Paradigm Academic Press
Journal of Innovations in Medical Research
ISSN 2788-7022
FEB. 2025 VOL.4, NO.1

Anatomy of Human Liver: A Theoretical Study

Haradhan Kumar Mohajan[1]

[1] Associate Professor, Department of Mathematics, Premier University, Chittagong, Bangladesh

Correspondence: Haradhan Kumar Mohajan, Associate Professor, Department of Mathematics, Premier University, Chittagong, Bangladesh.

doi:10.56397/JIMR/2025.02.03

Abstract

Liver is the largest and the most complex internal organ of the body. It is situated in the right upper quadrant of the abdomen and extents across the midline to the left upper quadrant. It is considered as a central essential vital organ for survival of human, animals, birds, fishes, etc. It plays many important roles in human body by breaking down nutrients that are found from digestion, storing energy and supplying this during fasting, fighting against infection and disease, reducing the effects of toxins and drugs, etc. Before and during various surgical and interventional radiologic procedures of the liver; physicians, anatomists, and radiologists need to determine the damage area. Therefore, they need accurate anatomical and clinical particularities of the liver before and during the essential interventional or surgical planning for the successful operations, such as hepatic artery infusion pumps, liver ablation, transplantation, transarterial chemoembolization, selective internal radiation therapy, and portal vein embolization. In this study anatomy of liver is discussed to improve the safety and feasibility of hepatic surgery.

Keywords: liver anatomy, bile ducts, hepatic lobes, portal vein, hepatic artery

1. Introduction

Anatomy is a field in the biological sciences that is concerned with the identification and description of the body structures of human and other different species of animals and fishes. Proper knowledge on anatomy of the liver is of critical importance for the determination of localization of disease processes and for their management, and for the essential liver transplant surgery for the survival of the patients. Also, knowledge on liver anatomy is essential for cholecystectomy, hepatobiliary, pancreatic, and upper gastrointestinal (GI) surgery (Elobu et al., 2021).

Liver is located within the peritoneal cavity, and is in the right upper quadrant of the abdomen. It is a wedge shaped organ. It performs various functions, such as digestion, bile production, drug metabolism, bilirubin synthesis, etc. A comprehensive analysis of the anatomical composition of the liver is necessary for the effective management of disorders for the surgical intervention and for the treatment of various liver diseases. At present liver resection is practicing worldwide widely to minimize morbidity and reduce mortality. On the other hand, microscopic anatomy is the study of structural units small enough to be seen only with a light microscope (Sumadewi, 2023).

2. Literature Review

The literature review section is an introductory unit of research that exhibits the works of previous researchers in the same field within the existing knowledge (Polit & Hungler, 2013). It assists all researchers to improve research questions and to move forward energetically in the current research (Creswell, 2007). Henri Bismuth has shown that the liver is divided into four sectors, some of them composed of two segments. In all, there are eight segments. He believes that a good knowledge of the anatomy of the liver is a prerequisite for anatomical surgery of this organ (Bismuth, 1982). Lukas Hettiaratchi has studied the anatomy, physiology and

pathophysiology of liver with the post-operative physiotherapy on a patient after liver transplantation (Hettiaratchi, 2022). Harold Ellis has provided morphologic liver anatomy with subdivisions (Ellis, 2011).

Kalpana Ramachandran and Robert Dinesh Kumar have studied the morphological variations of liver, such as changes in size, shape, presence of accessory lobes, fissures, and hypoplastic lobes (Ramachandran & Kumar, 2019). Komang Trisna Sumadewi has observed significant advancements in the comprehension of liver anatomy that have contributed to the notable progress in various surgical and interventional radiologic procedures, such as hepatic artery infusion pumps, liver ablation, transplantation, transarterial chemoembolization, selective internal radiation therapy, and portal vein embolization (Sumadewi, 2023).

Durand Lopez Cesar Augusto and Juana Raquel Durand Fernandez aim to shed light on the anatomy of segment V and to explore how it determines the number of portal segments of the liver (Augusto & Fernandez, 2021). Alex Emmanuel Elobu and his coworkers observe that a thorough knowledge of the liver anatomy and its variations is of critical importance for safe and successful procedures and surgeries involving the liver (Elobu et al., 2021).

Haobam Rajajee Singh and Suganthy Rabi have realized that the knowledge of normal and variant anatomy of the liver is important during radiological investigation and surgery. They believe that the congenital abnormalities of the liver are agenesis, atrophy or hypoplasia of lobes, accessory lobes, accessory fissures, etc. They have wanted to determine the gross anatomical variations of the liver in the South Indian population (Singh & Rabi, 2019).

