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All authors should have made substantial contributions to all of the following:

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Indexing

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Contents

Endoscopic Retrograde Cholangiopancreatography (ERCP) in Cirrhotic Patients

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See the article pages

Introduction

Endoscopic retrograde cholangiopancreato-graphy (ERCP) is an endoscopic technique in which a specialized side-viewing upper endoscope is guided into the duodenum, the bile and pancreatic ducts are opacified by injection of a contrast medium, and allowing for a variety of therapeutic interventions [1].

Patients with cirrhosis can tolerate ERCP to treat their biliary tract or pancreatic diseases. Patients with liver cirrhosis are 3 times more susceptible to cholelithiasis, than the non-cirrhotic population plus the biliary and pancreatic cancer and other disease. Child—Pugh classification is the determinative factor of ERCP treatment and the most important predictor of outcome in these patients. The main severe complication post—ERCP is bleeding [2].

Indications for ERCP

Indications for ERCP in cirrhotic patients are no different from those in general population. According to National Institutes of Health statement in 2002 [2,3]:

1. ERCP is sensitive and specific in diagnosis of choledocholithiasis.
2. ERCP with sphincterotomy and stone removal is a valuable therapeutic modality in choledocholithiasis with jaundice, dilated common bile duct, acute pancreatitis, or cholangitis.
3. In patients with pancreatic or biliary cancer, the principal advantage of ERCP is palliation of biliary obstruction when surgery is not elected.
4. Tissue sampling for patients with pancreatic or biliary cancer not undergoing surgery may be achieved by ERCP, but this is not always diagnostic.
5. ERCP is the best means to diagnose cancers of ampulla of vater .
6. In patients with severe biliary pancreatitis, early intervention with ERCP reduces morbidity and mortality compared with delayed ERCP.
7. ERCP with appropriate therapy is beneficial in selected patients who have either recurrent pancreatitis or pancreatic pseudocysts.
8. Patients with type I sphincter of Oddi dysfunction (SOD) respond to ERCP with sphincterotomy.
9. ERCP is the gold standard for diagnosis of primary biliary cirrhosis(PSC).
10. Diagnosis & treatment of portal biliopathy that includes abnormalities in the intrahepatic and extrahepatic biliary tract, gallbladder and cystic duct secondary to portal hypertension mostly caused by distended venous collaterals .

Contraindications for ERCP

According to American Society of Gastrointestinal Endoscopy guidelines in 2005 [4]:

1- Diagnostic ERCP should not be undertaken in the evaluation of pancreaticobiliary pain in the absence of objective findings on other imaging studies.
2- Routine ERCP before laparoscopic cholecystectomy should not be performed.

Other general contraindications [1]:

Acute pancreatitis (unless persistently raised or worsening bilirubin suggests ongoing obstruction)

- Previous pancreatoduodenectomy.
- Marked coagulopathy if sphincterotomy planned.
- Recent myocardial infarction.
- Inadequate surgical back-up.
- History of contrast dye anaphylaxis.
- Poor health condition for surgery.

- Severe cardiopulmonary disease.

Complications of ERCP

According to American Society of Gastrointestinal Endoscopy guidelines in 2005 [4]:
ERCP is associated with some complications and adverse events can be divided into two main groups:

1- Specific complications [6]:

Pancreatitis: The most frequent complication of ERCP, although most cases are mild and pass without complications.

Bleeding: Bleeding during ERCP typically develops after sphincterotomy.This is the most common & most serious in cirrhotic patients.

Infection: Infections occurring after ERCP are most often due to manipulation of an obstructed biliary or pancreatic system.

Perforation: ERCP may rarely be complicated by perforation of the esophagus, stomach, duodenum, or jejunum.

2- General complications :

Medication-related: complications related to Anticholinergic drugs, oversedation by benzodiazepines &/or opiates, contrast allergy [6,7].

Cardiopulmonary complications: such as aspiration, hypoxemia, gas embolisms and cardiac dysrhythmia [8].

Electrosurgical hazards: Excessive cautery can lead to perforation, while inadequate cautery increases the risk of bleeding. [5,8].

Miscellaneous complications: include gallstone ileus, colonic perforation, liver abscess, splenic, hepatic or vascular trauma, pneumothorax, impaction of retrieval baskets, complications related to biliary and pancreatic stents, biloma [6].

In this issue of the Afro-Egyptian Journal of Infectious and Endemic diseases, El-Naggar et al., performed free hand needle fistulotomy in the subgroup of cirrhotic patients with difficult cannulation. The maneuver was performed with high success rate and fewer complications. These findings emphasis that invasive techniques can be performed safely and successfully in well prepared cirrhotic patients. Cirrhosis is a major health problem in the Egyptian community and cirrhotic patients are not infrequently referred to the ERCP due to a variety of causes. The major problems that may face patients with cirrhosis are related to the bleeding tendencies and problems of anesthesia. According to El-Naggar et al., both can be controlled by proper preparation using the fresh plasma, vitamin K supplementation as well as step wise use of sedation. This study open the doors for application of further invasive techniques in cirrhotic patients without fear from further complications. However, this study have some limitations. Firstly, the limited number of patients in each arm. Secondly, exclusion of patients with Child C cirrhosis, in fact these patients represent challenge for all invasive procedures and are frequently seen with indications for ERCP, probably further studies focusing these patients may answer the question whether or not Child C cirrhotics can tolerate ERCP.

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Urinary Infection –One of The Most Common Bacterial Infections in Clinical Practice

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Urinary tract infection is one of the most common bacterial infections encountered in clinical practice. Most infections are uncomplicated. Complicated infections are caused by an abnormal urinary tract or a foreign body, the most common of which is catheter –associated urinary tract infection.

INTRODUCTION

Urinary tract infections may be referred to as cystitis or pyelonephritis, terms that refer to the lower and upper urinary tract, respectively. The terms bacteriuria and candiduria describe bacteria or yeast in the urine. Very ill patients may be referred to as having urosepsis. Urinary tract infections occur more commonly in women than men, with half of women having an infection at some point in their life. Recurrences are common. Risk factors include sexual intercourse as well as a family history. Pyelonephritis usually follows a bladder infection but may also occur from a blood borne infection. Diagnosis in young healthy women can be based on symptoms alone. In those with vague symptoms, diagnosis can be difficult, because bacteria may be present without there being an infection. In complicated cases or if treatment has failed, a urine culture may be useful. In those with frequent infections, low dose antibiotics may be taken as a preventative measure. In uncomplicated cases, urinary tract infections are easily treated with a short course of antibiotics, although resistance to many of the antibiotics used to treat this condition is increasing. In complicated cases, longer course or intravenous antibiotics may be needed, and if symptoms have not improved in two or three days, further diagnostic testing is needed. In women urinary tract infections are the most common form of bacterial infection with 10% getting urinary tract infections yearly.

PATHOPHYSIOLOGY

The urinary tract is normally sterile. Uncomplicated urinary tract infections, involves the urinary bladder in a host without underlying renal, metabolic, or neurologic diseases. Cystitis represents bladder mucosal invasion, most often by enteric coliform bacteria (eg., Escherichia coli) that inhabit the periurethral vaginal introitus and ascend into the bladder via the urethra. Because sexual intercourse may promote this migration, cystitis is common in otherwise healthy young women. Generally, urine is a good culture medium. Factors unfavorable to bacterial growth include a low pH (5.5 or less), a high concentration of urea, and the presence of organic acids derived from a diet that includes fruits and protein. Organic acids enhance acidification of the urine. Most uropathogens gain access to ascending route. The shorter length of the female urethra allows uropathogens easier access to the

bladder. The continuous unidirectional flow of urine helps to minimize urinary tract infections, and anything that interferes with this increases the host's susceptibility to urinary tract infections. Examples of interference include volume depletion, sexual intercourse, urinary tract obstruction, instrumentation, use of catheters not drained to gravity, and vesicoureteral reflux. Secretory defenses help promote bacterial clearance and prevent adherence. Secretory immunoglobulin A (IgA) reduces attachment and invasion of bacteria in the urinary tract. Women who are nonsecretors of the ABH blood antigens appear to be at higher risk for recurrent urinary tract infections.This may occur because of a lack of specific glycosyltransferases that modify epithelial surface glycolipids, allowing E. coli to bind to them better. In premenopausal women, lactobacilli are the predominant vaginal flora and serve to suppress vaginal colonization by the uropathogens.Most antibiotics, except sulfamethoxazole and the quinolones, can eradicate these protective bacteria. Urine itself has several antibacterial features that suppress urinary tract infections. Specifically, the pH, urea concentration, osmolarity, and various organic acids prevent most bacteria from surviving in the urinary tract.

MICROBIOLOGY OF UTI

E.coli, is the cause of 80-85% of urinary tract infections, with *Staphylococcus saprophyticus* being the cause in 5-10%[1]Rarely they may be due to viral or fungal infections. [2] Other bacterial causes include. *Klebsiella, Proteus, Pseudomonas,* and *Enterobacter*. These are uncommon and typically related to abnormalities of the urinary system or urinary catheterization.[3] Urinary tract infections due to Staphylococcus aureus typically occurs secondary to blood infections.[4]

CATHETERS

Urinary catheterization increases the risk of urinary tract infections.The risk of bacteriuria, is between three to six percent per day and prophylactic antibiotics are not effective in decreasing symptomatic infections. [5] The risk of an associated infection can be decreased by catheterizing only when necessary, using aseptic technique for insertion, and maintaining unobstructed closed drainage of the catheter.[6,7]

FAMILY HISTORY

A predisposition for bladder infections may run in families. Other risk factors include diabetes, [8] being uncircumcised, and having a large prostate. [9] Complicating factors are rather vague and include predisposing anatomic, functional, or metabolic abnormalities. A complicated urinary tract infections is more difficult to treat and usually requires more aggressive evaluation, treatment and follow-up. In children urinary tract infections are associated with vesicoureteral reflux and constipation. [9]

PROGNOSIS

The prognosis for most women with cystitis and pyelonephritis is good. However, the prognosis for emphysematous pyelonephritis is not as good. Infected cysts in polycystic kidney disease respond to treatment slowly. Although simple lower urinary track infections may resolve spontaneously, effective treatment lessens the duration of symptoms and reduces the incidence of progression to upper urinary track infections. Younger patients have the lowest rates of morbidity and mortality. Factors associated with an unfavorable prognosis include.

- Old age
- General debility
- Renal calculi or obstruction
- Recent hospitalization
- Urinary tract instrumentation or antibiotic therapy
- Diabetes mellitus
- Chronic nephropathy
- Sickle cell anemia
- Underlying cancer
- Intercurrent chemotherapy

IN CHILDREN

In young children, the only symptom of a urinary tract infection may be a fever. Because of the lack of more obvious symptoms, when females under the age of two or uncircumcised males less than a year exhibit a fever, a culture of the urine is recommended. Infants may feed poorly, vomit, sleep more, or show signs of jaundice. In older children, new onset urinary incontinence may occur.[9]

IN THE ELDERLY

Urinary tract symptoms are frequently lacking in the elderly. They may have vague presentations with incontinence, a change in mental status, or fatigue as the only symptoms. Diagnosis can be complicated by the fact that many elderly people have preexisting incontinence. Some elderly present to a health care provider with sepsis being the first symptoms [10].

CATHETER-ASSOCIATED URINARY TRACT INFECTION

Most patients with urinary tract abnormalities are referred to urologists. The closed urinary catheter system has a plastic bag fused to the distal end of a collection tube, allowing drainage so that the urine is always contained within a lumen closed to the environment. Even with meticulous attention to maintenance, the space between the external catheter and urethral mucosa provides an opportunity for direct entry of bacteria into the bladder. 10% to 30% of hospitalized patients with catheters develop bacteriuria. *E.coli* is the most common cause of catheter-related urinary tract infections, although it comprises only 25% of isolates. Other common causative organisms include *Enterococci, Pseudomonas aeruginosa, K.pneumoniae, P.mirabilis, Enterobacter sp., Staphylococcus epidermidis,* and *Staphylococcus aureus*. *Candida* may be isolated and appears to be increasing in prevalence, particularly when antibiotics are used .

