"INCIDENCE OF BACTEROBILIA IN PATIENTS WITH BILIARY OBSTRUCTION IN A TERTIARY CENTER"

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CERTIFICATE

This is to certify that this dissertation entitled **"Incidence of bacterobilia in patients with biliary obstruction in a tertiary center"** Submitted by **Dr.P.JAGADESAN** to the faculty of Medical Gastroenterology, The Tamilnadu Dr.MGR Medical University, Guindy, Chennai-600032, in partial fulfilment of the requirement for the award of DM Degree, Branch IV (Medical Gastroenterology) is a bonafide work carried out by him under my direct supervision and guidance.

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Incidence of bacterobilia in patients with biliary obstruction in a tertiary center

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CONTENTS

INCIDENCE OF BACTEROBILIA IN PATIENTS WITH BILIARY OBSTRUCTION IN A TERTIARY CARE CENTER

ABSTRACT

OBJECTIVES ;

Bacterobilia is commonly observed in patients with obstructed biliary system and is usually asymptomatic .Routine bile culture obtained during ERCP can help in predicting dreaded complications like cholangitis .We studied 30 consecutive bile samples and analysed the incidence of bacterobilia comparing benign and malignant etiology .

METHODS ;

30 Consecutive patients with biliary obstruction who have undergone ERCP at our hospital were studied.Study population included 13 males and 17 females .23 cases were of benign etiology .7 were malignant .After successful biliary cannulation ,bile was obtained and sent for microbiological analysis.

RESULTS ;

Bile cultures were positive in 16 patients .10 of them had benign etiology .6 of them were malignant .Organisms grown are mainly gram negative with Klebsiella in most of them .Response to cephalosporins were good and resistance to ciprofloxacin was observed .

CONCLUSIONS ;

This study confirms the importance of obtaining routine bile sample during ERCP in obstructed biliary system to predict and prevent dreaded complications like cholangitis .

KEY WORDS: Bacterobilia, Bile culture, Obstructive jaundice,Antibiotics.

INTRODUCTION

Bile in individuals with normal biliary tract is sterile. Presence of biliary obstruction leads to bacterial colonisation of bile. Ascending infection from duodenum and or bacterial translocation from portal vein are the likely sources of infection .Increase in the common bile duct pressure due to obstruction in the presence of infected bile promotes bacterial reflux into lymphatics and hepatic sinusoids resulting in cholangitis.

Studies that included both benign and malignant causes of biliary obstruction confirmed that bacterobilia is more common in benign biliary obstruction than malignant biliary obstruction. This is probably due to intermittent nature of benign obstruction facilitating bacterial colonisation.

RISK FACTORS FOR BACTEROBILIA

The risk factors or bacterobilia proportionately varies with underlying pathology .The most common causes are,

1. Common bile duct stones,
2. benign biliary strictures and
3. malignant strictures.

Other risk factors for bacterobilia are

1. Age >70 years ,
2. Diabetes mellitus and
3. previous biliary intervention .

Microbial flora commonly seen in infected bile include E.coli, Klebsiella, Enterococci, proteus ,salmonella and pseudomonas.

In this study, we evaluated the incidence of bacterobilia in patients who underwent ERCP for obstructed biliary system in our centre.We also evaluated the possible risk factors for bacterobilia in such cases .We also compared the incidence of bacterobilia in benign and malignant conditions presenting with biliary obstruction.We also studied the microbiological pattern of bile in such cases and their antibiotic sensitivity.

REVIEW OF LITERATURE

Extra-hepatic biliary obstruction occurs as a result of anatomical obstruction to common bile duct and,common hepatic duct. Causes include calculi, benign and malignant tumours, and benign strictures including primary sclerosing cholangitis.

PATHOPHYSIOLOGY OF OBSTRUCTIVE JAUNDICE

Obstruction to bile flow increases biliary pressure with dilatation of biliary tree .There is regurgitation of bile into the circulation and hepato-cellular damage. The degree of rise in biliary pressure depends upon the secreting capacity of the hepatocytes and ductular cells and distensibility of the biliary tract.

Some bile reaches the circulation via lymphatics .Paracellular flow is another route .Bile passage also occurs across the hepatocyte in intracellular vacuoles .Only a small rise in biliary pressure is necessary for regurgitation of bile into the circulation. Bile duct obstruction results in numerous changes in the hepatic structure and function.

The cause of hepatocellular injury is likely to be multifactorial. Retained bile salts have detergent properties and are cytotoxic in vitro. The toxicity increases with increasing hydrophobicity. Monohydroxy bile

salts such as lithocholate are more toxic than dihydroxy bile salts such as chenadeoxycholate or deoxycholate which in turn are more toxic than trihydroxy bilesalts such as cholate.

Copper which is normally excreted in bile is retained in patients with cholestasis.Mitochondrial respiratory enzyme activity and ketogenesis are impaired and take several weeks to recover after relief of obstruction .Hepatic mitochondrial response to oral glucose is impaired in patients with obstructive jaundice and relates to survival.

Hepatic transport process appears to remain intact. After relief of bile duct obstruction ,bile acid transport into bile begins virtually immediately and the serum non –sulfated bile acid concentration falls rapidly to normal.

In general, after relief of obstruction,serum bilirubin concentration falls with a half life of approximately 7 days. Persistent hyper bilirubinemia is seen when there is cholangitis, partial obstruction to drainage ,or when there are hepatic metastasis.

During prolonged obstruction ,serum albumin level falls even in the absence of sepsis.

SYSTEMIC EFFECTS

Fatigue is common with prolonged cholestasis. The exact mechanism is not clear. Alteration in central neurotransmission is postulated as one of the causes.

Itching is common with prolonged cholestasis and it usually disappears within few days of biliary decompression. Elevated serum bile acids and endogenous opioid peptides are probable mechanisms involved.

Cardio-vascular complications are subclinical .Reduced peripheral vascular resistance is common.

Exaggerated response to volume depletion is common ,though the resting blood pressure is unaffected.

Bile acids have a negative chronotropic effect. Jaundice induced cardiomyopathy can occur.

Acute tubular necrosis is a very common renal complication of obstructive jaundice particularly after surgery or any intervention[1,2,3]{8%}.

Haemorrhagic gastritis,anorexia, weight loss, hypoalbuminemia, impaired wound healing ,are other complications reported.

Absence of bile acids in the intestinal lumen impair the absorption of fat because of lack of miscelle formation. Plasma free cholesterol ,phospholipids and triglycerides are elevated in patients with obstructive jaundice [4].

Bone pain with fractures occur in patients with prolonged cholestasis and osteomalacia is a risk[5].

Bleeding tendencies are common. Low-grade DIC elevated FDP levels are seen. Platelet functions are impaired.

BILIARY OBSTRUCTION –CLINICAL FEATURES

Fever, jaundice abdominal pain are common features of biliary obstruction. Fever is more common with choledocholithiasis. When CBD stones are present, bacteria are usually seen in the bile .Ductal obstruction increases the biliary pressure and infected bile enters the circulation with systemic signs of sepsis.