3. Research Methodology of the Study

Research is the procedures of systematic investigations that requires collection, interpretation and refinement of data, and ultimately prepares an acceptable article, working paper, book chapter or a thesis by the appropriate use of human knowledge (Pandey & Pandey, 2015). A well-developed outline of the study and an efficient understanding are essential to reach the goal of a research (Tie et al., 2019). Methodology is a guideline for the accomplishment of a good research (Kothari, 2008). It relates to nature and power to science, truth, and epistemology (Ramazanoglu & Holland, 2002). Therefore, research methodology is a way to the researchers for organizing, planning, designing, and conducting a good research (Legesse, 2014).

To prepare this paper we have depended on the secondary data sources of anatomy related articles that are collected from published research papers, and books of famous authors. Some other valuable and essential materials are managed using internet, websites, etc. (Mohajan and Mohajan, 2023a-e, 2024a; Mohajan, 2017, 2018, 2020, 2024a-d).

4. Objective of the Study

Main objective of this article is to explore the basic concepts of liver anatomy. Some other related objectives of the study are as follows:

1) to highlight on structure and location of liver,

2) to focus history of liver anatomy, and

3) to enhance the approaches of liver anatomy.

5. Structure of Liver

Liver is the largest internal organ and the second-largest organ overall in the human body after the skin. It holds the most extensive visceral tissue situated within the abdominal cavity. It is pyramidal or wedge shaped, with the base of the wedge to the right and the apex to the left (Elobu et al., 2021). The inferior liver border in the normal patient should have an acute angled edge. Liver is dark pinkish-brown peritoneal organ, in an average adult human weighs 1.35-1.59kg, which is roughly 2-3% of the total body weight. Its size, as measured in the right mid-clavicular line, is about 12-15cm. It is consisted of two faces and four edges; visceral parietal faces, dorsal, ventral, right and left edges (Juza & Pauli, 2014).

Liver volumes vary depending on patients and are related to patient body surface area and weight. An average liver volume in healthy adult people is 1,225cm^3 (±217). However, when liver cirrhosis progresses, decrease in liver volume and Child-Pugh scores is used to assess the prognosis of the disease. Mean liver volumes of Child-Pugh class A is 1,100cm^3 (±337), of Child-Pugh class B is 1,040cm^3 (±365), and of Child-Pugh class C is 800 cm^3 (±205). These are required to determine the strength of the treatment and the necessity of liver transplantation (Cholongitas et al., 2005).

The liver consists of two major types of cells: hepatocytes and Kupffer cells. The main cells in the liver are known as hepatocytes that make up 80% of the cells of the liver. These cells are cuboidal epithelial and perform most of the functions of liver, such as metabolism, processing of hemoglobin, conversion of harmful ammonia to urea, regulating blood clotting, store and release of glucose, removing bacteria from the bloodstream, clearing

the blood of drugs and other harmful substances digestion, clearance of bilirubin, certain proteins production, and bile production (Bismuth, 1982). These are arranged in plates and separated by lacunae, the plates being in intimate contact with the portal tracts and the hepatic central canals that lie perpendicularly to each other. The portal tracts contain hepatic arterioles, radicals of the portal vein, lymphatics, and bile ductile (Elias, 1955). Kupffer cells are first observed by Baltic German anatomist Karl Wilhelm von Kupffer (1829-1902) in 1876 that are a type of macrophage, which capture and break down old, worn out red blood cells passing through the sinusoids (Nguyen-Lefebvre & Horuzsko, 2015).

The liver has two external surfaces: The parietal is a convex diaphragmatic surface (antero-superior), and the visceral is a concave surface (postero-inferior). The smooth and convex upper antero-superior surface fits closely beneath the curvature of the diaphragm, while the postero-inferior surface rests against the abdominal oesophagus, stomach, upper duodenum, hepatic flexure of the colon, right kidney and suprarenal gland, as well as carrying the gall bladder (Ellis, 2011).

6. Location of Liver

Liver is located in the upper right-hand portion of the abdominal cavity (right hypochondrium and epigastrium), below the diaphragm, on top of the stomach, right kidney, and intestines; and extends into the left hypochondrium. It is mostly protected by the lower right rib cage and maintains its position through peritoneal reflections, referred to as ligamentous attachments. The peritoneum connects the liver in four locations: the coronary ligament, the left and right triangular ligaments, and the falciform ligament (Krishna, 2013).