Many modifications have made to the closed catheter systems, but most have not markedly improved the ability of the system to postpone bacteriuria. The use of systemic antibiotics has been more successful. Up to 80% of patients receive antibiotics during, but not usually because of, catheterization, and most studies have demonstrated a lower incidence of bacteriuria. When antibiotics are used. However, antibiotics are usually effective only for the first several days, after which resistant organisms begin to appear. Most authorities believe that antibiotics are not indicated for postponing bacteriuria in catheterized patients because of side effects, cost and emergence of antibiotic-resistant bacteria. However, antibiotics may be appropriate in patients at high risk for the complications of catheter-associated bacteriuria (eg., renal transplant recipients and granulocytopenic patients). Two catheter - related principles are universally recommended:

-Keep the closed catheter system closed،

-Remove it as soon as possible.

Urine specimens should be obtained by needle and syringe, without opening the catheter-collection tube junction. Most catheter systems have parts on the distal catheter for needle aspiration of urine .If the catheter can be removed before bacteriuria develops, postponement of bacteriuria becomes prevention. Most episodes of short-term catheter-associated bacteriuria are asymptomatic. However, catheter-associated bacteriuria can be accompanied by fever, acute pyelonephritis, bacteremia, and death. In nursing homes, the incidence of catheter-associated bacteriuria is approximately the same as in hospitals. Because catheters in nursing home patients may be in place for months or years, almost all patients with indwelling catheters in nursing homes are bacteriuric. Indeed, polymicrobial bacteriuria is present in up to 95% of urine speciments from long-term catheterized patients. These colonizations are caused by common uropathogens, such as *E. coli, P. aeruginosa,* and *P. mirabilis,* as well as less familiar species, such as *providencia stuartii* and *Morganella morganii* .

Complications of long-term catheter-associated bacteriuria fall into two categories. The first category includes symptomatic urinary tract infections, such as those associated with short-term catheterization(i.e., fever, acute pyelonephritis, bacteremia, and death).The second category includes complications associated primarily with long-term catheterization, such as catheter obstruction, urinary tract stones, local periurinary infections, chronic renal inflammation, renal failure, and after years of catheterization, bladder cancer. There are few data justifying the use of antibiotics in catheterized patients. However, antibiotic treatment is often necessary for symptomatic patients.In the catheterized patient who develops fever and/or signs of bacteremia, the clinician should rule out sources of infection outside the urinary tract, catheter obstruction, and periurethral infection, such as apidedimitis or prostatitis in men; blood and urine cultures should be obtained. Those patients should be empirically treated with parenteral antibiotics at doses high enough to achieve concentrations in serum that are adequate to treat bacteremia .

Antibiotic selection should be based on knowledge of the organisms that are common in the medical unit and a Gram's stain of the patient's urine. Treatment should be modified on the basis of antibiotic susceptibilities. Seven to ten days of therapy is usually sufficient and may include oral administration. The occasional patient with bladder symptoms, such as lower abdominal pain without fever or other evidence of systemic infection, may, benefit from treatment with an oral antibiotic that is active against the causative organism in vitro. Because bacteria may be sequestered in a biofilm on the catheter surface, it may be reasonable to replace or remove the catheter. Candiduria may develop in catheterized patients, and the incidence is directly related to the duration of catheterization, hospitalization, and antibiotic use. The ideal approach to avoiding catheter-associated bacteriuria is to avoid catheterization .

Nursing care, patient training, and special garments and bed clothes can be used instead of catheterization in many situations. Other devices or techniques that assist in urinary drainage, including, condom catheters, intermittent catheterization, and suprapubic catheterization, should also be considered [6,8,10].

CONCLUSION

Anyone with a long-term indwelling urinary catheter is at risk of developing a urinary tract infection (UTI). Using a catheter can introduce bacteria into the bladder and cause a UTI. The longer the catheter stays in the bladder, the greater this risk so that, after 30 days, bacteria will inevitably be present in the urine. This bacteriuria may or may not cause symptoms, but bacteria multiply quickly in the urine and the constant friction of an indwelling catheter on the lining of the bladder ulcerates its surface, enabling the bacteria to invade the bladder wall and blood stream. From the bladder, infection can spread up the tubes or ureters to the kidneys. The catheter is held in the bladder by a balloon, which is filled with sterile water, and this prevents the bladder from emptying completely so that you always have some residual urine in the bladder, and that will be infected by bacteria. Secondly, the catheter has a protuberant tip and this can damage that surface lining in the bladder and the eye holes are in the tip of the catheter, not at the base of the bladder. So we have here a problem which does mean that the catheter is associated with a very high incidence of healthcare infections. In fact it accounts for more healthcare infections worldwide than any other medical device.

Proper adherence to the outpatient medical regimen should be stressed. Behavior modification such as good oral fluid intake to enhance diuresis, frequent voiding, and drinking fruit juices to acidify the urine are helpful in reducing recurrent infection.

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Pneumocystis jiroveci: Epidemiology and diagnosis

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The *Pneumocystis* organism was initially described in 1909 by Chagas. *Pneumocystis jiroveci* is an uncommon opportunistic organism, which induces a severe and mostly fatal pneumonia in immunocompromised people. Pneumocystosis comes from reactivation of latent infection acquired while childhood or active acquisition while immunosuppression state. The epidemiology of *Pneumocystis* pneumonia (PCP) has changed considerably through the course of the HIV/AIDS epidemic. The establishments of PCP prophylaxis in 1989 and effective combination antiretroviral therapy in 1996, have resulted in substantial reduces in the incidence of PCP. Due to the insufficient specificity of clinical symptoms as well as the possibility of toxicity with therapy, the affirmation of PCP is important details for correct patient management. The traditional method for diagnosis of PCP depends on the microscopic visualization of organisms in respiratory samples. PCR diagnosis of *P. jiroveci* was introduced experimentally in 1990. Molecular methods, could detect *P jirovecii* DNA in respiratory samples from patients without clinically apparent PCP. In this review both epidemiology and diagnosis of *Pneumocystis jiroveci* will be discussed.

INTRODUCTION

Pneumocystis jiroveci is an uncommon opportunistic organism, which induces a severe and mostly fatal pneumonia in immunocompromised people [1]. The *Pneumocystis* organism was initially described in 1909 by Chagas in Guinea pigs, and after that by Carini in rat lung [2]. Until 1980 *Pneumocystis* pneumonia (PCP) was unusual and primarily noticed in association with syndromes of immunodeficiency or intensive immunosuppression, particularly cancer chemotherapy. With the HIV-1 pandemic, however, PCP become the major AIDS defining disease in developed countries[3]. *Pneumocystis jiroveci*, consequently, continues to be an organism of clinical significance in today's practice [4]

ORGANISM

Pneumocystis organisms were primarily known and named *Pneumocystis carinii* at the beginning of last century [5]. In 2002, human *Pneumocystis* organism was recalled *Pneumocystis jiroveci* by the identification of its genetic and functional distinctness, in honour of Otto Jirovec, who is recognized for identifying the microbe in humans [6,7].

Pneumocystis was for an extended time defined as a protozoe according to morphologic features and the resistance to classical antifungal agents. Then again, in the late eighties, *P. carinii* was positioned in the fungal kingdom depending on phylogenetic analysis of ribosomal RNA (rRNA) sequences and observations of genome size. [8]. The organism has currently been fixed in a group of fungi entitled the Archiascomycetes. [9]

In the lung, two main forms of the organism could be identified by microscopy: They are usually called cystic form (cysts) and trophic form (trophozoites), however they more appropriately, considering the fungal reclassification, might be defined as sporangium and yeast cells[10] .

The cystic form (sporangium) is usually thick-walled oval, about 5 to 8 µ in diameter and include approximately eight daughter forms (spores or endospores, initially called intracystic bodies or sporozoites), which will eventually become trophic forms after excystation. The trophic form (yeast, previously trophozoite) is small (2 to 5µm), thin-walled, pleomorphic and commonly has an eccentric nucleus. The trophic forms are usually seen in clusters. A third form, the precyst, is infrequently encountered, but is believed to constitute an intermediate stage. There is no precise knowledge of the lifecycle as well as the mode of replication has not been absolutely demonstrated, but both asexual and sexual life cycles have been suggested according to electromicrographic observations of synaptonemal complexes [11,12]

TRANSMISSION

Reactivation of Latency

Traditional concepts have retained that pneumocystosis comes from reactivation of latent infection acquired while childhood. Detectable antibodies are found in most of children by four years of age. Moreover, presence of *P. jiroveci* in respiratory samples from clinically normal population sustains the reactivation theory [13,14]. Besides, host immune evasion by variation of major suface glycoprotein (MSG), species specificity of *P. jiroveci* and complicated in vitro cultivation are constant with extended carriage or latency in the host 15,16].

Active Acquisition

Almost all attempts to transfer *P. jiroveci* from one animal species to another have been failed. In natural environment, P. jiroveci deoxyribonucleic acid (DNA) has been found in water, air and in soil samples, however, whole organism has been practically never recognized from these sources. Navin et al [17] discovered that patients with *P. jiroveci* were usually have history of recent gardening, therefore suggesting soil exposure. Outbreaks in oncology and transplant units have increased the possibility of person to person transmission. Besides clinical cases, sub-clinical cases and a few number of immunocompetent persons with no evidence of clinical disease accommodate *P. jiroveci*, forming the reservoir. This source should not be disregarded without the presence of other evidences. In any case, the transmission occurs via an airborne route as alveolus is the site of infection. The vertical transmission is rarely reported and it couldn't be demonstrated by animal experiments [18].

EPIDEMIOLOGY

The epidemiology of PCP has changed considerably through the course of the HIV/AIDS epidemic. In the 1980s, PCP was the AIDS defining disease for about two-thirds of adults and adolescents with AIDS in the United States, and it was supposed that 75% of HIV-infected persons would acquire PCP through their lifetime [19]. At the beginning of the epidemic, the incidence of *Pneumocystis* pneumonia was approximately 20 cases per100 person-years in HIV-infected persons with CD4+ cell counts under 200 cells/l [20]. The establishments of PCP prophylaxis in 1989 and effective combination antiretroviral therapy in 1996 have resulted in substantial reduces in the incidence of *Pneumocystis* pneumonia. In the Centers for Disease Control and Prevention (CDC) Adult and Adolescent Spectrum of Disease (ASD) Project, the incidence of *Pneumocystis* pneumonia declined 3.4% per year for the period from 1992 to 1995 and then decreased 21.5% annually during 1996 to 1998, a time when effective combinations of antiretroviral therapy were starting to be applied [21]. In the Euro SIDA study, the incidence of *Pneumocystis* pneumonia reduced from 4.9 cases per 100 person-years before March 1995 to 0.3 cases per 100 person-years after March 1998 [22]. Even with its decreased incidence, PCP continues to be the common serious opportunistic infection among HIV-infected persons, and a considerable proportion of persons who develop *Pneumocystis* pneumonia are unconscious of their HIV infection or are outside of medical care, consequently minimizing opportunities for additional reductions in the incidence of the disease. A consideration, *Pneumocystis* pneumonia has been significantly reported in low- or middle-income countries (LMIC). One clinical study from Uganda observed that 38.6% of 83 HIV-infected patients who were admitted to the hospital with pneumonia and who had three expectorated sputum smears which were negative for acidfast bacilli had *Pneumocystis* pneumonia detected on bronchoscopy with bronchoalveolar lavage (BAL) [23,24].

DIAGNOSIS

CLINICAL DIAGNOSIS

The fungal pathogen *Pneumocystis jirovecii* is the source of PCP in humans [25]. Patients with PCP generally present non-specific respiratory symptoms, such as dyspnea, cough, and fever. Immunocompromised hosts commonly present a triad of progressive dyspnoea of many weeks, non-productive cough or with clear sputum and low-grade fever. They are more apt to be in respiratory distress coupled with severe hypoxemia [4]. On medical exam, tachypnoea, tachycardia, cyanosis and fine dry rales can be present [2]. While extrapulmonary involvement is exceptional, eye, ear, spleen, bone marrow, lymph node, liver, and meningeal involvement, have been mentioned [4].

Chest X-ray generally reveals diffuse interstitial or peri-hilar reticulonodular infiltrates but could be normal in one-third of cases. Other findings, including spontaneous pneumothorax, effusions or cavitary lesions may be seen in few numbers of cases [26].

BIOLOGICAL DIAGNOSIS

Due to the insufficient specificity of clinical symptoms as well as the possibility of toxicity with therapy, affirmation of PCP is important an essential details for correct evidence-based patient management [1]. Diagnosis of *P jirovecii* infection is hampered by the lack of a sustainable in vitro culture method. Elevated serum lactate dehydrogenase (LDH) > 460 IU/L has been noticed to be a sensitive test for this disease, but a variety of pathological conditions involving lungs indicate increased serum LDH level. Measurement of partial pressure of arterial oxygen (PaO2) gives a perfect negative predictive value for exemption of *P. jiroveci* infection as PaO2 < 75 mmHg correlates with the illness [27, 28].