Bile from patients with malignant obstruction is usually sterile. So, fever is rare except in patients who have been treated with endoscopic

or surgical stenting. This is because, bacteria adheres to the stent, bile is colonized and stent blockage results in systemic sepsis[6].

Pain is more common with stone disease but occur rarely in malignant obstruction.

Pruritus is more common with malignant obstruction and intra-hepatic cholestasis .Itching is rare with calculous obstruction because obstruction is rarely complete and may not be sufficiently prolonged to cause retention of pruritic agents. Relief of obstruction is followed by loss of itching in a few days. Weight loss is more common with malignant obstruction although it can occur in benign obstructive conditions with prolonged cholestasis.

History of previous cholecystectomy should raise the possibility of retained common bile duct stone. If surgery is recent and followed by abnormal drainage of bile through the wound or drain ,a traumatic bile duct stricture should be suspected.

Drug history is useful in patients with cholestasis. History of inflammatory bowel disease should raise the possibility of primary sclerosing cholangitis.

History of colonic malignancy in the past with those presenting with biliary obstruction leads to the suspicion of hepatic metastasis or biliary obstruction from lymph node involvement.

EXAMINATION

Examination should focus on jaundice, scratch marks, body mass index, signs of chronic liver disease to suggest long standing intrahepatic cholestasis, Liver may be palpable. Splenomegaly is usually seen with liver disease except in splenic vein block complicated by pancreatic malignancy.

A palpable gallbladder suggests malignant obstruction to distal CBD{ Courvoisier law .}

Lab investigations should include CBC, urea, creatinine, electrolytes, LFT and prothrombin time. Leucocytosis suggests cholangitis .Impaired renal function, hyponatremia, hypokalemia, prolonged prothrombin time, abnormal LFT with elevated serum bilirubin, serum alkaline phosphatase and GGT are other abnormalities seen.

When there is acute obstruction of bile duct, serum AST and ALT levels are very high reaching upto 30 times normal.

IMAGES ;

May be classified into non-invasive and invasive techniques . Ultra-sound abdomen is useful in detecting the site of obstruction in 2/3 rd of cases and cause of obstruction in 1/3 rd of cases.

MRCP is valuable in delineating ductal anatomy and serves as a roadmap for further work-up.

Invasive procedures include ERCP and PTC .The advantage of ERCP is that it serves both diagnostic and therapeutic purposes.

TREATMENT

Hydration and maintenance of fluid balance is ideal. Correction of coagulopathy with vitamin –k injection is useful. Antibiotics to combat infection is needed.

Management of pruritus include use of bile acid sequestrants, opiate antagonists, rifampin or antihistaminics. Biliary decompression with prophylactic stenting is indicated in all cases of biliary obstruction. Endoscopic sphincterotomy with removal of stone from the common bile duct helps in fastening recovery from obstructive jaundice.

BACTEROBILIA IN OBSTRUCTIVE JAUNDICE

Bacteria may enter the biliary tract by two routes.

1. Hematogenous[9,10] and
2. Retrograde [11] .

The hematogenous route involves the translocation of enteric bacteria across the bowel wall to portal vein, hepatic sinusoids and via the space of Disse into bile[12]. For the retrograde route, duodenal bacteria migrate through the ampulla and enter the biliary system[13] .

In a healthy biliary tract, there are anatomical barriers to both these routes .The tight junctions between hepatocytes prevent bacterial entry into bile and competence of sphincter of Oddi bans the retrograde route.

Additional anti-bacterial protection is provided by the physiology of the bile and the biliary system. Immunoglobins are excreted in to the bile predominantly IgA and may bind the bacteria[14].Bile salts have antibacterial action demonstrable in vitro [15].Finally flow of bile flushes any contaminating bacteria from the biliary system constantly.

Diseases of the biliary tract circumvents or negates these protective mechanisms and results in the presence of bacteria in the bile .{ BACTEROBILIA } Obstruction of biliary system from either benign or malignant cause has marked effect on the anti – bacterial defence mechanisms .

Obstruction reduces IgA production and prevents flushing of bacteria[20]. It increases the translocation of gut flora in to the portal vein[21]. It reduces Kupfer cell function[22]. It disrupts the tight junctions between the hepatocytes[23]. Bacterobilia is more common with benign obstruction than malignant obstruction. This is probably due to partial or intermittent nature of benign obstruction[32],facilitating bacterial colonisation. This implies that the retrograde bacterial colonisation is more important than the hematogenous route .

Bacterobilia varies with underlying pathology.

Common bile duct stones [24-29] -70 -80%

Benign biliary stricture[24,25] -85%

Malignant stricture [30,31] - 30 %

Other risk factors for bacterobilia are

Obstructive jaundice

Age > 70

Diabetes mellitus

. orthotopic liver transplantation .

Corticosteroid treatment and

Previous biliary intervention.

Bacterial flora almost always contain enteric organisms predominantly gram negative bacilli .

E.coli --55%

Klebsiella -20 -30 %

Proteus –5 %

Salmonella -0- 5 %

Pseudomonas[39,40] 0 – 25 % wide range exists may reflect prior instrumentation of the biliary tract or prior antibiotic usage.

Gram positive bacteria - mostly enterococci -15 -40 %

Anaerobic organisms -bacteroides 1 – 20 %

Clostridium 5 -15 %

It is noticeable that bacterobilia is found in patients without clinical sepsis. Once biliary pressure is raised ,regurgitation of bile in to systemic circulation occurs .The biliary contents reflux into sinusoids when biliary pressure rises to 25 cm of water .

Bile culture is superior to blood culture in detecting cholangitis. The high sensitivity of bile culture is plausible because the material for microbiological analysis is directly obtained from the place where the inflammation occurs.

It is important to differentiate asymptomatic bacterobilia from biliary sepsis[43-44].Polymicrobial bacterobilia is usually found in biliary sepsis, though systemic bacteremia is monomicrobial .

Charcot in 1877 described a triad of fever, right upper abdominal pain and jaundice. This triad occurs in 56 - 70 % of patients who have cholangitis .The most severe form , characterized by the additional clinical features of hypotension and alteration of consciousness {Reynold pentad] is uncommon and occurs only in 5 - 7 % of cases. Fever is the main symptom which is found in 90 % of cases. Abdominal pain is common in patients with cholangitis, Unlike the pain secondary to bile duct stones in the absence of infection it is relatively mild and intermittent .

Elderly and immune compromised patients may present with atypical symptoms and signs .The presence of fever ,leucocytosis and abnormal LFT is highly suggestive of cholangitis .

Broad spectrum antibiotics with adequate biliary excretion such as ampicillin-sulbactum ,piperacillin-tazobactum ,third or fourth generation cephalosporins , quinolones and carbapenam are beneficial

Antibiotics with enterococcal and anaerobic coverage may be added in patients with advanced age ,severe disease ,a biliary stent in situ or prior entero-biliary surgery.Biliary excretion of most antibiotics is compromised in the presence of biliary obstruction.Early biliary decompression is essential to restore good biliary excretion of antibiotics.

MANAGEMENT OF CHOLANGITIS

Initially ,supportive therapy that includes adequate hydration, correction of coagulopathy and metabolic derangements and antibiotic must be provided.

