SYMPTOMATIC GALL STONES AND THE RISK OF GALLBLADDER CANCER

THESIS

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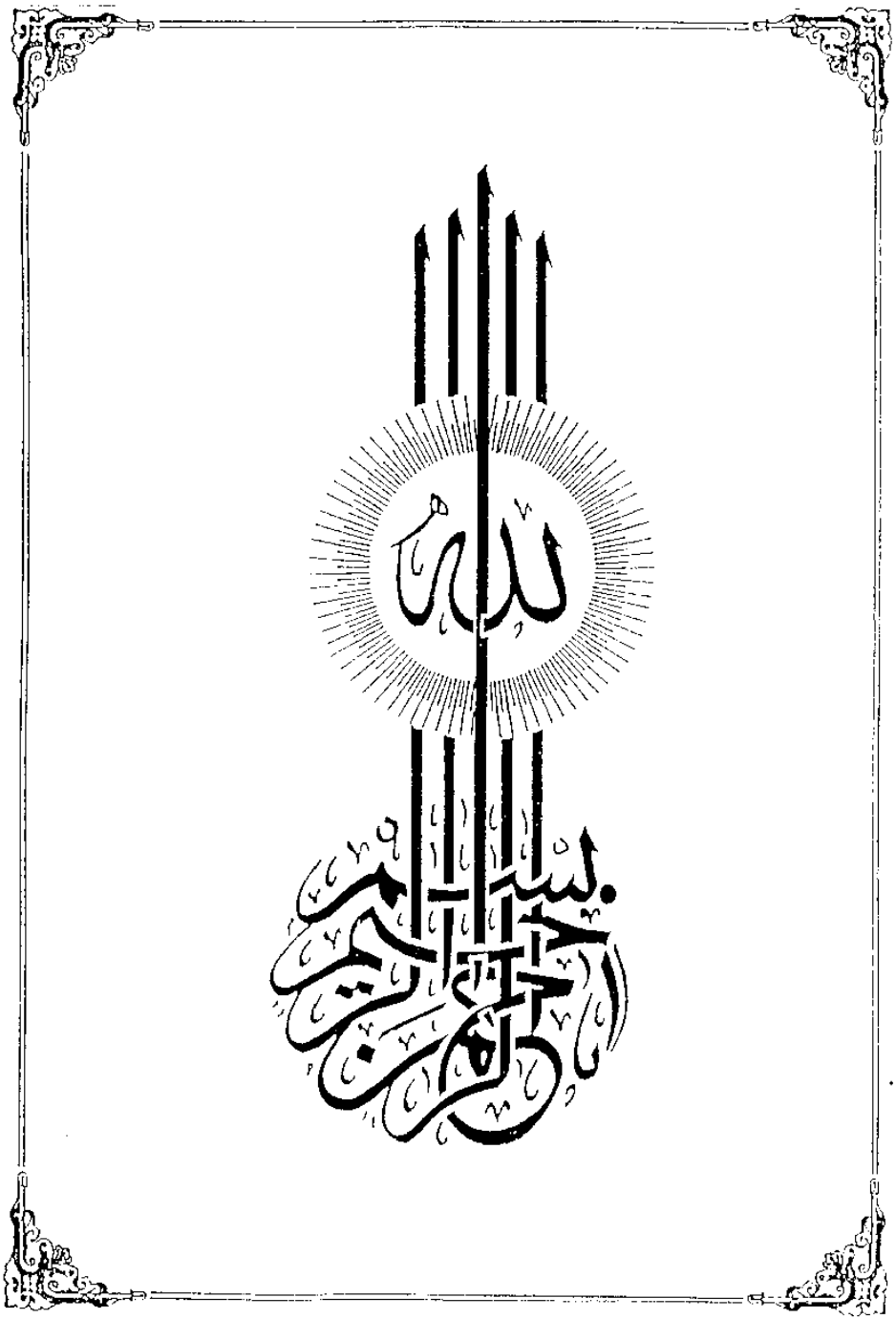

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List of Abbreviation

Ag-NORs	:	Silver staining Nucleolar Organizer Regions
AJCC	:	American Joint Committee on Cancer
CSI	:	Cholesterol Saturation Index
DNA	:	Desoxyribo Nucleic Acid
E.	:	Eosin Stain
G1	:	Gap 1
G2	:	Gap 2
HID	:	Hale's Iron Dialysis method, of staining
Hx.	:	Haematoxylin stain
NORA	:	The mean Nucleolar Organizer Region Area
NORAPs	:	Nucleolar Organizer Region-Association Proteins
NORDS	:	Nucleolar Organizer Regions Distribution Score
NORs	:	Nucleolar Organizer Regions
PAS	:	Periodic Acid Schiff Stain
pH value	:	A symbol for detection of the hydrogen ion concentration
rDNA	:	Ribosomal Desoxyribo Nucleic Acid
S-Phase	:	Phase of Synthesis
T1-NORs	:	Type 1 Nucleolar Organizer Regions
T2-NORs	:	Type 2 Nucleolar Organizer Regions
TNM	:	Tumour lymph NODE distant Metastasis

