Prevalence of Biliary Lithiasis in Chronic Renal Failure patients

Thesis by

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Abstract

Early recognition and prompt intervention are the most crucial steps in the management of gallstone-induced biliary disease. (Mansoor Ahmad et al., 2000).

- Gall stone formation is the primary underlying disease that results in gall bladder-related illnesses, The primary mechanisms that result in gallstone formation include supersaturation of bile products, nucleation factors (mucin, glycoproteins, and calcium), and bile stasis (Maurer KR et al, 1999).
- There are many Risk Factors for Gallstone Formation as Genetics (Pima Indians, Scandinavians, maternal family history of gallstones, female sex), Body habitus (Increasing age, obesity, rapid weight loss, pregnancy) , Drugs (Fibric acid derivatives, contraceptive , steroids and post-menopausal estrogens, progesterone, octreotide, ceftriaxone), Diet (Total parenteral nutrition, fasting), Diseases (Crohn's disease, ileal resection, gastrectomy, hyperlipidemia and diabetes mellitus) (Mansoor Ahmad et al., 2000) (De Santis A et al, 1997).

Key Words :

Biliary Lithiasis – Chronic Renal Failuye .

CONTENTS

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INTRODUCTION

Section A : Biliary Lithiasis

i. Introduction:

1-Anatomy of Gall bladder:

- The gallbladder is a reservoir of bile in the shape of a piriform sac partly contained in a fossa on the inferior surface of the right hepatic lobe.
- It extends from the right extremity of the porta hepatis to the inferior border of the liver.
- It is 7 to 10 cm long and 3 to 4 cm broad at its widest part, and can hold from 30 to 50 ml.
- The gallbladder is divided into a fundus, body, infundibulum and neck.(Wood D 1999).
    - The *fundus* extends about 1 cm beyond the free edge of the liver.
    - The *body* is the largest segment.
    - The *infundibulum* is the transitional area between the body and the neck.
    - *Hartmann's pouch* is a bulge on the inferior surface of the infundibulum.
- Gallstones may become impacted here and can cause obstruction of the cystic duct.
- *The neck* is the tapered segment of the infundibulum that is narrow and joins the cystic duct.
- The *cystic duct* is 3 to 4 cm long and passes posteriorly inferior and to the left from the neck of the gallbladder to join the common hepatic duct to form the common bile duct (CBD).
- The mucosa of the cystic duct is arranged with spiral folds known as the valves of Heister.(Wood D 1999).
- The arterial supply to the gallbladder is from the *cystic artery* which can originate from the right hepatic, left hepatic or the common hepatic artery, and it can be anterior or posterior to the common hepatic duct.

- The venous drainage is through the *cystic vein*, which drains into the portal vein, there are also some small veins that drain directly into the liver to the hepatic veins.
- The *lymphatic drainage* of the gallbladder proceeds mainly by four routes, which form two pathways that drain in the thoracic duct;

1. Superior and external, drains the fundus (around 6% of cases).

2. Superior and medial, drains the medial aspect of the gallbladder (around 10% of cases).

3. Inferior and external, drains the body of the gallbladder (present in 82% of cases).

4. Inferior and medial, from the body of the gallbladder (constant).

All four routes drain to both pathways, except the inferior and external which drain only to the inferior pathway.

- This is important in cases of gallbladder cancer, which can spread to the liver; because of its extensive lymph drainage to both pathways, cure by radical surgery is difficult.(Caplan I 1982).
- The gallbladder is *innervated* by the *vagus nerve* through its hepatic branch from the anterior vagal trunk.
- The gallbladder is also innervated by the *sympathetic nervous system* through the celiac plexus.
- Fibers in the *right phrenic nerve* may also be distributed to the gallbladder through the hepatic plexus.
- The *duct of Luschka* is a small bile duct, running in the bed of the gallbladder, outside the wall.
- It is present in 50% of individuals, this duct is surgically significant because it may be injured during cholecystectomy and may result in bile fistula unless ligated.(Kune GA 1989).
- Recent reports demonstrated a 1.5 to 2.0% incidence of bile leak from the duct of Luschka after laparoscopic cholecystectomy.

Ligation has no consequences as it is an end duct that drains an isolated segment.

- The *common bile duct* forms by the junction of the cystic duct with the common hepatic duct.
- Its course is divided into supraduodenal, retroduodenal, pancreatic and intraduodenal (joins the main pancreatic duct to form the sphincter of Oddi.
- The supraduodenal segment usually lies in the free border of the hepatoduodenal ligament; it runs to the right of the hepatic artery and anterior to the portal vein.
- The retroduodenal segment descends posterior to the first part of the duodenum and slightly obliquely from right to left.
- The pancreatic segment is related to the head of the pancreas; it can run entirely retropancreatic or travel through its parenchyma.
- The diameter of the common bile duct is often used as an indication of biliary pathology.
- Its “normal” size varies depending on the modality used to measure it, and a range of 4 to 13 mm has been reported.(Kune GA 1989) (Dowdy GS et al., 1962).
- The most common modality to examine the common bile duct diameter is ultrasound, and a diameter up to 6 mm is considered normal, some consider the equivalent in contrast radiology to be 10 mm; this depends on the magnification.(Padbury RTA 1993).
- The common bile duct enters the duodenum approximately 8 cm from the pylorus in the second part of the duodenum.
- The site entry is marked by a papilla (major papilla).
- Its position can be variable; in approximately 13% of individuals it can be located at the junction of the second and third part of the duodenum, or even more distally.(Lindner HH et al., 1976).
- A transverse fold of mucosa usually covers the *papilla* which is identified as a small nipple or pea-like structure in the lumen of the duodenum.(Boyden EA 1987).