Medical treatment alone is effective in approximately 80% of patients. Prompt and adequate biliary drainage is required in others to control the clinical symptoms .

Antibiotics should be given early when acute cholangitis is suspected, even before it is definitely established to control bacteremia and sepsis.

Choice of antibiotic depends on several considerations including host factors (renal function, allergic reaction) severity of disease, local antibiotic sensitivity pattern and presence of prior biliary intervention or surgery.

Broad spectrum antibiotics with adequate biliary excretion such as ampicillin-sulbactum, piperacillin-tazobactum, quinolones ,third or fourth generation cephalosporins are preferred.

Duration of therapy is based on clinical response and presence of bacteremia.For mild cases ,treatment for 5 to 7 days may be sufficient.Severe cases with a positive blood culture need antibiotic treatment for at least 10 to 14 days.

Biliary drainage is essential in patients with cholangitis. It can be performed by

1. endoscopic method

2 .percutaneous

3 .surgical drainage or

4 .multimodal approach.

Endoscopic approach has several advantages,

1. defining ductal anatomy

2. identifying simultaneous pathology such as biliary stricture or choledochal cyst.

3. collecting bile for microbiologial study

4. providing tissue sampling .

5. allowing definitive treatment in most cases and

6. less morbidity than the per cutaneous route .

Endoscopic biliary drainage is the procedure of choice.

Percutaneous drainage or surgical decompression is a useful alternative when endoscopic treatment is technically impossible or unsuccessful .

When ERCP is performed in the presence of active cholangitis and purulent bile ,care must be taken to avoid aggravating the

existing high intraductal pressure. Contrast injection during biliary cannulation should be minimized.

Once deep cannulation is successful, 20 to 40 ml of bile should be aspirated to decompress the bile duct and to provide a sample of bile for microbiological analysis . Then limited contrast can be injected to fill only the extra-hepatic ductal system to define the cause and location of the obstruction unless intrahepatic bile duct pathology is suspected. Definitive therapy of biliary endoscopic sphincterotomy with removal of stones is pursued in a stable patient who has confirmed bile duct stones . In an unstable patient , every effort should be made to shorten the procedure time while providing adequate biliary drainage.

Definitive therapy can be performed subsequently once the general condition of the patient is stabilized. Prolonging the procedure to attempt definite therapy in an unstable patient may increase the morbidity and mortality. In a patient with severe cholangitis, endoscopic biliary drainage can be achieved with plastic biliary stent or with nasobiliary catheter with or without biliary endoscopic sphincterotomy.

Concomittant sphincterotomy facilitates the placement of a large stent or multiple stents for more effective drainage and with a minimal risk of stent migration .Risk of post sphincterotomy bleeding correlates significantly with the presence of acute ascending cholangitis, even in the absence of coagulopathy .

Nasobiliary drainage provides the advantage of active decompression by intermittent or continuous negative pressure suction and the opportunity for sequential bacterial bile cultures. But used infrequently because of

1. patient discomfort
2. possibility of inadvertent dislodgement of the nasobiliary catheter.
3. risk of kinking with inadequate drainage and
4. the potential for electrolyte disturbance secondary to external diversion of bile.

Percutaneous transhepatic biliary drainage is generally reserved for patients in whom endoscopic method is unsuccessful or who have altered anatomy such as prior gastric bypass surgery.

Surgical drainage is done by either open or laparoscopic common bile duct exploration. In severely ill patients, the simplest procedure (like T-tube placement) should be performed to shorten the procedure time. The option of definitive therapy can be determined later when appropriate.Because of the operative risk, emergency surgical decompression is rarely performed. It is reserved for patients for whom both endoscopic and percutaneous approach are unsuccessful or who have altered anatomy which precludes such procedure.

DIAGNOSTIC CRITERIA AND SEVERITY ASSESSMENT OF ACUTE CHOLANGITIS -- TOKYO GUIDELINES

(K .Wada et al - journal of hepatobiliary pancreatic surgery[51] 2007 14—52-58)

Diagnosis is based on

1. history of biliary disease.
2. clinical manifestations
3. laboratory data indicative of presence of inflammation and biliary obstruction.

4. imaging findings indicative of biliary obstruction and or evidence of etiology were suitable making the diagnosis of acute cholangitis.

DIAGNOSTIC CRITERIA ;

A. clinical context and clinical manifestation.

1. history of biliary disease
2. fever with or without chills .
3. jaundice
4. abdominal pain - right upper quadrant or upper abdomen

B .Laboratory data –

5 .evidence of inflammatory response. –abnormal WBC count, increased c-reactive protein or other changes indicating inflammation.

6. abnormal liver function tests –increased serum alkaline phosphatase, GGT, altered AST or ALT levels.

C .imaging findings --

7 .biliary dilatation or evidence of an etiology suggestive of stricture, stone, stent etc.,

Suspected diagnosis -two or more items in A.

Definite diagnosis ;--

1. Charcot triad (2+3+4)

2. two or more items in A and both items in B and C .

PROGNOSTIC FACTORS ;

Can be divided in to

1. those related to organ dysfunction and

2. those unrelated to organ dysfunction.

Those related to organ dysfunction are

1. shock

2. mental confusion

3. elevated serum creatinine .

4. elevated BUN.

5. prolonged prothrombin time .

6. hyperbilirubimemia and

7. reduced platelet count .

Those unrelated to organ dysfunction are

1. high fever

2. leucocytosis

3. bacteremia

4. endotoxemia

5. hypoalbuminemia

6. liver abcess

7. medical co morbidities

8. elderly patients >75 years and

9. malignancy as etiology

SEVERITY ASSESSMENT ;

Can be classified in to mild, moderate and severe.

Mild --which responds to medical management.

Moderate -which does not respond to medical management but not having organ dysfunction.

Severe cholangitis –onset of dysfunction of any one of the following organs.

1. cardio-vascular –hypotension requiring dopamine infusion .
2. neurological –disturbance of consciousness .
3. respiratory -pao2/ Fi o2 ratio < 300
4. kidneys - serum creatinine > 2.0 mg/ dl
5. liver -PT-INR >1.5
6. platelet count < 1,00,000 / mcl

Elderly patients >75 years old and patients with co-morbid Illness should be monitored closely.

FACTORS THAT PREDICT MORTALITY IN CHOLANGITIS

(Bae WK et al Korean journal ofGastroenterology 2008)

1. Age > 50 years
2. Female gender
3. associated liver abscess
4. associated cirrhosis
5. cholangitis due to high grade malignant obstruction
6. cholangitis after trans hepatic choledochography and
7. Acute renal failure

Cholangitis due to malignant obstruction is increasing mainly due to frequent use of endoscopic or radiological biliary drainage procedures. One third of patients with malignant biliary obstruction had history of ERCP in the past.

However, studies reported a high incidence of bacterobilia and fungal colonisation associated with pre operative biliary drainage. (Jethwa et al alim. pharmacology 2007) High antibiotic coverage is needed and may be modified after bile culture report. Special cultures for fungal growth should be done and managed accordingly and appropriately.

