests of polyhedral cells/cuboidal cells ("zellballen") separated by highly vascularized fibrous stroma. The individual cells have a moderately abundant granular eosinophilic cytoplasm and round to ovoid nuclei. The cell boundaries are indistinct and mitotic figures are uncommon.

Discussion :

Chemodectomas/carotid body tumours (CBT) occur at an average age ranges from 19-72 years and there are no sex prevalence among the patients with chemodectomas[8]. Age of this male patient was twenty six years which agrees with the findings of Lahey FH and

Worren KW[9]. The average duration of symptoms before diagnosis was four years (range of 1 month to 20 years). The duration of symptoms of this patient was five years. This duration of symptom agrees with the finding of Wilson H[10]. Chemodectomas of head and neck are about ten times more frequent in persons living at high altitude than those at sea level[11]. These have been invariably benign and may actually represent exaggerated example of the well-known hyperplastic change that consistently occur in these organ when they are exposed to prolonged and severe pathologic or physiologic hypoxic stimulation[12]. The patient reported here presented with no history of exposure to pathologic or physiologic chronic hypoxaemia. This seem to be a less extent an atypical presentation of patient with chemodectoma.

A definite familial incidence has been detected[13]. Familial occurrence of chemodectomas (CBT) was first noted by Chase[14] and an autosomal mode of inheritance proposed by Kroll et al[15]. The familial chemodectomas are often multiple has been noted by Pratt LW 16 as has the fact that the carotid body is the most frequent site of involvement. Carney et all[17] have identified a syndrome characterized by exotic association of extra-adrenal paraganglioma, gastic malignant stromal tumour and pulmonary chondroma. Most of the cases have occurred in young females [18].

Farrar et al[19] classified chemodectomas into three groups according to the gross tumour-vessel relationship: localized tumours (group I), those adherent and partially surrounding the carotid vessels (group 2), and those intimately surrounding the carotid vessels (group 3). selective angiography, fine needle aspiration and incisional biopsy are the precise means of preoperative diagnosis of chemodectomas. Of these selective angiography proved to be the most informative preoperative diagnostic procedure. It is useful not only in providing a diagnosis, but in differentiating carotid body tumour (CBT), vagal body tumour (VBT), and glomus Jugulare tumour (GJT) and also in outlining the extent of tumour.

Chemodectomas /CBT occasionally are clinically malignant. The incidence of malignancy is low. However long term follow-up studies suggest that the real incidence of malignancy may be higher at least for some location[20]. There are no reliable morphologic criteria by which to separate the benign from the malignant forms, although high mitotic activity and decreased immunohisto-chemical reactivity for neuropeptide correlate with clinical malignancy[21]. It has also been shown that paragangliomas associated with benign clinical course have a greater representation of S-100 protein positive sustentacular cells than those with aggressive behaviour[22].

Chemodectomas are classified histologically as malignant on the basis of a combination of two or more of the following features: central necrosis of zellballen, invasion of vascular spaces and the presence of mitotic figures. Metastatic sites included cervical and mediastinal lymph node, lungs, bone, liver and occasional heart. The possibility of multicentric chemodectomas should always be considered before concluding that a given tumour has metastasized[23]. Biochemical assays of the tumour have confirmed the presence of norepinephrine and sometimes also of epinephrine and dopamine[24]. Immunohistochemically positivity has been found for neuron specific enolase, chromogranin, synaptophysim, neurofilaments, opiod peptides, serotonin, somatostanin and various other peptide hormones[25].

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COLLEGE NEWS

(J Bangladesh Coll Phys Surg 2002; 20 : 106-110)

The results of FCPS Part-I, FCPS Part-II and MCPS examinations held in January, 2002 are given below. A total of 996 candidates appeared in FCPS part-I in different specialties. 72 candidates were declared to have passed. A subjectwise result follows :

FCPS Part I Examination

	No. of candidates appeared.	No. of candidates qualified for viva.	Passed
Medicine	312	25	12
Surgery	239	76	21
Paediatrics	102	31	15
Obst. & Gynae	192	27	11
Ophthalmology	22	4	2
Otolaryngology	30	3	3
Psychiatry	4	0	0
Anaesthesiology	32	12	5
Radiology	8	1	1
Radiotherapy	1	0	0
Dermatology & Venereology	16	0	0
Physical Medicine	4	0	0
Dental Surgery	16	1	1
Haematology	9	0	0
Biochemistry	1	0	0
Microbiology	3	0	0
Histopathology	5	1	1
	996	181	72

177 candidates appeared in FCPS part-II examination in different subjects and 54 were declared to have qualified. A list of candidates who satisfied the board of examinations follows :

Roll No.	Name of Candidates	Graduated from	Speciality
012	Dr. Shaikh Amir Hossain	Sher-e-Bangla Medical College	Medicine
018	Dr. Neena Islam	Sir Salimullah Medical College	Medicine
021	Dr. Mohammad Ullah	Dhaka Medical College	Medicine
037	Dr. Md. Hafiz Sardar	Dhaka Medical College	Medicine
046	Dr. Quazi Mamtaz Uddin Ahmed	Dhaka Medical College	Medicine
051	Dr. Md. Abdul Quddus	Chittagong Medical College	Medicine
059	Dr. Molla Nazrul Islam	Dhaka Medical College	Surgery
063	Dr. Taufiqul Haque	Mymenshingh Medical College	Surgery