2-Physiology of the biliary tract:

- The *components of bile* are:

. Water
. Cholesterol
. Lecithin (a phospholipid)
. Bile pigments (bilirubin & biliverdin)
. Bile salts (sodium glycocholate & sodium taurocholate)
. Bicarbonate ions

- Bile fulfils two *major functions*; it participates in the absorption of fat and forms the vehicle for excretion of cholesterol, bilirubin, iron and copper.
- Bile acids are the main active component of biliary secretion.
- They are secreted into the duodenum and efficiently reabsorbed from the terminal ileum by the portal venous system.(Hofmann AF 1994).
- Bile is *secreted* by the hepatocytes through the canalicular membrane into the canalicular space.
- The secretory process is both active and passive and the active process generates bile flow.
- The products of active secretion are known as primary solutes and these are made up of conjugated bile acids, conjugated bilirubin, glutathione, conjugates of steroid hormones and leukotrienes.
- Filtrable solutes are generated by passive secretion induced by osmotic pressure and are called secondary solutes; these are mainly plasma, glucose, electrolytes, low-molecular-weight organic acids and calcium.
- The maximum secretory pressure developed by the liver is 30 cm.
- In the fasting state, the sphincter of Oddi has an average resting pressure of 12 to 15 cm H2O.
- Because the opening pressure of the cystic duct is 8 cm H2O and the gallbladder is 10 cm H2O, the pressure gradient favors the entry of bile into the gallbladder.(Everson GT 1991).
- Therefore, during fasting, most of the bile is diverted into the gallbladder where it is concentrated.

- Bile is *produced* by hepatocytes and cells of the intrahepatic ducts at a rate of 600 mL/day.
- The hepatic bile entering the gallbladder during fasting consists of approximately 97% water and 1 to 2% bile acids; Phospholipids, cholesterol, bile pigment and electrolytes make up the remainder.(Shaffer EA 1982) (Janson R 1978).
- Hepatic bile is iso-osmolar with plasma.
- Sodium, chloride and bicarbonate ions, with nearly an isotonic amount of water, are absorbed from the bile.
- The gallbladder is able to remove 90% of the water from hepatic bile.(Banfield WJ 1995).
- The gallbladder concentration of bile salts, bilirubin and cholesterol may rise 10-fold or more, relative to hepatic bile levels.
- The gallbladder partially empties during fasting in conjunction with the phases of the interdigestive cycle.
- After a meal, the gallbladder contracts and the sphincter of Oddi relaxes, leading to the delivery of bile to the duodenum.
- The gallbladder empties around 75% of its content, at the same time, hepatic bile bypasses the gallbladder and empties into the duodenum.
- At the end of the meal, the gallbladder relaxes and the sphincter of Oddi contracts, leading to the diversion of hepatic bile into the gallbladder once again for storage until the next meal.
- In individuals who have undergone a cholecystectomy, bile acids are stored in the proximal small intestine.(Hofmann AF 1998).
- After meal ingestion, the acids get transported to the distal ileum for absorption and maintenance of the enterohepatic circulation.

- The *reabsorption* of bile acids is through the enterohepatic circulation.
- Bile acids are absorbed from the terminal ileum and transported back to the liver by the portal system.

- This is achieved by passive and active transcellular absorption.
- The most important mechanism is a sodium-coupled transport system that is present in the apical membrane of the enterocytes; it is known as the ileal bile acid transporter (IBAT).(Wong MH et al., 1994).
- In the distal ileum and large intestine, intestinal bacteria deconjugate bile acids, which are absorbed passively in solution.(Hofmann AF 1994).
- A small amount of the bile acid is lost from the body in feces.
- This fecal loss is compensated by synthesis of new bile acids.
- In healthy adults, less than 3% of bile acids present in hepatic bile are newly synthesized.
- In the portal system, bile acids are bound to albumin and the ability of the albumin binding depends on the nuclear substitutes.
- For trihydroxy bile acids, this is around 75%, whereas it is 98% for dihydroxy bile acids.
- On the first pass, the hepatic circulation extraction is between 50 and 90%; the level of bile acids in the systemic circulation is directly proportional to the load presented to the liver, and it increases after meals.(Hofmann AF 1998).
- The plasma level of total bile acids is 3 to 4 mol/L in the fasting state and increases twofold to threefold after digestion.

ii. Biliary lithiasis:

1- INTRODUCTION:

- Gallstone disease is one of the most common and costly of all digestive diseases, the third National Health and Nutrition Examination Survey estimated that 6.3 million men and 14.2 million women aged 20 to 74 in the United States had gallbladder disease .
- Over the past two decades, a great deal has been learned about the epidemiology of and risk factors for gallstones.
- Ultrasonography has played a major role in this process, providing a rapid, risk-free method of screening large populations.
- Prior to the availability of ultrasound, most studies relied on highly selective autopsy data and limited oral cholecystography.(McSherry CK et al., 2005).