AIM OF THE STUDY

1. To evaluate the incidence of bacterobilia in patients with obstructive jaundice undergoing ERCP at our hospital.

2. To study the risk factors for bacterobilia.

3. To study the microbiological pattern of bile in obstructed biliary system.

4. To compare the frequency of bacterobilia in benign and malignant obstruction.

5. To study the drug sensitivity pattern of bacteria grown in bile culture in our center.

MATERIALS AND METHODS

PLACE OF STUDY:

Department of Digestive Health and Diseases

Government Peripheral Hospital

Anna nagar, Chennai.

TYPE OF STUDY:

Prospective ,observational and diagnostic study .

PERIOD OF STUDY

September 2011 to February 2012 .

ETHICAL COMMITTEE:

Approval obtained .

CONSENT :

Informed consent obtained from all participants of the study .

SELECTION OF PATIENTS:

INCLUSION CRITERIA

Age > 18 years

Evidence of cholestasis ;

1. Serum bilirubin > 2mg %

2. Serum alkaline phosphatase more than twice the upper limit of normal.

3. serum alanine transaminase more than twice the upper limit of normal.

4. Imaging -- ultrasound or CT abdomen showing dilated common bile duct.

30 consecutive patients who have documented evidence of obstructive jaundice who have undergone ERCP for biliary decompression and stenting at our centre during the study period were included.

EXCLUSION CRITERIA

1. Age less than 18 years .
2. Absence of informed consent .
3. Use of antibiotics within 7 days prior to ERCP .

METHODS

After ensuring adequate asepsis, biliary cannulation done after passing a guidewire under fluoroscopic guidance, around 10 ml of bile is aspirated before injecting contrast and the sample is collected and inoculated in bile broth and sent for microbiological analysis. Data collected were recorded for further work up.

Specific mention was made regarding the etiology benign or malignant, stone, stricture or growth .

Nature of fluid obtained, findings on cholangiogram if available are documented.

History of previous interventions ,number of attempts of

ERCP are all recorded .

STATISTICAL ANALYSIS

Statistical analyses were carried out to compare continuous variables using students test. Chi-squared analysis was used to evaluate categorical variables. A P value of <0.05 was considered statistically significant. All analysis were performed using SPSS 15.0 {SPSS.Inc.Chicago II}

P value

0 to 0.010 = ** =significant at 1% level

(Highly significant)

0.011 to 0.050 = * =significant at 5% level

(significant)

>0.05 = no star =not significant at 5% level

RESULTS AND STATISTICAL ANALYSIS

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age in years	30	24	86	50.77	15.364
BILIRUBIN	30	1	12	4.30	2.813
SAP	30	520	1000	734.67	122.568
TC	30	7000	11000	8283.33	971.697
Valid N (listwise)	30				

Frequency Table

Sex

		Frequency	**Percent**	**Valid Percent**
Valid	Male	13	43.3	43.3
	Female	17	56.7	56.7
	Total	30	100.0	100.0

ETIOLOGY

		Frequency	Percent	Valid Percent
Valid	Stone	17	56.7	56.7
	St.M	2	6.7	6.7
	St.B	6	20.0	20.0
	Growth	5	16.7	16.7
	Total	30	100.0	100.0

BILE C/S

		Frequency	Percent
Valid	Positive	16	53.3
	Negative	14	46.7
	Total	30	100.0

E.COLI

		Frequency	Percent
Valid	Positive	4	13.3
	Negative	16	53.3
	Total	20	66.7
Missing	System	10	33.3
Total		30	100.0

KLEBSILLA

		Frequency	Percent
Valid	Positive	8	26.7
	Negative	22	73.3
	Total	30	100.0

PSEUDOMONAS

		Frequency	Percent
Valid	Positive	4	13.3
	Negative	16	53.3
	Total	20	66.7
Missing	System	10	33.3
Total		30	100.0

CEFATAXIME

		Frequency	Percent
Valid	S	10	33.3
	R	6	20.0
	Total	16	53.3
Missing	System	14	46.7
Total		30	100.0

AMIKACIN

		Frequency	Percent
Valid	S	15	50.0
	R	1	3.3
	Total	16	53.3
Missing	System	14	46.7
Total		30	100.0

PIPERACILLIN - TAZOBACTUM

		Frequency	Percent
Valid	S	4	13.3
	R	5	16.7
	Total	9	30.0
Missing	System	21	70.0
Total		30	100.0

CEFTAZIDIME

		Frequency	Percent
Valid	S	6	20.0
	R	7	23.3
	Total	13	43.3
Missing	System	17	56.7
Total		30	100.0

CIPROFLOXACIN

		Frequency	Percent
Valid	S	2	6.7
	R	12	40.0
	Total	14	46.7
Missing	System	16	53.3
Total		30	100.0

Crosstabs

ETIOLOGY * BILE C/S

Crosstab

			BILE C/S		Total
			Positive	Negative	
ETIOLOGY	Stone	Count	9	8	17
		% within ETIOLOGY	52.9%	47.1%	100.0%
		% within BILE C/S	56.3%	57.1%	56.7%
	St.M	Count	2	0	2
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within BILE C/S	12.5%	.0%	6.7%
	St.B	Count	1	5	6
		% within ETIOLOGY	16.7%	83.3%	100.0%
		% within BILE C/S	6.3%	35.7%	20.0%
	Growth	Count	4	1	5
		% within ETIOLOGY	80.0%	20.0%	100.0%
		% within BILE C/S	25.0%	7.1%	16.7%
Total		Count	16	14	30
		% within ETIOLOGY	53.3%	46.7%	100.0%
		% within BILE C/S	100.0%	100.0%	100.0%

ETIOLOGY * E.COLI

Crosstab

			E.COLI		Total
			Positive	**Negative**	
ETIOLOGY	Stone	Count	3	9	12
		% within ETIOLOGY	25.0%	75.0%	100.0%
		% within E.COLI	75.0%	56.3%	60.0%
	St.M	Count	0	2	2
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within E.COLI	.0%	12.5%	10.0%
	St.B	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within E.COLI	25.0%	6.3%	10.0%
	Growth	Count	0	4	4
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within E.COLI	.0%	25.0%	20.0%
Total		Count	4	16	20
		% within ETIOLOGY	20.0%	80.0%	100.0%
		% within E.COLI	100.0%	100.0%	100.0%

ETIOLOGY * KLEB

Crosstab

			KLEB		Total
			Positive	**Negative**	
ETIOLOGY	Stone	Count	4	13	17
		% within ETIOLOGY	23.5%	76.5%	100.0%
		% within KLEB	50.0%	59.1%	56.7%
	St.M	Count	2	0	2
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within KLEB	25.0%	.0%	6.7%
	St.B	Count	0	6	6
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within KLEB	.0%	27.3%	20.0%
	Growth	Count	2	3	5
		% within ETIOLOGY	40.0%	60.0%	100.0%
		% within KLEB	25.0%	13.6%	16.7%
Total		Count	8	22	30
		% within ETIOLOGY	26.7%	73.3%	100.0%
		% within KLEB	100.0%	100.0%	100.0%