Roll No.	Name of Candidates	Graduated from	Speciality
065	Dr. Md. Shafiqur Rahman	Rajshahi Medical College	Surgery
066	Dr. Md. Shamsul Alam Chowdhury	Rajshahi Medical College	Surgery
069	Dr. Masud Anwar	Shere-Bangla Medical College	Surgery
070	Dr. Md. Burhan Uddin Khan	Shere-Bangla Medical College	Surgery
071	Dr. Md. Abdul Aziz	Sylhet MAG Osmani Medical College	Surgery
075	Dr. Md. Abid Hossain	Shere-Bangla Medical College	Surgery
077	Dr. Md. Atiar Rahman	Mymensingh Medical College	Surgery
079	Dr. Md. Atiqul Islam	Sir Salimullah Medical College	Surgery
081	Dr. Partha Sarathi Ray	Chittagong Medical College	Surgery
082	Dr. Tahmina Satter	Dhaka Medical College	Surgery
085	Dr. S.M. Nazrul Islam	Sir Salimullah Medical College	Surgery
087	Dr. Md. Rashidul Islam	Sir Salimullah Medical College	Surgery
091	Dr. Laila Shirin	Rangpur Medical College	Surgery
093	Dr. Md. Azharul Islam	Dhaka Medical College	Surgery
095	Dr. Abdus Salam	Sylhet MAG Osmani Medical College	Surgery
097	Dr. Abdullah Al Tarique	Sir Salimullah Medical College	Surgery
098	Dr. Md. A. Mottalab Hossain	Rajshahi Medical College	Surgery
100	Dr. Md. Aman Ullah	Rangpur Medical College	Surgery
102	Dr. Abu Tayab Md. Khurshed Alam	Sylhet MAG Osmani Medical College	Surgery
110	Dr. Md. Atiqur Rahman Khan	Rajshahi Medical College	Paediatrics
111	Dr. Arjun Chandra Dey	Chittagong Medical College	Paediatrics
113	Dr. Md. Abdul Khaleque	Mymensingh Medical College	Paediatrics
115	Dr. Probhat Ranjan Dey	Sylhet MAG Osmani Medical College	Paediatrics
116	Dr. Kiriti Prashad Deb	Chittagong Medical College	Paediatrics
120	Dr. Nahla Bari	Dhaka Medical College	Obst. & Gynae
122	Dr. Afrina Begum	Chittagong Medical College	Obst. & Gynae
124	Dr. Tanzina Latif	Mymensingh Medical College	Obst. & Gynae
125	Dr. Parveen Akhter Shamsunnahar	Dhaka Medical College	Obst. & Gynae
127	Dr. Shahin Akhter Zahan Habib	Rajshahi Medical College	Obst. & Gynae
128	Dr. Selina Parvin	Shere-Bangla Medical College	Obst. & Gynae
129	Dr. Fahmida Islam Chowdhury	Chittagong Medical College	Obst. & Gynae
130	Dr. Kulsum Haq	Chittagong Medical College	Obst. & Gynae
131	Dr. Gulshan Ara	Shere-Bangla Medical College	Obst. & Gynae
134	Dr. Touhida Ahsan	Mymensingh Medical College	Obst. & Gynae
138	Dr. Begum Maksuda Farida Akhter	Dhaka Medical College	Obst. & Gynae
141	Dr. Jobaida Sultana	Dhaka Medical College	Obst. & Gynae
143	Dr. Nasreen Haque	Chittagong Medical College	Obst. & Gynae
148	Dr. Shaheen Ara Anwary	Ins. of Post-gradiate Med. & Research	Obst. & Gynae
149	Anwara Begum	Chittagong Medical College	Obst. & Gynae
150	Rumana Nazneen	Sir Salimullah Medical College	Obst. & Gynae
158	Dr. Md. Mazharul Shaheen	Dhaka Medical College	Otolaryngology
162	Dr. Ashfaque Uzzaman Choudhury	Sylhet MAG Osmani Medical College	Psychiatry
164	Dr. Kazi Ashkar Lateef	Sir Salimullah Medical College	Anaesthesiology
169	Dr. Abdul Quddus	Sir Salimullah Medical College	Radiology
170	Dr. Md. Enamul Haque	Ins. of Post-gradiate Med. & Research	Radiology
176	Dr. Jissan Wajed	Dhaka Medical College	Haematology

271 Candidates appeared in MCPS examinations different Subjects. 39 were successful. List of Candidates who satisfied the board of examiners is as follows :