Conventional methods

The traditional method for diagnosis of PCP depends on the microscopic visualization of *P. jiroveci* organisms in respiratory samples. Given that only a few organisms can be found within the upper respiratory tract, lower respiratory secretions are often essential for certain diagnosis. Bronchoalveolar lavage (BAL) coupled with colorimetric as well as an immunofluorescent stain of BAL fluid is recognized as the technique of choice with sensitivity and specificity more than 95%. A different option is evaluation of material gotten by induced sputum. In spite of this, the sensitivity of that method is much more based on the experience of the personnel executing the procedure and checking the samples, with elevated variation in the diagnostic sensitivity noted (between 50 to 90%) [29,30,31,32] .

The usage of cytochemical stains for diagnosis is very slow process, and it could be complicated to preserve laboratory diagnostic expertise due to the reduced incidence of PCP after the introduction of significantly active antiretroviral therapy [33,34].

PCR methods

Since BAL is an invasive and irritating procedure that is not without risk, other non-invasive test were approved. PCR diagnosis of *P. jiroveci* was introduced experimentally in 1990 once Wakefield et al first identified DNA amplification of the multicopy mitochondrial ribosomal RNA gene. Since that time, numerous studies have evaluated PCR detection of *Pneumocystis* DNA in respiratory samples from HIV-1 positive and negative patients. To improve the diagnostic sensitivity of non-BAL specimens, distinct PCR methods have been considered, such as different gene targets and the use of nested PCR, during which a second round of PCR reamplifies the primary PCR product [1]. Molecular methods, on the other hand, could detect *P jirovecii* DNA in respiratory samples from patients without clinically apparent PCP [35,36] advocating asymptomatic carriage or ‘‘colonisation’’. Real-time PCR permits appropriate quantification of DNA as well as possibility to discriminate between asymptomatic carriage of *P jirovecii* and clinical disease depending on pathogen load.

CONCLUSION

P jirovecii is pathogen fungal organism witch continues to be an organism of clinical significance in today's practice and should not be disregarded because of the close link between this disease and HIV-infected persons. An earlier diagnosis with appropriate method could improve the prognosis of PCP and the correct patient therapy management.

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Predictors of Death and Prolonged Hospital Length of Stay in Dengue Fever Patients Admitted to a Tertiary Hospital in Makkah.

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Key words: Dengue fever, predictors, death, Makkah, hospital length of stay.

Background and study aim: Dengue fever is one of the commonest viral infections in tropical and subtropical areas and its main burden is related to patient's mortality and cost of hospital admission. Our aim was to study dengue fever patients admitted to a tertiary hospital as regards the predictors of patient's death and prolonged hospital length of stay (HLOS).

Patients and methods:This study included 123 patients. They were investigated for demographic, clinical and laboratory data that could predict the mortality and prolonged HLOS cases.

Results: Ninety one patients were males (74%) and average age was 30.6 ± 13.8 years. 119 patients (96.7%) improved and 4 patients (3.3%) died in the hospital. Out of the 119 patients, 38 patients (30.9%) were discharged after 5 days. Statistically significant predictors of prolonged HLOS (> 5 days) were leucopenia, INR > 1.25 and Creatine Kinase (CK) serum level > 488 IU/dl. Predictors of patient's death were male, non Saudi patients, age > 41.5 years, and complicated case (ICU admission , CNS hemorrhage and renal and/or liver failure). On multivariate logistic regression analysis; the laboratory independent predictors of death were AST > 610 IU/dl, ALT > 150 IU/dl, PT > 16.65 sec and INR > 1.4.

Conclusion: In a tertiary hospital in Makkah, the mortality rate of dengue fever patients was 3.3%.Predictors of patient's death were old age, male, non-Saudi patients, ICU admission, CNS hemorrhage, renal and liver failure and on multivariate logistic regression analysis, laboratory predictors were high serum levels of AST, ALT, PT and INR. About 31% of dengue fever patients needed hospital admission for >5 days and the statistically significant predictors were leucopenia, high INR and high CK serum levels.

INTRODUCTION

A dengue epidemic is one of the most important public health problems in the tropical and subtropical areas[1]. The geographical spread and severity are increasing dramatically, about 2.5 to 3 billion people are living in over 100 countries where dengue viruses can be transmitted. It is estimated that, there is 50 million new dengue infections happened every year, with 500,000 cases of DHF and at least 12,000 deaths. Epidemics of dengue like disease were reported in the Arabian Peninsula in the late 19th century (1870–1873), the disease appeared in Mecca, Madina, and Jeddah[2,3] . Results of a Saudi Arabian Ministry of Health (MOH) study showed that during the period 2006—2007, 1551 notified cases with an overall case-fatality rate of 0.52% [4]. Serious complications were uncommon, development of dengue hemorrhagic fever and dengue shock syndrome were rare but had a fatality rate of 2% to 5% [5]. Apart from fatality, the main burden is related to the cost of hospital admission.

This study was done on dengue fever patients admitted to Al Noor Hospital, Makkah during the year 2009; the aim of the study was to investigate the predictors that can help in the recognition of fatality cases and prolonged hospital length of stay cases, so the health care providers can early recognize the serious cases that need special care and can recognize the cases that can be safely discharged early.

PATIENTS AND METHODS

Study site and population:

This was a cross sectional, single center retrospective observational study done on dengue fever patients admitted to Al Noor specialist Hospital, Makkah, during the year 2009. Al Noor Specialist Hospital is a 600-bed, well-equipped hospital, it is the main hospital in Makkah.

Study design

All patients were diagnosed as a case of dengue fever and implemented on the Hospital Information System (HIS) according to the disease coding system ICD-10 AM (International Classification of Disease-10, Australian Modification), version 2006. Diagnosis depends on clinical presentation, serology and PCR study. The data studied included the demographic features (age, sex and nationality), Laboratory investigations (complete blood count, liver function tests, coagulation profile and serum Creatine Kinase (which is usually related to muscle injury). The hospital length of stay (HLOS) was the number of admission days including the admission and the discharge days. At Al Noor specialist hospital, dengue fever patients admitted for more than 5 days were considered to have "prolonged HLOS".

Course of the illness

Patients were discharged from hospital according to WHO criteria which include: absence of fever for at least 24 hours without the use of antipyretics, return of appetite, visible clinical improvement, good urine output, minimum of three days after recovery from shock, no respiratory distress, no ascites and platelet count of more than 50 thousands/cmm [6].

Statistical analyses:

The analysis was performed in SPSS version 17 (SPSS Inc., Chicago, IL, USA). Mean and standard deviation were calculated for quantitative variables and frequencies and percentages for qualitative variables. The Chi-square test was used to see the association among qualitative variables and student's *t*- test was used to see the differences in quantitative variable. Multiple logistic regression was used to predict a model of factors associated with mortality in patients with dengue fever. *P* value < 0.05 was considered statistically significant.

RESULTS

A total of 123 dengue fever patients were admitted to Al Noor Specialist Hospital, the males were 91 patients (74%), mean age of patients was 30.6 ± 13.8 years and 100 patients were Saudi (81%). Hospital Length of stay (HLOS) ranged from 2 to 14 days (mean ± SD 4.76 ± 2.25 days). Eighty one patients (65.8%) were discharged within 5 days, 38 patients were discharged after 5 days (30.9%) and 4 patients died during admission (3.3%) Figure (1).

When comparing the patients with regular (up to 5 days) and prolonged HLOS (more than 5 days), it is found that no significant difference between the two groups except low WBCs (p 0.00), high INR (p 0.03) and high CK serum level (p 0.03), (table 1), the cut off value for CK level was 488 IU/dl (sensitivity 100%, specificity 63.4%) and for INR the cut off value was 1.25 (sensitivity 100%, specificity 98.6%). Table (2)

Four patients died during admission, All patients were males (100%), only one was Saudi (25% vs. 83% p 0.003), and they were significantly older in age (p value 0.04), the number of admission days was (1, 2, 2 and 5 days, median 2 days and mean 3.3 days). Clinically; all mortality cases were admitted at the intensive care unit (ICU): two patients developed acute renal failure, one patient developed acute liver failure and one had septic shock. Three patients (75%) developed significant haemorrhage; (one had massive GI haemorrhage, one had subarachnoid haemorrhage and one had encephalitis with multiple small cerebral haemorrhagic spots). The laboratory results showed that: Hb was significantly lower (p value 0.029); WBCs were significantly higher (p value 0.000), marked reduction in platelet count (p 0.013), AST, ALT, PTT, PT and INR were significantly higher in mortality cases (p value 0.000), table (3). Independent predictors of patient death using logistic regression analysis were high AST and ALT serum levels and prolonged PT , table (4). Table (5) showed the cut off value for predictors of patient's death; they were the age (41.5 years), AST (610.5 IU/dl), ALT (150.5 IU/dl), PT (16.65 sec) and INR (1.4); sensitivity and specificity were demonstrated.

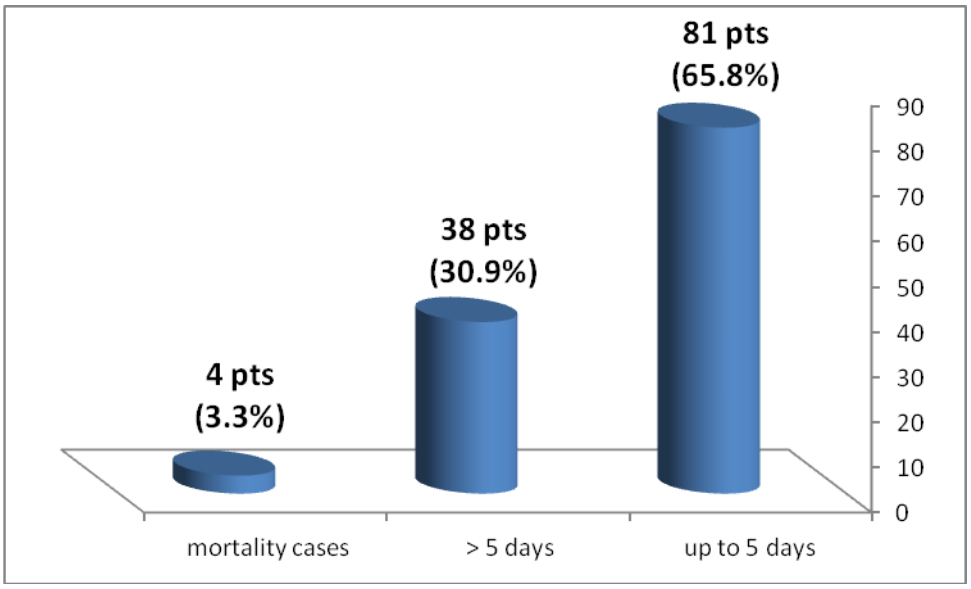

Figure (1): Number of dengue fever patients as regards early and late discharge and fatality cases.

Table (1): comparison between early and late discharge dengue fever patients.

Parameter (no, %), (m ± SD)	LOS up to 5 d 81pt (65.8%)	LOS > 5 days 38 pt (30.9%)	P value
Age (yr)	31.1 ± 14.1	33.5 ± 16.1	>0.05
Male (no, %)	59 (72.8%)	28 (73.7%)	>0.05
Saudi (no, %)	67 (82.7%)	32 (84.2%)	>0.05
Hb (gm %)	13.96 ± 1.7	13.6 ± 1.8	>0.05
WBCs (10^3/cmm)	3.3 ± 1.4	2.9 ± 1.2	0.000*
Plat (10^3/cmm)	96.6 ± 43	100.2 ± 62.3	>0.05
AST (IU/ml)	117 ± 112	151 ± 145	>0.05
ALT (IU/ml)	98 ± 105	101 ± 88	>0.05
PTT (sec)	37.1 ± 5.6	37.4 ± 6.3	>0.05
PT (sec)	11.7 ± 1	12.3 ± 1.2	>0.05
INR	0.96 ± 0.1	1 ± 0.1	0.03*
CK	506 ± 519	1162 ± 1672	0.03*

M mean, SD=standard deviation

ALT=alanine aminotransferase *(normal value < 40 U/L*)

AST=aspartate aminotransferase *(normal value < 40 U/L)*

PTT=partial thromboplastin time

WBCs=white blood cells

Table (2): cut off values for predictors of patient's prolonged HLOS.

parameter	value	sensitivity	specificity
CK (TOTAL)	488 IU/dl	100%	63.4%
INR	1.25	100%	98.6%

Table (3): Comparison between dengue fever discharged patients and mortality cases.