ETIOLOGY * PSEUDO

Crosstab

			PSEUDOMONAS		**Total**
			Positive	Negative	
ETIOLOGY	Stone	Count	3	9	12
		% within ETIOLOGY	25.0%	75.0%	100.0%
		% within PSEUDO	75.0%	56.3%	60.0%
	St.M	Count	0	2	2
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within PSEUDO	.0%	12.5%	10.0%
	St.B	Count	0	2	2
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within PSEUDO	.0%	12.5%	10.0%
	Growth	Count	1	3	4
		% within ETIOLOGY	25.0%	75.0%	100.0%
		% within PSEUDO	25.0%	18.8%	20.0%
Total		Count	4	16	20
		% within ETIOLOGY	20.0%	80.0%	100.0%
		% within PSEUDO	100.0%	100.0%	100.0%

ETIOLOGY * CEFATAXIME

Crosstab

			CEFATAXIME		Total
			S	R	
ETIOLOGY	Stone	Count	4	5	9
		% within ETIOLOGY	44.4%	55.6%	100.0%
		% within CEFTAX	40.0%	83.3%	56.3%
	St.M	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within CEFTAX	10.0%	16.7%	12.5%
	St.B	Count	1	0	1
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within CEFTAX	10.0%	.0%	6.3%
	Growth	Count	4	0	4
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within CEFTAX	40.0%	.0%	25.0%
Total		Count	10	6	16
		% within ETIOLOGY	62.5%	37.5%	100.0%
		% within CEFTAX	100.0%	100.0%	100.0%

ETIOLOGY * AMIKACIN

Crosstab

			AMIKACIN		Total
			S	R	
ETIOLOGY	Stone	Count	8	1	9
		% within ETIOLOGY	88.9%	11.1%	100.0%
		% within AMIK	53.3%	100.0%	56.3%
	St.M	Count	2	0	2
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within AMIK	13.3%	.0%	12.5%
	St.B	Count	1	0	1
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within AMIK	6.7%	.0%	6.3%
	Growth	Count	4	0	4
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within AMIK	26.7%	.0%	25.0%
Total		Count	15	1	16
		% within ETIOLOGY	93.8%	6.3%	100.0%
		% within AMIK	100.0%	100.0%	100.0%

EIOLOGY * PIPERACILLIN- TAZOBACTUM

Crosstab

			PIPERACILLIN TAZOBACTUM		Total
			S	R	
ETIOLOGY	Stone	Count	2	1	3
		% within ETIOLOGY	66.7%	33.3%	100.0%
		% within P - TAZ	50.0%	20.0%	33.3%
	St.M	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within P – TAZ	25.0%	20.0%	22.2%
	Growth	Count	1	3	4
		% within ETIOLOGY	25.0%	75.0%	100.0%
		% within P – TAZ	25.0%	60.0%	44.4%
Total		Count	4	5	9
		% within ETIOLOGY	44.4%	55.6%	100.0%
		% within P – TAZ	100.0%	100.0%	100.0%

ETIOLOGY * CEFTAZIDIME

Crosstab

			CEFTAZIDIME		Total
			S	R	
ETIOLOGY	Stone	Count	1	5	6
		% within ETIOLOGY	16.7%	83.3%	100.0%
		% within CEFTAZIDIME	16.7%	71.4%	46.2%
	St.M	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within CEFTAZIDIME	16.7%	14.3%	15.4%
	St.B	Count	1	0	1
		% within ETIOLOGY	100.0%	.0%	100.0%
		% within CEFTAZIDIME	16.7%	.0%	7.7%
	Growth	Count	3	1	4
		% within ETIOLOGY	75.0%	25.0%	100.0%
		% within CEFTAZIDIME	50.0%	14.3%	30.8%
Total		Count	6	7	13
		% within ETIOLOGY	46.2%	53.8%	100.0%
		% within CEFTAZIDIME	100.0%	100.0%	100.0%

ETIOLOGY * CIPROFLOXACIN

Crosstab

			CIPROFLOXACIN		Total
			S	R	
ETIO-LOGY	Stone	Count	0	9	9
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within CIPROFLOXACIN	.0%	75.0%	64.3%
	St.M	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within CIPROFLOXACIN	50.0%	8.3%	14.3%
	St.B	Count	0	1	1
		% within ETIOLOGY	.0%	100.0%	100.0%
		% within CIPROFLOXACIN	.0%	8.3%	7.1%
	Growth	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within CIPROFLOXACIN	50.0%	8.3%	14.3%
Total		Count	2	12	14
		% within ETIOLOGY	14.3%	85.7%	100.0%
		% within CIPROFLOXACIN	100.0%	100.0%	100.0%

Crosstabs

ETIOLOGY * Sex Crosstabulation

			Sex		Total
			Male	**Female**	
ETIOLOGY	Stone	Count	4	13	17
		% within ETIOLOGY	23.5%	76.5%	100.0%
		% within Sex	30.8%	76.5%	56.7%
	St.M	Count	1	1	2
		% within ETIOLOGY	50.0%	50.0%	100.0%
		% within Sex	7.7%	5.9%	6.7%
	St.B	Count	5	1	6
		% within ETIOLOGY	83.3%	16.7%	100.0%
		% within Sex	38.5%	5.9%	20.0%
	Growth	Count	3	2	5
		% within ETIOLOGY	60.0%	40.0%	100.0%
		% within Sex	23.1%	11.8%	16.7%
Total		Count	13	17	30
		% within ETIOLOGY	43.3%	56.7%	100.0%
		% within Sex	100.0%	100.0%	100.0%

E.COLI * CEFATAXIME

Crosstab

			CEFATAXIME		Total
			S	R	
E.COLI	Positive	Count	2	2	4
		% within E.COLI	50.0%	50.0%	100.0%
		% within CEFATAXIME	20.0%	33.3%	25.0%
	Negative	Count	8	4	12
		% within E.COLI	66.7%	33.3%	100.0%
		% within CEFATAXIME	80.0%	66.7%	75.0%
Total		Count	10	6	16
		% within E.COLI	62.5%	37.5%	100.0%
		% within CEFATAXIME	100.0%	100.0%	100.0%

E.COLI * AMIKACIN

Crosstab

			AMIKACIN		Total
			S	R	
E.COLI	Positive	Count	4	0	4
		% within E.COLI	100.0%	.0%	100.0%
		% within AMIKACIN	26.7%	.0%	25.0%
	Negative	Count	11	1	12
		% within E.COLI	91.7%	8.3%	100.0%
		% within AMIKACIN	73.3%	100.0%	75.0%
Total		Count	15	1	16
		% within E.COLI	93.8%	6.3%	100.0%
		% within AMIKACIN	100.0%	100.0%	100.0%

E.COLI * PIPERACILLIN - TAZOBACTUM

Crosstab

			PIPTAZ		**Total**
			S	**R**	
E.COLI	Negative	Count	4	5	9
		% within E.COLI	44.4%	55.6%	100.0%
		% within P - TAZ	100.0%	100.0%	100.0%
Total		Count	4	5	9
		% within E.COLI	44.4%	55.6%	100.0%
		% within P – TAZ	100.0%	100.0%	100.0%