Introduction

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Cholelithiasis is the most prevalent disease of the biliary system and it has increased markedly in the last decades. It occurs in persons over 40 years of age, and females are more commonly affected than males (2-4:1). Although gallstones may be clinically silent, symptomatic patients are common. The symptomatology of these gallstones is varied, often non-specific. The symptoms may be acute or chronic.

Cholecystectomy for symptomatic gallstones, is usually done to avoid potential complications. Gallbladder cancer may occur in 18% to 50% of patients with gallstones, followed for 20 years *(Stephen S. Sternberg, 1989)*.

Therefore, there is a common association between carcinoma of the gallbladder and gallbladder stones, but whether gallstones are precancerous or not, is still debatable.

Aim of the Work

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The aim of this work, is to detect any malignant or premalignant changes in the wall of the gallbladder, in cases of symptomatic gallbladder stones and to study the relation of these changes if any, with the chemical composition and the relative age of the stones.

Anatomy of the gallbladder

The gallbladder is a pear shaped, distensible reservoir located on the undersurface of the liver within the cystic fossa. The gallbladder has a capacity of 30 to 50 ml, and consists of a fundus, body, and a neck or infandibulum. The fundus is the rounded portion of the gallbladder that usually extends beyond the edge of the liver. The body of the gallbladder extends from the fundus to the tapered portion, or neck, of the gallbladder. The neck occupies the deepest part of the gallbladder fossa and lies in the free portion of the hepatoduodenal ligament. Dilation of the gallbladder neck creates the Hartmann's pouch which may obscure the junction between the cystic and the common bile duct. The gallbladder may occasionally be partially or completely embedded within the liver parenchyma or abnormally positioned beneath the left lobe of the liver *(David et al., 1993)*.

Arterial Supply:

The arterial supply of the gallbladder is by means of the cystic artery, which arises from the hepatic artery within the hepatocystic triangle in approximately 80% of individuals *(David et al., 1993)*.

Near the gallbladder, the cystic artery usually divides into a superficial branch and a deep branch. The superficial branch courses along the anterior surface of the gallbladder, whereas the deep branch passes between the gallbladder and the liver in the cystic fossa ***(Scott-Conner et al., 1992).***

Based upon anatomic dissections, three anatomic variations are recognised in the course of cystic artery, the commonest being an accessory or double cystic artery arising from the right hepatic artery, the second common is the caterpillar hump which is a cystic artery arising from the convex angle of a humped portion of the hepatic artery and the least common is the cystic artery which pass anterior to the common bile duct or the common hepatic duct ***(David et al., 1993).***

Lymphatic drainage:

Lymph drainage of the gallbladder passes into three main pathways namely the right, left and the hilar routes. The right route which is the commonest passes in the right half of the hepatoduodenal ligament along the common bile duct into the superior retropancreaticoduodenal or retroportal nodes. The left route which is less significant passes to the common hepatic nodes and finally the hilar route ascends in the

hepatoduodenal ligament to drain in the hilar group of lymph nodes *(Katsuhiko et al., 1996).*

Histology of the Gallbladder

The gallbladder wall has several layers and is somewhat different structurally than the other hollow organs of the gastrointestinal tract. The mucosa is thrown into a variable number of folds, depending on the degree of organ distention. The epithelial lining consists of uniform tall columnar cells which contain oval basally located nuclei and pale cytoplasm. The apical cytoplasm contains scant amounts of sulfomucin. Occasional narrow or pencil cells and oval basal cells may also be found. Argyrophil cells are absent. The lamina propria is composed of loose connective tissue containing blood vessels and lymphatics. The muscular layer directly abuts on the lamina propria, without an intervening submucosa. its thickness is variable. There are no defined circular and longitudinal layers, and thus it resembles the muscularis mucosa. The perimuscular connective tissue layer (subserosa, adventitia) is composed of variable amounts of collagen, elastic tissue and fat. Blood vessels, lymphatics, nerves and scattered paraganglia are found. The serosal layer (peritoneum) lined the portion of the gallbladder not directly attached