Parameter/ No (%)	Discharged patients 119 (96.7%)	Mortality cases (4 pt) (3.3%)	P value
Age yr (m ± SD)	30.14 ± 13.4	44.3 ± 20.1	0.04*
Male (no, %)	87 (73%)	4 (100%)	>0.05
Saudi (no, %)	99 (83%)	1 /4 (25%)	0.003*
Hb (gm %)	13.4 ± 1.9	11.1 ± 4.8	0.029*
WBCs (10^3/cmm)	3.04 ± 1.4	8 ± 4.1	0.000*
Plat (10^3/cmm)	106.2 ± 66	22.5 ± 14.9	0.013*
AST (IU/ml)	129.2 ± 128	5311 ± 4735	0.000*
ALT(IU/ml)	97.3 ± 92.9	2024 ± 1907	0.000*
PTT(sec)	37.4 ± 5.6	78.5 ± 30.2	0.000*
PT(sec)	11.9 ± 0.9	28.9 ± 10.9	0.000*
INR	0.98 ± 0.1	2.5 ± 0.9	0.000*
CK(IU/ml)	655.3 ± 963	1573 ± 904	>0.05

Table (4): Independent predictors for patient death using logistic regression analysis.

parameter		95% C.I.for EXP(B)		Sig
	Exp(B)	Lower	Upper	P value
AST	1.029	1.001	1.058	0.044*
ALT	0.965	0.934	0.997	0.032 *
PT	0.017	0.001	0.549	0.022*

Table (5): cut off values for predictors of patient's death

parameter	value	sensitivity	specificity
Age	41.5 yrs	75%	81.5%
AST	610.5 IU/dl	100%	98%
ALT	150.5 IU/dl	100%	86%
PT	16.65 second	100%	100%
INR	1.4	100%	100%

DISCUSSION

Dengue fever is typically a self-limiting disease, dengue fever patients usually have a very low mortality rate (less than 1%) and survivors usually recover without sequelae and develop immunity to the infecting serotype. In dengue hemorrhagic fever (DHF), the mortality rate varies from 2 - 5% in treated cases and up to 50% in untreated cases[7].

In a study on 1695 dengue fever patients from 8 American and Asian countries, the average illness lasted 11 days for hospitalized patients. Overall mean costs were more than double for hospitalized cases[8].

In this study, male patients were more infected (74%); this is also noticed in other studies from Makkah and Jeddah (males were 51%- 67%) [9,10,11,12]. Contrary to that, females

were more often infected than males in a study from Brazil (females 59.3%)[13]. Male preponderance may be related to changes in immune system related to gender[14]. Also, females were less exposed to mosquitoes[15] .

In this study, the mean age of patients was 30.6 ± 13.8 years, this is close to other studies from Makkah and Jeddah (23 ± 9 years [11] , 25.6±16.1 years[10] and 27.6 ±11.2 years[12]. In South and South East Asia, dengue fever is an infectious disease of children and the peak age ranged from 5 to 10 years[16]. In Latin America, dengue fever is a disease of adults[17], Saudi Arabia is a part of Asia but the age pattern of infection is related to Latin American pattern, and this may be due to the dengue genotype prevalent[10].

Fatality rate in this study was 3.3%, in two studies from Saudi Arabia; the fatality rate was 0.5 and 0.6%[18,10]. Internationally, the mortality rates were 1.3% in Indonesian study[19], 6% in Cuban epidemic[7] and 0.06% and 1.7% in two studies from Singapore[20,21]. The variation in the case fatality rate depends on the percentage of severe cases included in the study.

In this study, all patients died were males (100%) and median age of 46.5 years (m ± SD: 44.3 ± 20.1), all were admitted to ICU and death occurred at a median of 2 days after admission to ICU (range 1 – 5 days). In a study from Singapore, the median age of patients who died was 59 years and 67.9% of patients were males, also, 70% of them were admitted to ICU and the median duration of ICU stay was 3 days (range, 1-32 days)[22].

In this study, mortality cases had significantly low HB and platelets and high WBCs, AST, ALT, PTT, PT and INR (table 3). On using logistic regression analysis, the independent predictors of patient death were AST, ALT and PT levels (p=0.04, p=0.3 and p=0.02 respectively) (table 4) and table (5), showed the cut off values of age (41.5 yrs), AST (610.5 IU/dl), ALT (150.5 IU/dl), PT (16.65 sec) and INR (1.4). Similar results were observed in a study from Pakistan where the mortality predictors were; high WBCs count (p=0.02), PTT (56.8 versus 36.8, p=0.01) and ALT (802 versus 176, p=0.01) and on multivariate logistic regression analysis, ALT > 300 *IU/*dl, bleeding, an altered mental status and shock at presentation were all significantly associated with mortality (p=0.008, p<0.001, p<0.001, p<0.001, respectively)[23] . The impaired level of consciousness in dengue patients is usually related to dengue encephalopathy[24,25]., which may be due to direct dengue encephalitis or associated liver failure[24].

In this study, clinical predictors of death during admission were old age, male, non Saudi patients, admission to ICU, developing haemorrhage especially CNS haemorrhage and acute renal and/or liver failure. These results are supported by reports other parts of the world where the following mortality predictors were listed: old age (Taiwan[26], Singapore[21] and Puerto Rico[27], spontaneous bleeding[28], the presence of chronic diseases[21], renal disease [29] and ethnicity[21]. In a study from Singapore[22], clinical predictors of death were platelet count <20 × 10^9/L, acute renal impairment, impaired consciousness and severe hepatitis, while in a study from Pakistan, high white cell count, uremia, acidosis and deranged liver function were the laboratory predictors of death[30].

One of the important laboratory predictors of patient's death is liver damage which manifests as increase in AST and ALT serum levels and deranged coagulation parameters. In persons with fatal dengue hepatitis, direct virus infection was demonstrated in more than 90% of hepatocytes and Kupffer cells[31,32]. There was a correlation between liver enzymes and the severity of dengue infection and in patients who presented with encephalopathy, AST and ALT values usually exceeded 200 IU/dl[33,34]. In rare cases, dengue fever may present as an acute liver failure[35]. In contrast to other viral infections which involve the liver, dengue hepatitis is associated with AST higher than ALT levels[33,29,10], this difference could be due to the release of AST from skeletal muscle as muscle damage in dengue infections has been reported, this muscle damage may also explain the increased CK serum levels[36].

In this study three out of four mortality cases were non Saudi, the foreigners are more prone to poorer prognosis[10,11] , this may be related to the lower socioeconomic status and often living in poorer areas with inadequately developed infrastructures[11] which increases the incidence and prevalence of dengue and dengue haemorrhagic fever[37,38] .

The strength of this study is that, to our knowledge, it is the first study from Saudi Arabia which identified the factors associated with mortality in a multivariate analysis. There were some limitations; it is a single center study, it is of retrospective type and the small number of mortality cases.

CONCLUSION

Identification of prolonged HLOS predictors may help the health care providers to safely discharge patients early and to decrease the final cost of care of dengue fever patients, these predictors were leucopenia, INR < 1.25 and CK serum level < 488 IU/dl. Clinical predictors of death were non Saudi male patients, aged above 41.5yrs, ICU admission, CNS hemorrhage and acute renal or liver failure. Mortality laboratory predictors were high WBCs, AST > 610 IU/dl, ALT >150 IU/dl, INR >1.4 and PT> 16.65; patients presented with these symptoms should be admitted in high dependency units.

Abbreviations:

HLOS: hospital length of stay.

AST: Aspartate Transaminase.

ALT: Alanine Transaminase.

CK: Creatine Kinase.

PT: prothrombin Time.

INR: International Ratio.

IU: International Unit.

Dl: Deciliter.

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Needle-Knife Fistulotomy as a Rescue Access of the Common Bile Duct in Cirrhotic Patients: Feasibility and Outcome

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Key words:
Endoscopic retrograde cholangiopancreatography; needle-knife fistulotomy; cannulation, cirrhosis, common bile duct; pancreatitis

Background and study aim: Cannulation of the common bile duct may require invasive procedures; such procedures may carry an increased risk of complications. This study aimed at comparing the safety and efficacy of the needle-knife fistulotomy with other techniques in cirrhotic patients after failure of the standard cannulation using the free hand needle knife.

Patients and methods: Seventy cirrhotic patients were included and were divided into: Group A; 15 patients who underwent a needle-knife fistulotomy using the needle–knife after failure of transpapillary wire – guided cannulation. Group B : 15 patients who underwent a precut using the standard pull sphincterotome after failure of transpapillary wire – guided cannulation. Group C : 20 patients who underwent a conventional transpapillary wire – guided cannulation without sphincterotomy. Group D : 20 patients who underwent a conventional transpapillary wire – guided cannulation with standard sphincterotomy. Cannulation was evaluated for duration, number of trials, use of aiding instruments and success rate.

Results: Success rate of CBD cannulation and fair dye drainage was reported in 93.3% and 73.3%, 86.7% and 80%, 85% and 70%, 85% and 80% of patients in groups A,B, C and D respectively, with no statistically significant difference among the four groups. The only complication reported in group A was bleeding (three patients). No statistically significant difference among the four groups regarding post-procedural complications was noticed.

Conclusion: Suprapapillary needle – knife fistulotomy can be used in cirrhotic patients when standard biliary cannulation proves to be difficult, it is associated with a high success rate and a low complication risk.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is the standard approach for the diagnosis and treatment of a wide variety of hepatopancreaticobiliary diseases. Since its development, it has gained widespread use and has become a therapeutic tool in that field [1].

Cannulation of common bile duct (CBD) requires many techniques, these include standard transpapillary biliary cannulation techniques with the use of catheters and papillotome [2] with or without the use of a guide wire [3]; placement of a pancreatic guide wire (or stent) to assist biliary cannulation [4]; precut "access" papillotomy, by using a needle knife or a traction papillotome [5]; and papillectomy [6] may also be used. The suprapapillary needle puncture technique is another technique that could be added to those techniques in cases with difficult cannulation [7].

Operations (including ERCP) in patients with existing liver disease are not uncommon and the peri-operative risk increases with advanced stage of liver disease [8].

The aim of this work was to evaluate and compare the safety and efficacy of the needle-knife fistulotomy technique in cirrhotic patients using the free hand needle knife with other techniques used for biliary access after failure of the standard transpapillary biliary cannulation as regard immediate and long term outcomes.

PATIENTS AND METHODS

Study design: Prospective randomized.

Study setting and time: This study was conducted on patients from the Gastrointestinal Endoscopy Units of both the Internal Medicine and Tropical Medicine Departments –Zagazig University Hospitals, Egypt in the period from March 2011 to September 2012 and operated upon at ERCP unit of the Tropical Medicine Departments –Zagazig University Hospitals, Egypt. One experienced endoscopist with annual ERCP rate of >200 case/year performed all cases.

Patients: Out of 322 ERCP patients, 70 cirrhotic patients (Child A and B) were included.

Exclusion criteria : Exclusion of patients with

- Prior ERCP.
- Prior gastric surgery.
- Child–Pugh class C patients.
- The patient did not consent for all or part of the expected procedures.

The severity of hepatic dysfunction in patients with chronic liver disease has been classified according to the modified Child–Pugh classification [9] as shown in Table 1.

Study groups:

■ **Group A :** 15 patients who underwent a needle-knife fistulotomy using the needle–knife as an access to the CBD after failure of transpapillary wire – guided cannulation.

■ **Group B :** 15 patients who underwent a precut using the standard pull sphincterotome as an access to the bile duct after failure of transpapillary wire – guided cannulation.

■ **Group C :** 20 patients who underwent a conventional transpapillary wire – guided cannulation without sphincterotomy.

■ **Group D :** 20 patients who underwent a conventional transpapillary wire – guided cannulation with standard sphincterotomy.

Definitions :

Cannulation failure: defined as up to three unintended cannulations of the pancreatic duct or failure of biliary cannulation attempts within a time limit of 10 minutes [10].