E.COLI * CEFTAZIDIME

Crosstab

			FORTUM		Total
			S	R	
E.COLI	Positive	Count	1	2	3
		% within E.COLI	33.3%	66.7%	100.0%
		% within CEFTAZIDIME	16.7%	28.6%	23.1%
	Negative	Count	5	5	10
		% within E.COLI	50.0%	50.0%	100.0%
		% within CEFTAZIDIME	83.3%	71.4%	76.9%
Total		Count	6	7	13
		% within E.COLI	46.2%	53.8%	100.0%
		% within CEFTAZIDIME	100.0%	100.0%	100.0%

E.COLI * CIPROFLOXACIN

Crosstab

			CIPROFLOXACIN		Total
			S	R	
E.COLI	Positive	Count	0	4	4
		% within E.COLI	.0%	100.0%	100.0%
		% within CIPROFLOXACIN	.0%	33.3%	28.6%
	Negative	Count	2	8	10
		% within E.COLI	20.0%	80.0%	100.0%
		% within CIPROFLOXACIN	100.0%	66.7%	71.4%
Total		Count	2	12	14
		% within E.COLI	14.3%	85.7%	100.0%
		% within CIPROFLOXACIN	100.0%	100.0%	100.0%

KLEB * CIFRAN

Crosstab

			CIFRAN		Total
			S	R	
KLEB	Positive	Count	2	5	7
		% within KLEB	28.6%	71.4%	100.0%
		% within CIFRAN	100.0%	41.7%	50.0%
	Negative	Count	0	7	7
		% within KLEB	.0%	100.0%	100.0%
		% within CIFRAN	.0%	58.3%	50.0%
Total		Count	2	12	14
		% within KLEB	14.3%	85.7%	100.0%
		% within CIFRAN	100.0%	100.0%	100.0%

PSEUDO * TAXIM

Crosstab

			TAXIM		Total
			S	R	
PSEUDO	Positive	Count	2	2	4
		% within PSEUDO	50.0%	50.0%	100.0%
		% within TAXIM	20.0%	33.3%	25.0%
	Negative	Count	8	4	12
		% within PSEUDO	66.7%	33.3%	100.0%
		% within TAXIM	80.0%	66.7%	75.0%
Total		Count	10	6	16
		% within PSEUDO	62.5%	37.5%	100.0%
		% within TAXIM	100.0%	100.0%	100.0%

PSEUDO * AMIK

Crosstab

			AMIK		Total
			S	R	
PSEUDO	Positive	Count	4	0	4
		% within PSEUDO	100.0%	.0%	100.0%
		% within AMIK	26.7%	.0%	25.0%
	Negative	Count	11	1	12
		% within PSEUDO	91.7%	8.3%	100.0%
		% within AMIK	73.3%	100.0%	75.0%
Total		Count	15	1	16
		% within PSEUDO	93.8%	6.3%	100.0%
		% within AMIK	100.0%	100.0%	100.0%

PSEUDO * PIPTAZ

Crosstab

			PIPTAZ		Total
			S	R	
PSEUDO	Positive	Count	2	1	3
		% within PSEUDO	66.7%	33.3%	100.0%
		% within PIPTAZ	50.0%	20.0%	33.3%
	Negative	Count	2	4	6
		% within PSEUDO	33.3%	66.7%	100.0%
		% within PIPTAZ	50.0%	80.0%	66.7%
Total		Count	4	5	9
		% within PSEUDO	44.4%	55.6%	100.0%
		% within PIPTAZ	100.0%	100.0%	100.0%

PSEUDO * FORTUM

Crosstab

			FORTUM		Total
			S	R	
PSEUDO	Positive	Count	1	3	4
		% within PSEUDO	25.0%	75.0%	100.0%
		% within FORTUM	16.7%	42.9%	30.8%
	Negative	Count	5	4	9
		% within PSEUDO	55.6%	44.4%	100.0%
		% within FORTUM	83.3%	57.1%	69.2%
Total		Count	6	7	13
		% within PSEUDO	46.2%	53.8%	100.0%
		% within FORTUM	100.0%	100.0%	100.0%

PSEUDO * CIFRAN

Crosstab

			CIFRAN		Total
			S	R	
PSEUDO	Positive	Count	0	4	4
		% within PSEUDO	.0%	100.0%	100.0%
		% within CIFRAN	.0%	33.3%	28.6%
	Negative	Count	2	8	10
		% within PSEUDO	20.0%	80.0%	100.0%
		% within CIFRAN	100.0%	66.7%	71.4%
Total		Count	2	12	14
		% within PSEUDO	14.3%	85.7%	100.0%
		% within CIFRAN	100.0%	100.0%	100.0%

Crosstabs

ETIOLOGY * BILE C/S Crosstabulation

			BILE C/S		Total
			Positive	**Negative**	
ETIOLOGY	B	Count	10	13	23
		% within ETIOLOGY	43.5%	56.5%	100.0%
		% within BILE C/S	62.5%	92.9%	76.7%
	M	Count	6	1	7
		% within ETIOLOGY	85.7%	14.3%	100.0%
		% within BILE C/S	37.5%	7.1%	23.3%
Total		Count	16	14	30
		% within ETIOLOGY	53.3%	46.7%	100.0%
		% within BILE C/S	100.0%	100.0%	100.0%

BILE C/S

	Observed N	Expected N	Residual
Positive	16	15.0	1.0
Negative	14	15.0	-1.0
Total	30		

30 Consecutive cases who have undergone ERCP at our institution, and successful biliary cannulation were studied .Among them ,13 were males 43.3% and 17 (56.7% were females .

Mean age was 50.77 with standard deviation of 15 .364 .

Among the 30 cases ,23 have benign disease and 7 have malignant disease.

17 patients had common bile duct stones (56.7%)

5 patients had malignant growth .(16.7 %)

6 had benign biliary stricture (20 %)

2 had malignant biliary stricture .(6.7)

Bile culture was positive in 16 patients .(53 .3%) and negative in 14 patients .(.46 .7 %) .Benign -10 malignant-6 .(p-value <0.05).

Almost all positive bile cultures grew gram negative bacilli.9 out of 16 have grown Klebsiella .(p-value-significant at 5% level)

4 cultures were positive for E.coli .

Pseudomonas was grown in 3 cultures .

Almost all except one growth on culture were monomicrobial.

Most of the organisms grown in bile were sensitive to Amikacin , cefotaxime and ceftazidime (p-value-not significant)

Most of them were resistant to ciprofloxacin .

DISCUSSION

In our study ,we found that asymptomatic bacterobilia was more common than earlier reports.(53.3 %).

Variation with underlying pathology is common.

Among the risk factors ,common bile duct stones are the commonest . (56.7% sensitive).

Only 20 % of benign biliary stricture had a positive bile culture .

Malignant biliary strictures showed 6 .7 % positivity.

Micro-organisms grown in bile culture were predominantly gram negative bacilli .

Klebsiella was predominant E .coli comes the next .

Unusual bacteria like pseudomonas and staphylococci may grow in culture and may be due to iatrogenic introduction of bacteria by poorly sterilized endoscope or a percutaneous drain .Incidence ranges from 0 to 25 % and may reflect prior biliary intervention or

antibiotic usage .In our case, no such history available in the subgroup with pseudomonas positivity by culture.