Roll No.	Name of candidates	Speciality
001	Dr. Md. Shahedur Rahman Khan	Medicine
006	Dr. Arun Kumar Sharma	Medicine
009	Dr. Md. Abdul Ali Mia	Medicine
010	Dr. A.K.M. Murshed	Medicine
012	Dr. Md. Abdul Quddus	Medicine
014	Dr. Adnan Yusuf Choudhury	Medicine
019	Dr. Tarek Ahmed Choudhury	Medicine
020	Dr. Shah Noor Sarmin	Medicine
023	Dr. Md. Nurul Huda	Medicine
035	Dr. Md. Golam Mustafa	Medicine
036	Dr. Mohd. Harun-or-Rashid	Medicine
039	Dr. Rafique Ahmed Bhuiyan	Medicine
048	Dr. Chitta Ranjan Debnath	Medicine
050	Dr. Md. Mahbubur Rahman	Medicine
051	Dr. Md. Ashraf Ali	Medicine
052	Dr. A.K.M. Mokhlesuzzaman	Medicine
059	Dr. Pradip Kumar Karmakar	Medicine
076	Dr. Md. Abdur Rakib	Surgery
089	Dr. Asim Kumar Saha	Paediatrics
095	Dr. Md. Tarek Azad	Paediatrics
126	Dr. Md. Akbar Hossain	Obst. & Gynae
154	Dr. Sufia Khatun	Obst. & Gynae
177	Dr. Nazma Begum	Obst. & Gynae
199	Dr. A. H. M. Delwar	Otolaryngology
204	Dr. A.B.M. Tofazzal Hossain	Otolaryngology
205	Dr. A.K.M. Asaduzzaman	Otolaryngology
207	Dr. Anjoli Roy	Anaesthesiology
232	Dr. Md. Azraf Hossain Khan	Dermatology & V.
235	Dr. Sushanta Kumar Biswas	Dental Surgery
238	Dr. Md. Mozaharul Islam	Forensic Medicine
243	Dr. Md. Mozahedul Hoque	Family Medicine
249	Dr. Md. Mahbubur Rahman	Family Medicine
251	Dr. Muhammad Shibbir Ahmed Osmani	Family Medicine
252	Dr. Md. Badruzzaman	Family Medicine
253	Dr. Md. Rowshanul Karim	Family Medicine
255	Dr. Kazi Habib Ibrahim Rahmat Ullah	Family Medicine
257	Dr. Dilip Kumar Saha	Family Medicine
263	Dr. Md. Sirajul Islam	Clinical Pathology
267.	Dr. Md. Afzalur Rahman	Clinical Pathology

College Convocation held

The 8th Convocation of Bangladesh College of Physicians and Surgeons for the year January 1998 to July 2001 was held on 28th January, 2002, in the Bangladesh China Friendship Conference Centre. The Hon'ble Prime Minister of the People's Republic of Bangladesh, Begum Khaleda Zia, graced the occasion as the Chief Guest and gave out the Certificates to the Fellows and Members.

The following is list of the total recipients of the convocation certificate

	Fellows	Members
January 1998	60	53
July 1998	42	34
January 1999	54	29
July 1999	43	35
January 2000	52	52
July 2000	23	43
January 2001	41	45
July 2001	28	60

Twelve eminent academicians who were conferred Honorary Fellowship over these years also received their certificates

1.	Dr. Afroze Sherali	Pakistan
2.	Dr. Farrukh Zaman	Pakistan
3.	Dr. Shabeer Hossain	Pakistan
4.	Dr. Abdullah Jan Jaffar	Pakistan
5.	Dr. Azhar Hossain	Pakistan
6.	Dr. Saghir Ahmed	Pakistan
7.	Dr. Mahesh Khakure	Nepal
8.	Dr. A.P.R Aluwihare	Srilanka
9.	Dr. Syed Mukarram Ali	Bangladesh
10.	Dr. Munir Uddin Ahmed	Bangladesh
11.	Dr. Maleka Khatun	Bangladesh
12.	Dr Shahla Khatun	Bangladesh

Intercollegiate Scientific Conference-2002

Bangladesh College of Physicians & Surgeons organized "Intercollegiate Scientific Conference-2002" with the theme "Challenges and Prospects of the new Century". It was held during 28 – 31st January of this year in the college premises.

Bangladesh College of Physicians & Surgeons, The Royal College of Physicians & Surgeons of Glasgow, the College of Physicians & Surgeons, Pakistan & the Institute of Medicine, Tribhuvan University, Nepal joined as partners in progress to meet the challenge and to explore the prospects.

The inaugural ceremony was held at Bangladesh China Friendship Conference Centre on 28th January with His Excellency President of People's Republic of Bangladesh, Prof. AQM Badruddoza Chowdhury as Chief Guest.

There were about 1000 participants from home & abroad (800 local & 160 foreign delegates). Sessions included were state of Art Lectures, Plenary Sessions, Symposia, Panel Discussions, Free Paper, Posters & Video presentation.

298 scientific papers were presented (279 oral, 18 posters, 1 video).

There was a pre-conference workshop on "Education Planning & Evaluation". There was also a post conference CME programme on "Assisted Reproductive Technique" (ART).

It is the first time that this type of a multi-disciplinary international conference was held in Bangladesh in collaboration with other three premier institutes of the world. The conference ended successfully with due applause from foreign delegates.