Difficulty of cannulation was graded according to the total number of attempts on the major papilla with all devices, before final cannulation of the CBD. Difficulty of cannulation was described as *"easy"* one to five attempts, *"moderate"* six to fifteen attempts, and *"difficult"* more than fifteen attempts [11]**.**

Primary outcome: was successful cannulation of the CBD with comparison of the four procedures as regard the time needed for successful cannulation and adverse events.

Secondary outcomes: were post– ERCP adverse events.

Diagnostic failure was considered when the CBD could not be cannulated. **Therapeutic failure** was defined as the lack of adequate duct drainage when necessary.

ERCP was considered successful i.e. clinically effective if there were partial or complete relief of symptoms associated with sonographic evidence of relief.

Post-ERCP Pancreatitis : Defined as the recording of pancreatic enzymes levels greater than three times the normal upper limits, associated with severe abdominal pain requiring narcotic analgesics for at least 24 hours (requiring more than one night of hospitalization) [12].

Cholangitis: Defined as a fever greater than 38º C for more than 24 hours that was thought to have biliary causes, chills, elevated liver enzymes, and/or positive blood culture within 48 hours after the procedure [12].

Perforation: Defined as slight leakage of contrast during ERCP or evidence of retroperitoneal or free air on abdominal radiographs and computed tomography (CT) [12].

Bleeding : Defined as either *"immediate"* if it is apparent during precut or sphincterotomy and required endoscopic hemostasis, and *"delayed"* if the patient post–procedural develop melena or drop in hemoglobin (Hb) level greater than 2 g/dl or the need for a blood transfusion [12].

Adverse events were classified as mild if the length of hospital stay was less than or equal to 3 nights; moderate 4-9 nights and severe if: 10 or more nights admission, admission to an intensive care unit, or required surgery. As regard timing, adverse events were considered *"immediate"* if they occurred during or shortly after the

procedure within one hour ; *"early"* if they occurred within 1 – 48 hours ; and *"delayed"* if occurred after 2 days [14].

Ethical Considerations:

The study was approved by *the Ethical Committee of the Faculty of Medicine, Zagazig University*. The patient or his custodian gave a written consent for the procedure after explaining the risk/benefit ratio as well as expected hazards and interventions.

All patients were subjected to:

- **Before ERCP :**
  - Thorough history taking.
  - Thorough clinical examination.
  - Investigations including :

A. Laboratory: Liver function tests, kidney function tests, prothrombin time (PT), complete blood count (CBC) and serum amylase.

B. Radiological**:** Abdominal ultrasound ± CT ± MRCP.

C. Other investigations: Chest X – ray, ECG and Echocardiography (for selective cases).

D. Preparation of the patients for ERCP:

a- Patients received vitamin K (Phytonadione solution IV, 10 mg/day) for 3 days before ERCP. Fresh frozen plasma (10 – 15 ml/kg) was given immediately before the endoscopy if the prothrombin time was > 16 seconds [15]**.**

- **During ERCP :**
  - ERCP was performed under general anesthesia with intravenous 1 % propofol in the presence of an anesthesiologist in 64 patients. The remaining 6 patients were deeply sedated with intravenous *Pethidine* (50 mg) and *Midazolam* (10 mg) due to their advanced Child class B score.
  - ERCP was done and cannulation was viewed from four perspectives, namely :
    - Duration.
    - Number of trials (each targeting was considered as an individual trial).
    - Use of aiding instruments and methods
    - Success rate.

A. Suprapapillary needle – knife fistulotomy CBD:

Performed by using a needle knife at a point corresponding to the proximal third of the line between the transversal fold and the papillary ostium, at least five millimeters above the orifice, perpendicular to the papilla at 11–12 O'clock position, and three millimeters deep to the surface (over the most bulging point of the pregnant papilla; on the bulged intraduodenal segment of the CBD extending upward or downward over the papillary mound).

After needle puncture of the CBD was confirmed by easy insertion of a guide wire parallel to the spine in the direction of the CBD then injection of the contrast medium to obtain a cholangiogram (here there is no pancreatogram). If the guide wire insertion into the CBD did not occur easily, gentle lateralization movements were carried out, with simultaneous attempts to pass the guide wire.

The procedure was completed according to the diagnosis in each case (stone extraction, biliary dilatation and brush cytology, stent insertion in selected cases).

B. Precut by pull sphincterotome:

It is an incision of the papillary roof which is carried out from the papillary orifice along the midline of the papilla. The incision is made in small increments by using pure cutting current to ensure a clean cut. The aim is to slit open the papillary roof in order to expose the orifice of the CBD.

C. Transpapillary cannulation without sphincterotomy :

It is the standard cannulation of the CBD through the papillary orifice by using diagnostic biliary cannulae of different sizes, the guide wire was used to facilitate cannulation.

D. Transpapillary cannulation with standard sphincterotomy:

It is the standard cannulation of the CBD through the papilla, but by using a sphincterotome for both cannulation and standard sphincterotomy.

- **Post ERCP :**
  - Patients were allowed to drink and eat as soon as they have fully recovered from anesthesia and intestinal movements were regained, except if adverse events were expected when

nil per os *(NPO)* and infusion of intravenous fluids were followed for variable durations.

- Patients received IV antibiotics *(Cefotaxime),* vitamin K, antispasmodics whenever needed.
- All patients were admitted for at least one day (the night after the procedure) and the patients with evident or suspected post – ERCP adverse events had longer durations of hospital stay**,** and upon discharge the patients and their relatives were given detailed instructions about symptoms of post – ERCP adverse events and were informed to report by phone or to come to the emergency unit or outpatient clinics if any symptoms suggestive of post–ERCP adverse events developed.
- Repeated clinical evaluation of all patients daily during hospital stay.
- Investigations were done one day after the procedure, and within one week in patients with suspected early post–ERCP adverse events.

Follow up of all patients during the hospital stay and for 2 weeks after discharge as outpatients for detection of clinical efficacy of the procedure. Cases with failed ERCP were subjected to either repetition of ERCP (but were not re-included in this study), referral to surgery or percutaneuos transhepatic drainage according to the individual situation. Recording mortality during hospital stay and for 2 weeks after discharge.

Statistical analysis:

Data were checked, entered and analyzed using SPSS version 15. Data were expressed as mean ± SD for quantitative variables, number and percentage for qualitative ones. Chi-squared (X^2) or Fisher exact, t test and paired t test were used when appropriate. P <0.05 was considered significant.

RESULTS

Out of 322 ERCP cases presented to our units in the study period, 70 cirrhotic cases Child A and B were enrolled in a percent of 21.7%, this reflects the high prevalence of chronic liver diseases in our community. The base line characteristics of patients are shown in Table 2. A total of 37 females (53%) and 33 males (47%) with mean age 56.3 years (range 28 – 78 years) were included. The commonest indication for ERCP was CBD stones followed by pancreatic masses.

A total of 30 patients (42.8%) had co-morbidities. Cardiovascular diseases (hypertension, ischemic heart diseases and heart failure were the comments associated morbidities) followed by diabetes and COPD. These associated co-morbidities were not associated with an added risk to ERCP adverse events in this study (Figure 1).

Cannulation of the CBD succeeded in group A in 93.3% of cases with fair drainage of the dye in 73.3% of them, 86.7% of cases in group B with fair drainage of dye in 80% of them, 85% of cases in group C with fair drainage of dye in 70% of them and lastly 85% of cases in group D with fair drainage of dye in 80% of them, with no statistically significant difference among the studied groups regarding the cannulation success rate (p= 0.87) or the fair drainage of the biliary tree(p= 0.76) (Figure 2).

No post ERCP pancreatitis was reported in group A, while the incidence was 6.7%, 5% and 10% in groups B, C and D respectively. Regarding the severity of pancreatitis according to Cotton et al., [12] , one case in group B and another one in group C presented by mild form, while in group D the two cases presented by moderate degree. They were treated conservatively in the hospital then discharged within 8 – 10 days. There were no severe cases and there was no mortality related to pancreatitis.

Bleeding was the most common complication in this study. Intra-operative bleeding was reported in two, one, one and two cases in groups A, B, C and D respectively. Bleeding was mild and stopped either by cautery or after diluted adrenaline flushing, while delayed bleeding (all presented with melena) was reported in one case in each of groups A, B and C and two cases in group D, and was treated conservatively and with blood transfusion, neither surgery nor therapeutic angiography were needed in all cases.

A case of cholangitis was reported in group D which resolved with medical treatment, while there were no cases in the other groups. Hepatic encephalopathy (HE) developed in one case of Child's class B (score 9) in group C. No cases of perforation were recorded in this study.

The developed adverse events when translated to terms of prolonged hospital stay (more than 3 days) occurred as follow: three cases in group A,

three cases in group B, five cases in group C and seven cases in group D.

The only case of mortality among the groups was recorded in group C and he died due to HE in spite of admission to the hepatology intensive care.

In this study there was a significant relation of post – ERCP pancreatitis with the number of trials and the duration taken for cannulation, with more attempts to cannulate more time is elapsed and more risk to develop post-ERCP pancreatitis (Table 4). There was a significant relation of ERCP related bleeding and the prolonged prothrombin time and this is reflected in terms of intra-operative and delayed bleeding episodes, although the bleeding was not fatal (Table 5). Only one case of cholangitis was reported in this series. She was a female patient in the group D and this was controlled with iv levofloxacin injection once daily for 5 days.

The total number of cases achieved an overall success were 58 cases (82.85%). Group A showed a better overall success which was achieved in 14 cases (93.3%), group B showed an overall success in 13 cases (86.6%), group C showed an overall success in 17 cases (85%) and group D showed an overall success in 14 cases (70%) with no statistically significant difference among the studied groups. The parameters assessed to evaluate the overall success were: Successful CBD cannulation and absence of post – ERCP adverse events (Figure 3).

Table (1): The modified Child – Pugh classification

Parameter	Numerical score		
	1	**2**	**3**
Ascites	None	Slight	Moderate to severe
Encephalopathy	None	Grade I – II	Grade III – IV
Bilirubin	< 2 mg/dl	2 – 3 mg/dl	> 3 mg/dl
Albumin	> 3.5 mg/dl	2.8 – 3.5 mg/dl	< 2.8 mg/dl
Prothrombin time (seconds > control)	1 – 3	4 – 6	> 6

Child – Pugh class A= score 5-6, class B= score 7-9, class C= score 10-15

Table (2): shows base line data of the studied patients

	Group A (n = 15) n (%)	**Group B (n = 15) n (%)**	**Group C (n =20) n (%)**	**Group D (n = 20) n (%)**	**F**	**P**
Age (years) Mean± S.D. Range	54.3±13.7 31 – 75	53.7±12.7 28 - 71	57.5±9.4 39 - 73	59.7±10.3 36 - 78	1.079	0.36
					X^2	**P**
Gender Male Female	8 (53.3%) 7 (46.7%)	6 (40%) 9 (60%)	10 (50%) 10 (50%)	9 (45%) 11 (55%)	0.64	0.88
CBD stone	7 46.7	6 40	8 40	9 45	5.18	0.99
Passed stone	1 6.7	2 6.7	1 5	1 5		
Distal CBD stricture	2 13.3	2 13.3	4 20	4 20		
Proximal CBD stricture	0 0	1 6.7	1 5	2 10		
Pancreatic mass	3 20	4 26.7	5 25	4 20		
Intra-operative biliary trauma	2 13.3	1 6.7	1 5	0 0		

Table (3): Reported complications in the studied groups.

		Group A (n = 15)		Group B (n = 15)		Group C (n = 20)		Group D (n = 20)		Total (n = 70)		P value
		N	%	n	%	n	%	N	%	n	%	
Pancreatitis (n = 4)		0	0	1	6.7	1	5	2	10	4	5.7%	0.65
Bleeding (n = 11)	immediate	2	13.3	1	6.7	1	5	2	10	6	8.5%	0.82
	delayed	1	6.7	1	6.7	1	5	2	10	5	7.1%	0.39
Cholangitis (n = 1)		0	0	0	0	0	0	1	5	1	1.4%	0.46
Hepatic encephalopathy (n = 1)		0	0	0	0	1	5	0	0	1	1.4%	0.65
Prolonged hospital stay (n = 18)		3	20	3	20	5	25	7	35	18	25%	0.7
Mortality (n = 1)		0	0	0	0	1	5	0	0	1	1.4%	0.65

Table (4): The possible risk factors for post-ERCP pancreatitis among the studied groups.