It is noticeable that bacterobilia is found in patients without biliary sepsis . Obstruction leads to sepsis ,as increase in biliary pressure induces regurgitation of bile. The biliary contents reflux into sinusoids when biliary pressure increases to 25cm of water.

Regarding treatment with antibiotics ,studies have shown that antibiotics used should be active against gram negative bacilli. Quinolones are preferred because they are effective when given orally .They effectively penetrate in obstructed biliary tree.

In our study most organisms grown on culture are resistant to ciprofloxacin. (E.coli-100 % , Klebsiella-71 .4 % pseudomonas -100 %)

Most organisms responded to cefotaxim ,ceftazidine and amikacin.

Patients with CBD stone disease have a higher incidence of bacterobilia . Previous studies around 84 % in a study of 70 patients (Keighley et al), 83 % in a study of 545 patients (Maluenda et al) and 82 % in a study of 65 patients .(Pitt et al)

Patients with malignant obstruction have lesser incidence of bacterobilia , Previous studies also confirm the same.

(46 % Pitt et al .,30 % Keighley et al .,21 % Maluenda et al)

Benign biliary strictures have a higher incidence of bacterobilia in earlier studies which are consistent with our findings Pre-operative biliary drainage in malignant obstruction could be beneficial in patients with sepsis ,co-agulation abnormalities and malnutrition .(Dig .surg 2001 18 84—89).

Pre -operative biliary drainage is associated high incidence of bacterobilia and fungal colonisation . (Alim . pharma cology 2009 Jethwa et all).

None of the patients in our study presented with clinico imaging suggestive of cholangitis .None had previous biliary intervention. Bacterobilia is present only in obstructed biliary system .Bile is usually sterile in normal individuals . Hatfield et al [19] observed 0% growth in a study of 10 patients in normal individuals .Csenda et al[16] also observed 0 % growth in normal bile in a study of 20 patients .Nielson and Justesen et al[17] observed 0 % growth in unobstructed bile in a study of 38 patients .

Bacterobilia is commonly present in obstructed biliary system due to common bile duct stone and is documented in various studies .Keighly et al[24] in a study of 70 patients with common bile duct stone disease observed bacterobilia in 84% of cases .Pitt et al [25]observed 82 % bacterobilia in a study of 65 patients .

Maluenda et al [26]observed 83 % bacterobilia in 545 patients studied .Kosowski et al[27] in a study of 34 patients observed 82 % of bacterobilia in stone disease .Leung et al [28]in a study of 896 patients with stone disease observed 64 % of bacterobilia .Landau et al [29]in his study of 436 patients with stone disease observed 61% of bacterobilia .Wells et al (30) in his study of 73 patients of stone disease observed 73 % of bacterobilia .

Recent studies by Ahamed et al[50] quoted in GI endoscopy 2010 also observed positive bile cultures in 18 out of 20 cases with CBD stone disease.

Sahu et al[52] in their study published in IJG sept 2011 observed bacterobilia in 88 of 95 patients studied.

Bacterobilia in malignant obstruction were comparatively less than those observed with stone disease,as observed in previous studies.

Pitt et al - 46% in 35 patients studied.

Well et al 31 % in 16 patients studied.

Keighley et al - 30% in 102 patients studied.

Mannala et al - 27 % in 91 patients[31]

Nielson and Justesen 0 % in 28 patients.

Our study also observed the same finding with bacterobilia predominant in benign biliary obstruction , most commonly due to common bile duct stone disease .

Growth pattern in bile culture varied in different studies

In a study published in Alimentary pharmacological therapy 1995, the microbiological profile observed are as follows.

E .coli 55%

Klebsiella 20- 30 %

Proteus -5 %

Salmonella -0-3%

Pseudomonas –0-25%

Pitts et al of 25 patients

E coli -52 %

Klebsiella -34%

Pseudomonas -25%

Malusuda et al –of 230 patients

Ecoli 52 %

Klebsiella 14 %

Pseudomonas 0%

Recent studies by Sahu et al [52]and Ahamed et al[50] also confirmed E.coli as a predominant organism grown in bile culture . But in our study, the predominant organism grown was klebsiella. (9 out of 16 positive cases. whereas E .coli was grown in 4 cultures.

Antibiotic sensitivity is consistent with earlier studies in that most of them respond to cephalosporins and amikacin. But in contrast to earlier studies, sensitivity to ciprofloxacin was not

consistent .In fact ,most of the organisms grown on culture are resistant to ciprofloxacin.

Gram positive bacteria and anaerobes were not grown in culture in our study.

Thawee Ratanachu et al[47], in a study published in world journal of gastroenterology 2007, studied the role of ciprofloxacin in patients with cholestasis after ERCP. They observed that ciprofloxacin was effective in the study population .

An Indian study conducted by Shivaprakash et al reported high resistance to ciprofloxacin, correlates with our observation [53]

Aggarwal et al conducted a study in2006 in patients with cholangitis.70% of patients of 175 studied had common bile duct as etiology[54]

Bacteria % positive bile culture	Maluenda *et al.*[26] 230 pts with CBD stones clear bile 76%	Maluenda *et al.*[26] 315 pts with CBD stones turbid bile 92%	Pitt *et al.*[25] 134 pts with obstructive jaundice 66%	Leung *et al.*[28] 896 pts with CBD stones 80% cholangitis 67%	Meijer & Schmitz[48] 934 pts for biliary surgery 35%	Sung *et al.*[44] 76 pts with suppurative cholangitis 89%
E. Coli	52%*	57%	52%	58%	58%	44%
Klebsiella spp.	14%	18%	34%	36%	22%	29%
Enterobacter spp.	8%	10%	10%	17%	5%	13%
Citrobacter spp.	6%	3%	2%	6%	0%	4%
Proteus spp.	3%	7%	10%	6%	4%	9%
Pseudomonas spp.	0%	0%	25%	15%	0.3%	13%
Bacteroides spp.	0.5%	1%	18%	3%	5%	9%
Other Gram-negative	2%	6%	16%	0%	13%†	28%
Enterococcus spp.	13%	11%	40%	36%	0%	53%
Other Gram-positive	8%	5%	35%	21%	39%‡	44%
Clostridium spp.	16%	10%	5%	4%	10%	7%
Salmonella spp.	5%	3%	0%	0%	0%	0%
Polymicrobial	23%	29%	0%	71%	36%	82%

* Percentage of positive cultures. Because of polymicrobial infections the sum of percentages may be greater than 100.

† Labelled 'other organisms'.

‡ Including 34% labelled 'aerobic streptococci'.

21 % had malignancy .

Shimada et al in 1981 ,studied 23 bile cultures in aged population .All had a positive bile culture .Out of them ,15 yielded both aerobic and anaerobic growth and 8 had only anaerobic growth .E.coli,klebsiella,enterococci and bacteroides fragilis were isolated .He also suggested that treatment of anaerobic infections in the elderly is mandatory .