2-Background:

- Biliary colic and cholecystitis are in the spectrum of biliary tract disease, this spectrum ranges from asymptomatic gallstones to biliary colic, cholecystitis, choledocholithiasis, and cholangitis.
- In the United States, autopsies have shown that at least 20% of women and 8% of women older than 40 years have gallstones.
- Gallstones are divided into 2 categories: Cholesterol (80%) and pigment (20%), ones temporarily obstruct the cystic duct or pass through into the common bile duct, gallstones become symptomatic, and biliary colic develops.

- Cholecystitis occurs when this obstruction is prolonged (usually several hours) resulting in inflammation of the gallbladder wall.
- Choledocholithiasis occurs when the stones become lodged in the common bile duct, resulting in possible cholangitis and ascending infections.(Hourdat R et al., 1995).

3-Pathophysiology:

- Cholecystitis is an inflammation of the gallbladder caused by obstruction of the cystic duct.
- A gallstone usually causes the obstruction (calculous cholecystitis).
- The inflammation may be sterile or bacterial.
- The obstruction may be acalculous or caused by sludge.
- This obstruction can result in gallbladder distention, gallbladder wall edema, ischemia, and necrosis.
- Additional inflammatory mediators, specifically prostaglandins, are released resulting in increased gallbladder inflammation.
- Bacterial infection is thought to be a consequence, not a cause, of cholecystitis.
- In the early stages of acute cholecystitis, bile is sterile.
- Approximately 20-75% of bile cultures are eventually positive with the most common organisms being *Escherichia coli, Klebsiella* species, *Enterococci*, and *Enterobacter*. Common bile duct stones (choledocholithiasis, 10%) are either secondary (from the gallbladder) or primary (formed in bile ducts).(Singer AJ et al., 1996).

4- EPIDEMIOLOGY :

- Epidemiologic data are now available from a number of large European and American populations.
- These studies have revealed a marked variation in overall gallstone prevalence between different ethnic populations.
- In general, there appears to be higher rates of cholelithiasis in western Caucasian, Hispanic, and Native American populations and lower rates in eastern European, African American, and Japanese populations.(Torvik A et al., 1996) (Attili AF et al., 1995).
- In the United States, the age standardized prevalence of gallbladder disease was estimated based upon a sample of more than 14,000 persons aged 20 to 74 in whom gallbladder disease was detected by the presence of gallstones or cholecystectomy on ultrasonography.(Everhart JE et al., 1999).
- The following prevalence rates were observed: 8.6 and 16.6 percent among non-Hispanic white men and women, respectively 8.9 and 26.7 percent among Mexican American men and women, respectively 5.3 percent and 13.9 percent among non-Hispanic black men and women, respectively
- In other studies, Native Americans had the highest prevalence of cholelithiasis in North America. As an example, 73 percent of female Pima Indians over the age of 25 years have gallstones(Sampliner RE et al., 2000) ; similar high rates have been found in multiple other Native American populations.(Thistle JL et al., 2001) (Williams CN et al., 1990).
- As illustrated above, African Americans appear to have the lowest prevalence of cholelithiasis. Autopsy based studies performed in the 1950s found that African Americans had one-half to one-quarter the risk of cholelithiasis compared to Caucasian Americans(Cunningham JA, Hardenbergh FE 1996) (Newman HF,

Northup JD 1999) ; later reports have shown a 40 percent lower risk of hospitalization for gallstone related disease.(Sichieri R et al., 1990).

- Large ultrasound based studies from Europe have characterized both gallstone prevalence and incidence. As an example, the Multicenter Italian Study of Cholelithiasis (MICOL) examined nearly 33,000 subjects aged 30 to 69 years in 18 cohorts in 10 Italian regions. The overall rate of gallstone disease was 18.8 percent in women and 9.5 percent in men.(Attili AF et al., 1995).
- Similar results were noted in the Sirmione study in which an overall prevalence rate of 11 percent in 1930 Italian subjects between the ages of 18 and 65 years was noted. (Barbara L et al., 1993). Ultrasound examinations were repeated on the same patients at five-year intervals. The 10-year cumulative incidence of new gallstones was 4.6 percent.

5-RISK FACTORS:

In addition to the variability of gallstones in different ethnic populations, a number of other risk factors for this condition have been identified.

- *Age:*

- Age is a major risk factor for the gallstones.
- Gallstones are exceedingly rare in children except in the presence of hemolytic states; in addition, less than 5 percent of all cholecystectomies are performed in children.
- Age 40 appears to represent the cut-off between relatively low and high rates of cholecystectomies.
- This observation was validated in the Sirmione study in which the incidence between the ages of 40 and 69 years was four times higher than that in younger subjects.