		Patients with post-ERCP pancreatitis (n = 4)	Patients without post-ERCP pancreatitis (n = 66)	X^2	P
Age (years)		48 ± 8.2	56.3 ± 9.4	0.07	0.99
Gender	Male	1 (25%)	32 (48%)	0.56	0.45
	Female	3 (75%)	34 (52%)		
Co-morbidities		1 (25%) DM 1 (25%) COPD	8 (12%) DM 2 (3%) COPD	2.07	0.15
Bilirubin (mg/dl)	Total	8.3 ± 3.6	9.6 ± 4.8	0.42	0.67
	Direct	6.2 ± 3.3	7.4 ± 4.1	0.61	0.54
S. Amylase (U/L)		52 ± 12.7	48.9 ± 13.2	0.05	0.95
S. Alkaline phosphatase (U/L)		680 ± 170	549 ± 168	0.49	0.62
Cannulation	No of trials	6.2 ± 1.6	3.63 ± 1.98	3.48	< 0.05
	Duration(minutes)	22 ± 8.5	14.5 ± 6.7	2.47	0.014
Pancreatogram		0 % abnormal	16 % abnormal	0.03	0.85
Cholangiogram		1 (25%) CBD stricture	13 (20%) CBD stricture	0.03	0.85
		3 (75%) CBD stone	33 (50%) CBD stone	0.23	0.63
Use of Sphincterotomy		2 (50%)	15 (23%)	1.15	0.29
Use of Precut		1 (25%)	12 (18%)	1.2	0.26
Use of suprapapillary puncture		0 (0%)	14 (21%)	0.06	0.75

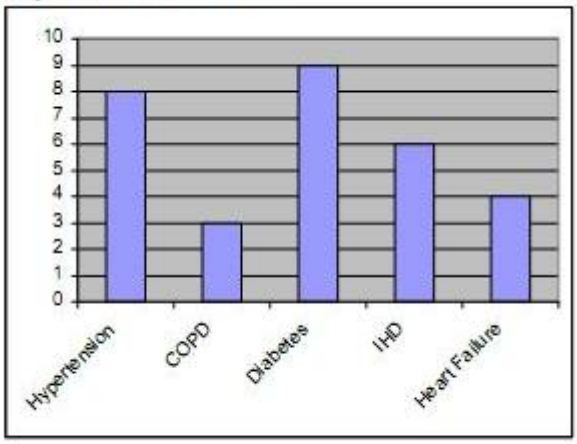
Table (5): The possible risk factors for bleeding among the studied groups.

		Patients with bleeding (n = 11)	Patients without bleeding (n = 59)	X^2	P
Age (years)		47 ± 6.2	54 ± 8.4	0.05	0.85
Gender	Male	9 (81%)	24 (40%)	0.55	0.45
	Female	2 (19%)	35 (60%)		
PT (seconds)		14 ± 1.5	11.8 ± 1.16	2.3	< 0.05
Platelets (x 10^3/cc)		149.5 ± 73	236 ± 76	1.32	0.22
Cannulation	No of trials	3.7 ± 2.1	3.8 ± 1.3	0.71	0.51
	Duration (minutes)	15 ± 9.5	14.6 ± 8.2	0.6	0.55
Cholangiogram		7 (65%) CBD stone	29 (49%) CBD stone 14 (24%) CBD stricture	0.28	0.59
Use of Sphincterotomy		4 (36%)	13 (22%)	0.14	0.7
Use of Precut		2 (18%)	13 (22%)	0.55	0.52
Use of suprapapillary puncture		3 (27%)	12 (20%)	0.89	0.62

Table (6): The possible risk factors for post-ERCP cholangitis among the studied groups.

Factor		Patients with cholangitis (n = 1)	Patients without cholangitis (n = 69)	X^2	P
Age (years)		60	56.3 ± 11.5	1.2	0.72
Gender	Male	0 (0%)	33 (48%)	0.01	0.92
	Female	1 (100%)	36 (52%)		
Co-morbidities		1 (100%) DM	8 (11.5%) DM	1.43	0.23
Bilirubin (mg/dl)	Total	15	9.75 ± 5.1	0.13	0.88
	Direct	11	7.27 ± 4.2	0.07	0.93
S. Amylase (U/L)		51	48 ± 4	0.41	0.68
S. Alkaline phosphatase (U/L)		655	547 ± 75	1.35	0.12
Cannulation	No of trials	6	3.8 ± 1.2	0.85	0.6
	Duration (minutes)	20	14.5 ± 9.4	0.46	0.64
Pancreatogram		0 (0%) Abnormal	11 (16%) Abnormal	1.2	0.27
Cholangiogram		1 (100%) CBD stone	31 (45%) CBD stone	1.06	0.3
Use of Sphincterotomy		1 (100%)	16 (23%)	0.14	0.7
Use of Precut		0 (0%)	15 (22%)	1.43	0.23
Use of suprapapillary puncture		0 (0%)	14 (20%)	0.1	0.75

Figure (1): The patients' co-morbidities



COPD chronic obstructive pulmonary disease, IHD ischemic heart disease

Figure (2): The successful cannulation rates among the studied groups.

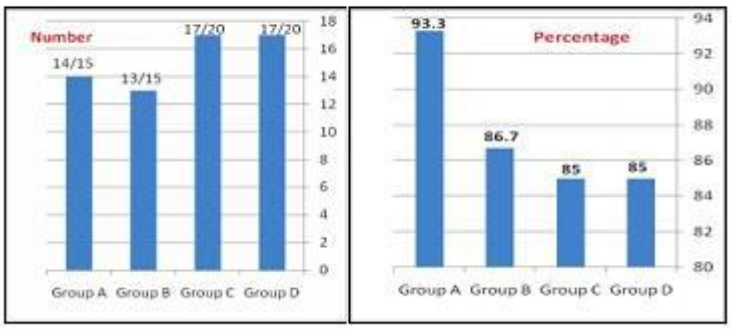
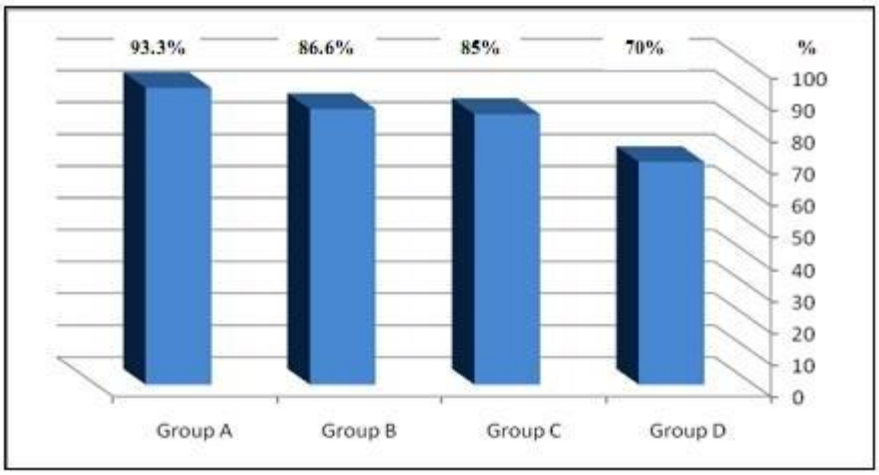


Figure (3): The overall success rates among the studied groups.



DISCUSSION

Cannulation of the CBD remains the most important and challenging aspect of the ERCP. Even in experienced hands the cannulation through the papillary orifice may be difficult [16]. Consequently, several techniques have been developed to facilitate cannulation of the papilla during ERCP [17]. The problem of canulation is expected to be more difficult in cirrhotic patients who are known to be more vulnerable to operative risks in particular the bleeding episodes.

In this study, we look to the suprapapillary puncture technique previously used by Everson et al in 2007 [7] who accomplished this technique by a specially designed needle as a rescue in order to overcome difficult cannulation in the subgroup of cirrhotic patients who tolerate invasive techniques poorly. Because of unavailability of this needle in our work, needle – knife was used for the fistulotomy technique

The mean age of our patients was 56.3 ± 9.4 years. Therapeutic ERCP is safe and effective and well tolerated in elderly patients so advanced age per se should not impinge on decisions relating to its use [18]. This study confirmed that elderly cirrhotic patients can tolerate therapeutic ERCP when properly selected and prepared.

Although, liver diseases in Egypt are common in males than females [19], females predominates in this study and this may be related to the biliary stone disease that was the comments indication for ERCP in this series a finding agrees with other studies [20], such category of diseases are more frequent in females.

Irrespective of the technique used, successful cannulation of the CBD was achieved in 87% (61/70) of cases, 85% (53/61) of the successfully cannulated cases achieved fair drainage of the biliary tree. These results lie central within the range of cannulation success rates reported by many authors varying from 80% to 95% [21-23].

In the present study, suprapapillary needle – knife fistulotomy appeared to be superior to other methods, as successful cannulation of the CBD was achieved in 93.3% of cases, while other precut techniques using the sphincterotome achieved 86.6% and 85% success rate for the remaining two groups with no added risk.

The high success rate with the needle-knife fistulotomy of 93.3% (14/15) in our study is comparable with rates of 86%-90.5% reported by many authors [24-25]. Precut techniques success rate was 86.6% (13/14) in the present study and is comparable to Vandervoort et al., [26] who reported a rate of 86% (120/140) and Deng et al., [23] who reported a rate of 89% (247/277).

The adverse events following the ERCP can occur approximately in 10% of cases and mortality in about 1% [11]. This is the range within which figures from a great number of published series lay and also our study lies.

Regarding the post – ERCP pancreatitis that has been developed after the procedure, the overall incidence in our study was 5.7% with no statistically significant difference among the

studied groups, which is in line with the reported rates of 4-5.5% in other studies [27,28].

There were no reported cases of pancreatitis after the suprapapillary puncture technique in our study. This is because the potential mechanisms that precipitate pancreatitis associated with conventional transpapillary biliary cannulation and endoscopic sphincterotomy were avoided. .

Chemical, allergic and hydrostatic injury to the pancreatic duct from inadvertent injection of contrast into the pancreatic duct is eliminated by totally avoiding the pancreatic duct injections and selectively injecting into the bile duct only after confirmation of the position of the guide wire in the bile duct.

Thermal injury from conventional biliary sphincterotomy was also avoided, because balloon dilation of the puncture tract was used to enlarge the orifice for removal of stones in selected cases. The hypothesis that avoidance of thermal injury to the pancreatic duct by means of cutting above the papillary orifice minimizes risk for pancreatitis seems to be reinforced by the results of this study, although the concept remains controversial [29].

The question about the needle – knife technique is whether or not the observed adverse events rate is a function of the technique itself, or merely a reflection of the fact that the repeated unsuccessful cannulation after standard techniques has been difficult and the prolonged attempts to achieve cannulation may result in trauma and inflammation of the papilla with the resultant edema accounting for the increased rate of pancreatitis. Before the needle – knife was used in difficult biliary cannulation, the risk of overall adverse events had already reached 14%, but with the early institution of the needle – knife the successful biliary access was increased while the overall adverse events rate was reduced to 11.8% [30].

We used all measures to minimize the risk of post – ERCP pancreatitis such as tapered catheters, avoiding repeated pancreatic cannulations and effort to cannulate the CBD in a programmed, step – by – step manner, for no more than 10 minutes and, we also tried to use coagulation current and avoidance of working on non – dilated CBD. However, the higher rates of post – ERCP pancreatitis recorded were assumed to be related to the repeated cannulation attempts that have been occurred before precut. These repeated cannulation attempts also mean that precut was almost performed under difficult conditions, on an already edematous and distorted papilla.

The incidence of pancreatitis following standard sphincterotomy in the present study was 10% which is relatively higher than 5.4% rate reported by Freeman et al., [11], this may be attributed to the relatively long duration for cannulation in group D patients 18.4 minutes (range 8 – 40 minutes) and the use of sphincterotome as the cutting wire tend to inadvertently injure the juxtapapillary portion of the pancreatic duct, leading to a cascade of events that culminates in pancreatitis.

The possible risk factors for post – ERCP pancreatitis in our study were significantly related to the number of trials for transpapillary cannulation ($p < 0.05$) and also to the duration spent for attempting transpapillary cannulation ($p = 0.014$).

As regard the overall bleeding risk in the present study it was 8.5% for immediate bleeding and 7.1% for the delayed bleeding with no statistically significant difference among the studied groups. As regard the bleeding risk in the needle – knife fistulotomy group (group A) it was 13.3% for immediate bleeding and 6.7% for delayed bleeding that agreed with results of Donnellan et al. [31].