Condition	% bacterobilia	Number of patients	Reference
Normal	0%	10	Hatfield *et al.*[19]
	0%	20	Csendes *et al.*[16]
	0%	38	Nielsen & Justesen[17]
Biliary obstruction: malignant	46%	35	Pitt *et al.*[25]
	31%	16	Wells *et al.*[30]
	30%	102	Keighley *et al.*[24]
	27%	91	Mannella *et al.*[31]
	0%	28	Nielsen & Justesen[17]
Biliary obstruction: benign stricture	90%	86	Keighley *et al.*[24]
	86%	14	Pitt *et al.*[25]
CBD stones	84%	70	Keighley *et al.*[24]
	83%	545	Maluenda *et al.*[26]
	82%	65	Pitt *et al.*[25]
	82%	34	Kosowski *et al.*[27]
	64%	896	Leung *et al.*[28]
	61%	436	Landau *et al.*[29]
	32%	73	Wells *et al.*[30]
Post-endoscopic sphincterotomy	88%	17	Sand *et al.*[13]
Ascending cholangitis	100%	23	Shimada *et al.*[43]
	92%	113	Maluenda *et al.*[26]
	89%	76	Sung *et al.*[44]
Post t-tube	100%	133	Sheen-Chan *et al.*[39]

CONCLUSION

Bacterobilia is common in obstructed biliary system and are usually asymptomatic.

It is more common in benign biliary obstruction than malignant biliary obstruction.

Most common risk factor for bacterobilia observed in our study is common bile duct stone.

Other risk factors identified in our study include malignant growth and biliary strictures.

Biliary decompression with stent placement helps in symptomatic relief.

Bile culture is useful in early diagnosis and prevention of complications.

Gram negative bacilli infection is very common in obstructed biliary system.

Klebsiella is the commonest organism grown in our study.

Escherichia.coli is the second commonest organism isolated from bile culture in our study.

Pseudomonas aeroginosa is the third commonest organism grown in our study.

Microbiological sensitivity pattern is different in our study.

Most of them respond ed to third generation cephalosporins and amikacin and resistance to ciprofloxacin was common. In conclusion, routine bile cultures done for all patients during ERCP in patients presenting with biliary obstruction can help in predicting early biliary sepsis which will respond to antibiotics and prevent dreaded complications.

BIBLIOGRAPHY

1. Green J and Better os -- journal of American society of nephrology 1995 ; 5 ;1853- 71.

2. Bomson A Jacob G and Better os --The kidney in liver diseases -Baltimore ,Hanley and Belfur -1996 ;423-46.

3. Fogarty B .Parker R.W-British Journal of Surgery 1995;62; 877-84.

4. Harry DS and Mc Lyntyre et al – Liver Biliary diseases . 3rd edn .London W.B.Saunders 1992; 61-78.

5. Hay J.E. –Gastroenterology 1995 ;108;276-283.

6. Kimmings AN et al –Journal of American college of surgery1995 ;181 ;567-81 .7

7. BaeWKet al-Korean journal of GE 2008;51(4) 248-54.

8. Kaorushimada et al –journal of clinical n-micro ;nov1981 522-526.

9. Scott A J et al Lancet 1967 ;2 ;790-92 ..

10. Sung JY et al Hepatology 1991;14 ;113-17.

11. Dowidar et al Scandinavian Journal of Gastro enterology 1991 ;26 ; 113-44.

12. Han ke et al Langenbeck Arch Chir 1980; 353 121-7.

13. SandJ et al -American journal of surgery 1992 ;58;324-8.

14 . Nagura et al - journal of immunology 1987 ;126 ;587-95.

15. Sung JU et al -Dig .Dis .Science 1993;38 ;2104 -12.

16. Csendes et al –American journal of surgery 1975 ;129 ;629-31

17. Nielson et al - Scandinavian Journal of gastroenterology 1976 ;11 ;437- 46 .

18. Edlund et al - Acta chir Scand 1959 ;116 ;461- 76 .

19. Hatfild et al -Journal of infectious diseses -1982 ;4 ;119 -25 20. Sung JU et al –GI endoscopy 1994 ;40 ;127

21. Deitch et al -American journal of surgery .1990 ;15;979-84 .

22. Pain J.A et al –British journal of surgery .1987 ;74 ;1091-94

23. Robenek et al –American journal of pathology 1980 ;100;93-114 .

24. Keighley et al -surgery of liver and biliary tree – Churchill Livingstone 1987 ;121-137 .

25. Pitt H A et al – Archives of surgery 1982 ;117 ;445-9.

26. Malueda et al –Hepatogastroenterology .1989;36;132-5 .

27. Kosowski et al – European journal of clinical microbiology .1987 ;6; 575-8 .

28. Leung et al -GI endoscopy 1994 ;40;716-21.

29. Landau et al - world journal of surgery 1992 ;16 ;962-5.

30. Wells GR et al - British journal of surgery 1989 ;76; 374-7 .

31 ‘Mannala - Minerva medicine 1985 ;76; 1917-20 .

32. Wang et al .- Chinese journal of surgery 1931;28-278-80-

33. Bapat et al –Indian journal of gastroenterology 1996 ;15;126-8 .

34. Cryan FM - journal of hospital infection 1984 ;5 ;371-6 .

35. Basi et al –S .African med journal 1990 ;77;509-11.

36. Helm et al Disch med Wochenschr 1984 ;109 ;697-701 .

37. Doherthy et al –Dig .Dis .Sci - 1982 ;27 ;169-70

38. Siegmann et al -Scand journal of infective diseases -1987 ;19 ;527-30 .

39. Shen Chen et al -- Archives of surgery 1995;130 ;20-3.

40. Audisio et al - surgery 1988;103;507-12.

41. Mothe et al -- Gastroenterology 1991 ;101;1374-81 .

42. Brook et al –journal of clinical microbiology 1989;27; 2373-5 .

43. Shimada et al -- journal of clinical microbiology1987;14;422-6

44. Sung et al - journal of anti bacterial chemotherapy-1995;35;855-64.

45. Niekson et al –Scandinavian journal of gastroenterology -- 1976;11;265-72.

46. JM.Subhan et al - Alimentary pharmacology and therapeutics – 1999 ;13 ;103-116 .

47. Thawee Ratanachu et al W J G-January 2007 .

48. Jagannath et al -ISG- 2003 Jan-Feb2003 vol 22.

49. Attasaranya et al - MCNA 2008(92) 925- 960.

50. Ahamed et al -GI endoscopy –vol -72 no.2 ; 2010.

51. Wada et al -- journal of hepatobiliary pancreatic surgery-2007;14;52-58.(Tokyo guidelines .)

52. Sahu et al-indian journal of gastroenterology sep-oct 2011 30(5)204-2

53. Shivaprakash et al –Indian journal of patho and micro 2006;49;464-7.

54. Agarwal et al –world journal of gastroenterology2006;12;6551-5.

PROFORMA

DDHD No

ERCP No

Name of the patient:

Age and sex:

Presenting symptoms-

fever, abdominal pain, pruritus,

Loss of appetite and weight, jaundice,altered sensorium

Past history of jaundice,ERCP,HT,DM,CAD,Abdominal surgery,drug intake,organ transplantation,

Exposure to STD,alcohol consumption,smoking.

Urine routine, complete haemogram, blood urea, blood sugar, LFT

Chest x-ray, USG abdomen,

CT abdomen, MRCP

Blood culture and sensitivity;Bile culture and sensitivity

Present and previous ERCP-indications and complications