The relatively high rate of bleeding in our study is directly related to the underlying liver disease (prolonged PT) and might be also related to the use of pure cutting current for fistulotomy and other precutting techniques. We expected a higher rate of bleeding episodes than we reported and we assume that iv pre-operative vitamin K and fresh frozen plasma are responsible for this reduction.

In the present study, HE after ERCP has occurred in one patient (1.4%). The only significant risk factor for its development was advanced chronic liver disease (Child's class B). The enhanced effect of sedation with the relatively long procedure time could explain the development of HE in this patient.

In our study, prolonged hospital stay (more than three days) occurred in 25% of cases. This could be explained by the high rate of co-morbidity (42.8%) in this study; association of liver cirrhosis with other chronic diseases explains the long hospital stay for complicated cases.

Mortality rate was 1.4%, as only one patient died 7 days after the procedure from HE. Mortality rate in our study lies close to mortality rates reported by many authors that range from 0.16% to 1% [26,27,32].

CONCLUSION

In this study we concluded that suprapapillary needle – knife fistulotomy can be used when standard biliary cannulation proves to be difficult, it is associated with a high success rate and a low complication risk in experienced hands even in cirrhotic patients it can be used as an alternative method, at least in difficult patients.

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Ethical approval: Was granted by the hospital ethics committee and informed consent was obtained from each patient prior to inclusion in the study.

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Case 2-2013: Eosinophilic Ascites (EA); Pathophysiology, Differential Diagnosis and Therapeutic Challenges

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Key words: Ascites, Eosinophilic gastroenteritis, EGE, Eosinophilic ascites , EA, Montelukast, Steroids

Eosinophilic ascites (EA) is a rare disorder of unknown etiology that has been reported in both adult and pediatric patients. It is a part of the eosinophilic gastroenteritis (EGE) syndrome, which is characterized by the presence of non specific abdominal complaints in association with eosinophil-driven inflammation of any or all layers of the gut wall. Peripheral eosinophilia may or may not be present. Here, we report a case of EA, a rare presentation of the serosal variant of EGE that developed in a thirty years old Egyptian female. She complained initially from nonspecific GI symptoms associated with diffuse abdominal pain and distention for several weeks. Her physical examination was significant for moderate ascites. Initial work-up demonstrated: very high peripheral eosinophilia, normal liver function tests, thickening of the small and large bowel walls, and normal total serum IgE. Upper endoscopy and extensive testing for malignancy and parasitic infections failed to establish a diagnosis. Ascetic fluid analysis showed significant eosinophilia. Further, a duodenal biopsy showed marked eosinophilic infiltration of the lamina Propria. This report adds to the scarce data on serosal involvement, "the rarest form of presentation" and illustrates that EGE complicated by ascites can be effectively treated with a combination therapy of steroids and the leukotriene receptor antagonist "Montelukast" after other systemic disorders associated with peripheral eosinophilia have been ruled out. The pathophysiology, differential diagnosis as well as therapeutic challenges associated with EGE are discussed.

INTRODUCTION

Eosinophilic gastrointestinal disease (EGE) is a rare chronic inflammatory bowel condition of unknown etiology that was originally described by Kaijser in 1937 [1]. EGE is a spectrum of gastrointestinal (GI) disorders characterized by inflammation rich in eosinophils without evidence of other known causes of eosinophilia (i.e., parasitic, infectious, drug reaction, or malignancy) [2]. The disease can affect one segment or several segments of the GI tract from the esophagus to the rectum, giving rise to various clinical presentations. Three distinct subtypes of EGE are recognized. The most common "mucosal" form (58% of cases) typically presents with nausea, vomiting, abdominal pain, diarrhea and malabsorption, while involvement of the muscularis (30% of cases) may manifest with symptoms of obstruction. Serosal involvement is rare, occurring in less than 13% of cases of EGE, and can result in abdominal pain and eosinophilic ascites (EA) [3]. Most reported cases of EA are idiopathic, often accompanied by an atopic condition, such as asthma, food or medication allergy. Peripheral eosinophilia is a usual finding in most cases of EA [4,5]. EGE is primarily a polygenic allergic disorder involving mechanisms that fall between IgE-mediated food allergy and cellular-mediated hypersensitivity disorders [2]. Steroids are the main therapy for cases in which diet restriction is not feasible or has failed. The recent researches suggest a similar pathophysiology to asthma. Cysteinyl leukotrienes are known to have potent chemo- attractant properties for eosinophils. Together with interleukins 3 and 5 they play a major

role in the recruitment of eosinophiles into the tissue causing damage .Disrupting this vicious circle provides the rationale for treating EGE patients with the leukotriene receptor antagonists (LTRA) [6, 7].

Case report

We present a 30-year-old single female working as a school teacher from a rural area not known to have any previous chronic medical illness. She experienced intermittent nausea, non-bloody vomiting and diarrhea for several weeks, accompanied by upper abdominal pain and distention which was increased after meals. There was no obvious aggravating or relieving factors for her abdominal pain. She received nonspecific treatment in the form of domperidone, omeprazole, and an anti-flatulent without improvement. However, her abdominal distention was worsening and associated with sever bloating. She denied any history of fever, night sweats, weight loss, blood transfusion, recent travel, respiratory symptoms, rash, allergies, or ill contact. There was no history of liver or heart disease. She was not consuming alcohol or any illicit drug, and was taking neither medications nor supplements. She had a regular menses with no gynecologic troubles. She had no family history of liver disease, atopy or coagulation disorders. On physical examination, the patient was alert, well built, and showed no signs of distress. She was afebrile and hemodynamically stable and her skin and mucosa were anicteric and clear without spider angiomata, no lymphadenopathy or pedal edemas were detected. The cardiovascular and thyroid examinations were normal. Chest examination revealed; dullness to percussion over the right lower lobe, with auscultation we demonstrated decreased breath sounds over the right lower lobe, no wheezing or crackles but increased egophony was detected. The abdomen was distended and diffusely tender with active bowel sounds and positive bilateral shifting dullness; no *caput medusae*, rebound or guarding were observed, no hepatosplenomegaly were detected. Her investigations were as follow: Hgb 12.9 g/dL, Htc 38, PLT 415,000 /mL, WBC 11.800/mL, differential: segmentonuclear neutrophils 48%, lymphocytes 9%, monocytes 1%, eosinophils 42% (absolute count, 7200). ESR was 9 mm/ hour. Serum electrolytes, urine analysis, renal functions, serum amylase &lipase, coagulation studies, thyroid and liver tests were all normal. HIV (human immunodeficiency virus) ELISA, hepatitis markers (HbsAg & HcvAb) as well as autoantibody screen were all negative. . Cancer Antigen-125 (CA-125), CEA, CA19-9, and alpha feto-protein were all negative. She had a positive tuberculin (purified protein derivative or PPD) skin test of 12 ml induration diameter after 48 hours. Total IgE was normal: 147 U/ ml (range 5 to 200). Parasitic infestations were excluded by repeated negative stool studies and negative serology for Echinococcusis, Strongyloidiasis, and Toxocariasis. However, we gave her a precautionary course of oral albendazole (400 mg twice a day for 5 days) with no change in her current state for almost two weeks until the investigations were completed. On abdominal ultrasonography, the liver was normal in size and echogenicity, and all vessels were patent. There was a moderate amount of pelvic and abdominal ascites and a mild right-sided pleural effusion. Chest x was normal apart from the mild RT sided pleural effusion. Computed tomography (CT) of the abdomen and pelvis revealed moderate volume ascites with no solid organ tumors, lymphadenopathy, or omental deposits but with thickening of the small intestinal and colonic walls. Diagnostic ascetic aspirate revealed straw colored fluid with no cytological signs of malignancy, with protein level 5.5 g/dL, albumin 3.4 g/dL (low SAAG of 0.8), RBC 1200/ mL, WBC 1.780/ mL with eosinophilic predominance of 73%. Ascetic fluid for bacterial culture and for tuberculosis had no growth, ascetic adenosine deaminize (ADA) as well as PCR for tuberculosis were negative. Ascetic Glucose, amylase, and LDH had normal values. Bone marrow biopsy demonstrated an increased myeloid-to-erythroid ratio with an increase of eosinophilic component (up to 35% of the myeloid precursors); there was no evidence of dysplasia. Upper GI endoscopy demonstrated patchy erythema in the lower eosophagus and gastric antral regions, and duodenal edema. Mucosal biopsies were obtained, and were consistent with mild reflux esophagitis and antral gastritis manifested as mild nonspecific acute inflammation predominantly lymphocytic but no eosinophilic infiltration could be detected. However the duodenal biopsies demonstrated eosinophilic infiltration in the lamina propria of more than 20 eosinophils/high power field. Unfortunately, the patient refused colonoscopy or laparoscopy which would have been the next steps in the clinical work-up of eosinophilic gastroenteritis. The constellation of clinical

features, eosinophilic ascites, thickening of intestinal and colonic walls, eosinophilic infiltration in the lamina propria of the duodenum and peripheral eosinophilia were all consistent with the diagnosis of EGE after exclusion of other possible causes of such condition. She was empirically treated with a combination regimen of prednisone (40mg/day) plus montelukast (10 mg/day) for two weeks. The dose of steroid was tapered off over the following 2 weeks and the patient was left on montelukast alone to avoid the serious long term adverse effects of steroids. After completion of steroids, the patient's abdominal pain and physical finding of ascites had completely resolved and peripheral blood count revealed an absolute eosinophil count of 378/μl (nL < 450). Furthermore, chest x was normal with complete resolution of the RT sided pleural effusion. CT imaging of the abdomen and pelvis showed disappearance of the ascites and small and large bowel thickening. Four months have elapsed since treatment was initiated and the patient remained asymptomatic on montelukast alone. As there is no clear treatment end point for montelukast in the literature, we intend to keep our patient on this safe drug for one year to avoid the commonly met with relapses after cessation of steroids.

DISCUSSION

Eosinophilic gastroenteritis (EGE) is a rare condition characterized by recurrent [8] eosinophilic infiltration of portions of the gastrointestinal tract presenting with nonspecific GI symptoms in association with peripheral eosinophilia in most of the cases [9, 10]. In a study conducted on 15 patients with EGE, Chen et al. reported that abdominal pain and diarrhea were the most common presenting symptoms. Our patient complained of similar presentations for several weeks with no response on nonspecific treatment. One-third of the patients in Chen et al study, had history of allergy and more than 80% were found to have peripheral eosinophilia [8]. Peripheral eosinophilia was marked in our patient, with 42% eosinophilic predominance (normal range 1-3%). Although profound peripheral eosinophilia in EGE is usually associated with the serosal form, it should be noted that eosinophil count can be normal at presentation in up to 23% of EGE patients in general, which may further obscure the diagnosis and require an extensive and invasive work up and surgery [3, 12]. EA is a rare presentation of EGE and should be considered when facing a patient with ascites in the absence of liver disease, and with refractory gastrointestinal symptoms, especially in the presence of a concomitant allergic condition [29, 30]. The most common classification of EGE based on the involved layer of the GI tract is known as Klein's classification. Subsequently, there are three subtypes of EGE (mucosal, muscular, and subserosal), with some degree of overlap [3, 9]. Data are insufficient in regard to the true prevalence of EGE and each of its subtypes. However, the mucosal form is the most common followed by muscular and lastly subserosal [2]. The stomach and duodenum are the most commonly affected sites in EGE, with colonic involvement being less common. However it is unclear whether this represents bias related to accessibility to endoscopic biopsy [3, 27]. The etiology and pathogenesis of EGE remain unclear. The role of allergy in recruitment of eosinophils to the GI tract remains controversial. Several studies have shown that half of the patients with EGE had a preexisting history of atopy [3, 11]. Moreover, Alfadda, et al; confirmed the presence of strong association with atopy in 80% of EGE patients reporting a personal history of asthma, eczema, allergic rhinitis or drug allergy. The association with atopy suggests a genetic component and unsurprisingly approximately 16% of patients with EGE have a family member with a similar condition. They added that activated eosinophils release an array of cytotoxins by degranulation, including Major Basic Protein (MBP), Eosinophil Cationic Protein (ECP) and others, producing tissue damage both directly and by downstream production of cytokines and leukotrienes. Eosinophil degranulation also triggers the release of histamine from mast cells, further perpetuating inflammation and cell damage [27]. In addition, serum IgE levels were elevated in some patients; which was not the situation in our case as she denied any history of allergy or food intolerance and her IgE level was normal. Although rarely IgE antibodies are directed against identified food allergens, yet in an interesting case report presented by B. Rodreguez et al, they found that Skin prick tests and patch tests with different allergens were all negative in their EGE confirmed patient. The patient's eosinophil cationic protein (ECP) level was very high. Given that one of the most common causes of this condition is allergy to cow's milk, ECP levels were determined during

a diet with and without cow's milk. ECP levels were considerably elevated during the diet with milk, although it returned to normal values several months after milk was withdrawn. The favorable clinical outcome and normalization of ECP levels point to a very probable association with cow's milk in EGE presented in that patient. On the other hand, hypoallergenic diets have not been shown to be of significant benefit in treating EGE specially the serosal variant of the disease. Regardless of the initial trigger, activated tissue eosinophils are known to release various chemo-attractive cytokines resulting in recruitment of more eosinophils into the affected tissues [2, 10, 12, 21]. Symptoms of EGE are nonspecific and overlap with many other GI and systemic diseases. Mucosal subtype of EGE often presents with abdominal pain, nausea, vomiting, and/ or diarrhea. Eosinophilic infiltration of the tunica muscularis results in a thickened rigid gut that produces symptoms of intestinal obstruction [6, 8]. Finally, patients with the exceedingly rare serosal EGE have ascites as the source of their symptoms [2, 9–11]. Furthermore, this subgroup is clinically distinct in having abdominal bloating, higher eosinophil counts, and dramatic response to steroid therapy [3, 29]. Eosinophilia is a distinguishing feature of ascites in patients with serosal EGE. Further characterization of 42 patients with this subtype of EGE by Durieu et al. revealed female predominance with 75% of the patients being females 40 years and older. Moreover, the study showed that 69% of these patients had peripheral eosinophilia and 11% had pleural effusion which was almost similar to our case. The diagnosis of EGE is established on high clinical suspicion in conjunction with suggestive histopathologic findings. Although peripheral eosinophilia is very common in all subtypes of EGE, it can be absent in as high as 23% of cases. In addition, 25% of the patients may have moderately elevated erythrocyte sedimentation rate (ESR) which was not the case in our patient [3]. Thus, tissue samples are essential for confirming the diagnosis and classical findings include sheaths of eosinophils in the involved layer [12]. Nevertheless, this is not always an easy task as multiple endoscopic biopsies may be required due to the patchiness of the disease and diagnosis can be missed in up to 25% of cases [3]. Moreover, in cases where the diagnosis remains uncertain, CT imaging can help in localizing areas of thickened bowel suitable for surgical full thickness biopsy [12, 14]. In contrast to the other two types, serosal EGE may be confirmed by ascetic fluid analysis, which in the majority of cases reveals predominant eosinophilia reaching up to 99% of the white cells [15, 16]. No test specific for EGE is available and prior to establishing such a diagnosis, a number of GI and systemic diseases should be excluded. Many of these disorders have similar presentations and may be associated with eosinophilia. The differential diagnosis should include parasitic infections with Visceral larva migrans as "Toxocariasis, Strongyloides, Trichinosis, Echinococcusis, Ascaris suum, Capillaria hepatica, and Anisakis" [17, 22]. In any case, it is essential that parasitic infection is completely out-ruled prior to treatment of EGE, as initiation of corticosteroid therapy in the presence of occult parasitic infection may result in catastrophic disseminated disease [25]. Other differential diagnosis include, malignancies such as "intestinal lymphoma; gastric cancer; colon cancer and ovarian malignancy", Para neoplastic eosinophilia, inflammatory bowel disease, and more rarely connective tissue diseases as SLE with overlap syndrome [24,25, 26], systemic vasculitides such as polyarteritis nodosa and Churg-Strauss syndrome. The distinctive histologic features of EGE are absent in these diseases. Another major differential diagnosis of EGE is idiopathic hypereosinophilic syndrome (HES), a condition associated with marked peripheral eosinophilia and gastroenteritis. In addition to possible involvement of the GI tract, this systemic entity may involve the heart, lungs, brain, and kidneys and frequently has a progressive course, while EGE lacks any extra-intestinal manifestations [2, 3]. Further investigations to exclude the HES may be indicated in certain cases, and investigations should assess for each of several pathogenetically distinct variants of the HES. For example, clonality of eosinophils on phenotyping implies a diagnosis of chronic eosinophilic leukemia. A subset of these patients has F/P-associated HES, in which a sporadic hematopoietic stem cell chromosomal rearrangement occurs, producing the F/P fusion gene on 4q12. The F/P fusion gene can be detected using reverse transcription polymerase chain reaction or fluorescent in situ hybridization for surrogate markers of the chromosomal abnormality. In contrast, lymphocytic-HES occurs when a proliferating T cell population overproduces interleukin-5 resulting in reactive polyclonal hypereosinophilia. Analysis of T cell

subsets to detect a phenotypically aberrant T cell population, and assessment of T cell receptor gene rearrangement patterns to assess for clonality may reveal an underlying primary T cell disorder as a cause for eosinophilia [28]. These investigations are essential in suspected HES cases as certain variants; in particular F/P-associated HES demonstrate dramatic therapeutic response to the tyrosine kinase inhibitor imatinib. Finally, when EGE presents as a part of HES, patients should be referred for appropriate hematological evaluation, since eventual malignant transformation is a possibility [28]. Available data on the natural history and therapy of EGE remains scarce. Untreated patients can remit spontaneously [22] or progress to develop severe malabsorption. In most cases, the disease is essentially benign and pharmacologic therapy is not always indicated [14]. Many patients have been reported to spontaneously recover over a period of days however; others have a relapsing-remitting course and require long-term treatment with steroids, usually at a low dose of prednisone (5 to 10 mg/day). [13, 18, 19] . The outcome of EA in particular was favorable in 90% of patients while relapses occurred in 26% of 42 cases studied by Durieu et al. [11]. More symptomatic patients require therapy with prednisone (20 to 40 mg/day) which is considered the current standard treatment. A two-week course produces dramatic clinical improvement regardless of the histological subtype of EGE. Rapid tapering over another two weeks is sufficient to keep the majority of patients in remission [2, 12, 19]. For localized disease or where systemic corticosteroid treatment is not well tolerated, topical corticosteroid therapy in the form of swallowed fluticasone or non-enteric coated budesonide may be of benefit. It is unclear whether topical corticosteroid treatment is as efficacious in serosal EGE as compared with the mucosal variant [25, 31]. In cases that fail to respond to corticosteroids, treatment with azathioprine or 6-mercaptopurine should be considered [20]. Multiple therapeutic strategies have been tried in order to avoid steroid side effects (steroid sparing regime). Novel approaches in the treatment of patients with EGE include the use of sodium cromoglycate for its mast cell stabilizing properties, especially in individuals with a strong history of atopy or elevated serum IgE and mucosal predominant disease [32]. Another therapeutic option is the leukotriene receptor antagonists " Montelucast" which has been successfully used in treatment of serosal EGE with EA [33]. Moreover, Monoclonal antibodies directed against IgE and IL-5 (omalizumab and mepolizumab respectively) as targeted treatments for EGE and other eosinophilic conditions show some promise in early clinical studies [34, 35]. In addition to the above pharmacological approaches, it may be possible to significantly reduce steroid dependence in patients with documented food allergies through elimination, oligoantigenic or elemental diets [27]. These medications offer a steroid-sparing approach to treatment of EGE which aids in avoiding the serious side effects of steroid therapy. The latter is especially important in the younger patient population.

CONCLUSION

EGE is a rare condition characterized by recurrent eosinophilic infiltration of portions of the GI tract and presenting with nonspecific GI symptoms in association with peripheral eosinophilia. Its etiology and pathogenesis remain obscure and its symptoms overlap with many GI and systemic diseases. Thus, the diagnosis of this readily treatable and easily missed disease requires a high index of suspicion accompanied by the judicious application of tests. We presented a case of EA which is considered one of the rare presentations of EGE and is typically associated with the serosal variant of the disease; also it behaves in a manner distinct from the more common mucosal EGE. Our patient was a thirty years old female who presented with non-specific abdominal symptoms. Investigations revealed large volume eosinophil-rich ascites and a markedly elevated peripheral eosinophil count. Histopathological diagnosis is essential and is usually complicated by the patchy nature of mucosal disease and the paucity of mucosal infiltration in the serosal predominant form. In our patient, we could not perform colonoscopy or laparoscopy due to patient's refusal. However, duodenal biopsies; markedly elevated peripheral eosinophilia; and eosinophilic ascites as well as bowel thickening by imaging studies and, otherwise, negative workup for TB, parasitic infections and malignancy confirmed the diagnosis of EGE. So she was put on a combination regimen of prednisone (40mg/day) plus montelukast (10 mg/day) for two weeks. The dose of steroid was tapered off over the following 2 weeks and the patient was left on montelukast alone. Four months after her initial presentation, the patient is asymptomatic with a normal absolute

eosinophilia. Fortunately, novel targeted pharmacologic therapies provide promise for steroid-free remission for patients with EGE. As there is no clear treatment end point for montelukast in the literature; we intend to keep our patient on this safe drug for one year.

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Video Case: Autologous Blood Injection for Actively Oozing Gastric Ulcer

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Comment

A 64-year old Egyptian male presented by first attack hematemesis and melena. On endoscopic examination actively oozing gastric ulcer was seen. A total of 8 cc autologous blood (withdrawn from the cupital vein of the patient) was injected along the edges of the ulcer and bleeding stopped (defined as stoppage of bleeding at the time of endoscopy and stoppage of hematemesis and melena 24 h after autologous blood injection).

Video Case: Sphincterotomy after Small Pre-cut of the Major Duodenal Papilla using Standard Sphincterotome

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Comment

A 29-year old Egyptian female presented by pain in the right hypochondrium. Abdominal ultrasonography revealed mild dilatation of the common bile duct (CBD). On endoscopic retrograde cholangiopancreatography (ERCP) cannulation of the CBD was difficult. Small pre-cut for few millimeters upwards starting from the orifice of the major duodenal papilla using the standard sphincterotome was performed .Then Cannulation of the CBD and sphincterotomy were successful. Small stone was extracted from the CBD by balloon .

Image Case: Diverticulosis of the Sigmoid Colon in a 63 Years Old Male

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In this case a 63 years old Egyptian male presented by lower left abdominal pain and was diagnosed by CT as having diverticulosis of the sigmoid colon. Colonoscopy confirmed the diagnosis and excluded malignancy .

Colonic-diverticulosis in middle eastern population was found in a study done by Azzam et al., to have a low prevalence, be predominantly left-sided and associated with adenomatous-polyps. Age, hypertension and rectal bleeding predict the presence of diverticular disease[1].

Acute diverticulitis occurs in 10-25% of patients with diverticulosis. Nowadays, elective or emergency resection is generally recommended as therapy of first choice. However, contrary concepts with merely conservative treatment or drainage - even for perforated diverticulitis - are emerging. Colonoscopy is advised 6 weeks after an attack of acute diverticulitis in order to completely evaluate the colon lumen and exclude a potential malignancy.[2,3].

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Diverticular bleeding occurs due to rupture of a vas rectum at the fundus of the diverticulum. Conservative and endoscopic management is the first line and surgical resection plays a role as salvage-strategy in case of recurrent and life-threatening bleeding. Localising the bleeding, i.e., with angiography, is crucial prior to surgery [3].

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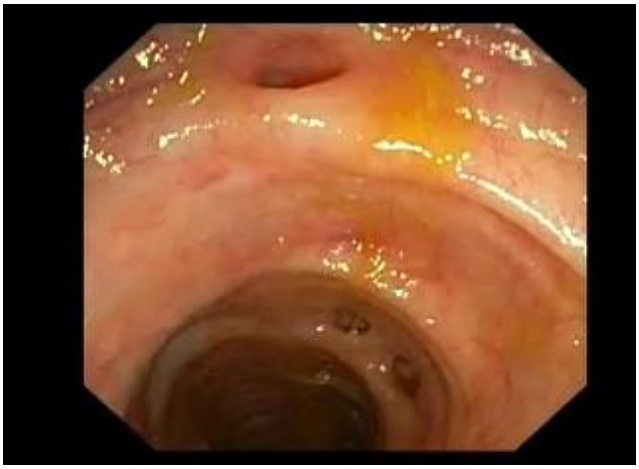

Figure 1: Diverticula of the sigmoid colon