The common hepatic artery is originated from the celiac trunk that is responsible for delivering oxygenated blood to the liver and serves as this organ’s primary source of blood supply. The convergence of the central veins results in the formation of the hepatic veins. These veins facilitate the direct blood flow from the liver to the inferior vena cava (IVC), bypassing the diaphragm (Kalra et al., 2023).

7. History of Liver Anatomy

The development of liver anatomy has occurred over hundreds of years. Greek physician, surgeon, and philosopher laudius Galenus (130-216BC) was one of the first who described the anatomy of liver. He thought that the liver was five-lobed (Rocca, 2003). In 1784, Swiss anatomist, physiologist, naturalist, encyclopedist, bibliographer and poet, Albrecht von Haller (1708-1777) described the external liver surface (Frixione, 2006).

British physician and anatomist Francis Glisson (1598-1677) was the first to disclose the internal structure of the liver. He has examined the venous structures and the network of bile ducts in the liver by injecting them with water or milk and then removing the liver tissue (van Gulik, 2022). In 1957, French surgeon and anatomist, Claude Couinaud (1922-2008) has studied segmental anatomy of the liver (Couinaud, 1954). He has closely examined the intrahepatic anatomy and demonstrated that hepatic functional anatomy is based on vascular and biliary relationships rather than external surface anatomy. He has improved the safety and feasibility of modern hepatic surgery (Abdel-Misih & Bloomston, 2010).

8. Approaches of Liver Anatomy

Scholars from various countries have used various anatomical markers on the surface and inside of the liver to divide the liver into multiple independent functional units, and the different liver segments are essentially not related to each other; each of which has its own blood supply and drainage channels (Liu et al., 2021). There are two different surgical approaches of liver anatomy: i) morphological anatomy, and ii) functional anatomy.

8.1 Morphological Anatomy

Morphological anatomy is the anatomy of the liver depending on external appearance. It describes the liver into two main lobes and two accessory lobes. The liver consists of two lobes: i) the right lobe (larger), ii) the left lobe (smaller) that are divided by the plane of middle hepatic vein (Bismuth, 1982). The right lobe is divided into anterior and posterior sectors by the plane of the right hepatic vein. The left lobe is divided into a medial and lateral sectors by an oblique plane connecting the left hepatic vein and the falciform ligament. Both lobes are separated by the falciform ligament that connects the liver to the abdominal wall. These consist of 1,000 lobules that are connected to small ducts, which are connected with larger ducts to form the common hepatic duct. Each of these lobules has a duct flowing toward the common hepatic duct, which drains bile from the liver (Emma, 2022).

Other two smaller parts of liver are i) caudate lobe, and ii) the quadrate lobe. The caudate lobe on the posterior surface and the quadrate lobe on the inferior surface lie to the right of these two fissures posteriorly, separated from each other by the porta hepatis (Ellis, 2011). This approach is not sufficient for the needs of modern radiology, hepatology, and hepatobiliary surgery (Bismuth, 1982).

8.2 Functional Anatomy

Functional anatomy is the functional segments of the liver on the basis of the anatomy of hepatic vessels and bile ducts. It is necessary to meet the needs of modern radiology, hepatology, and hepatobiliary surgery (Skandalakis et al., 2004). It permits the description of a hepatic segmentation based upon the distribution of the portal pedicles and the location of the hepatic veins. It is initiated in 1898 by British physician James Cantlie (1851-1926) (McIndoe & Counseller, 1927). John E. Healey and Paul C. Schroy have taken first attempt to divide the liver into functional parts. They have divided the liver into left and right livers and five segments: medial, lateral, posterior, anterior and caudate (Healey & Schroy, 1953).

French surgeon and anatomist Claude Couinaud (1922-2008) has suggested that the liver should be subdivided into eight segments, based on portal scissura and later modified by French surgeon Henri Bismuth (Couinaud, 1954). Each segment is the functional unit with a branch of hepatic artery, portal vein, bile duct, and biliary drainage (Couinaud, 1999). The subsegmental descriptions of Bismuth have more anatomic detail that are useful for current surgical techniques. The resection of the right hemiliver involves subsegments V, VI, VII, and VIII and that of the left hemiliver involves subsegments II, III, IVA, and IVB (Figure 1) (Bismuth, 1982). The left lateral section is subdivided into Segments II superiorly and III inferiorly, the left medial section form segments IVA superiorly and IVB inferiorly. The right anterior section forms segment V and VIII while the right posterior forms segment VI and VII superiorly and inferiorly accordingly (Figure 1). Segments II and III is a left-lateral segmentectomy; segments VI and VII is a right-lateral segmentectomy also known as a right posterior segmentectomy; and segments IV, V, and VIII is a median segmentectomy (Leslie et al., 2017).

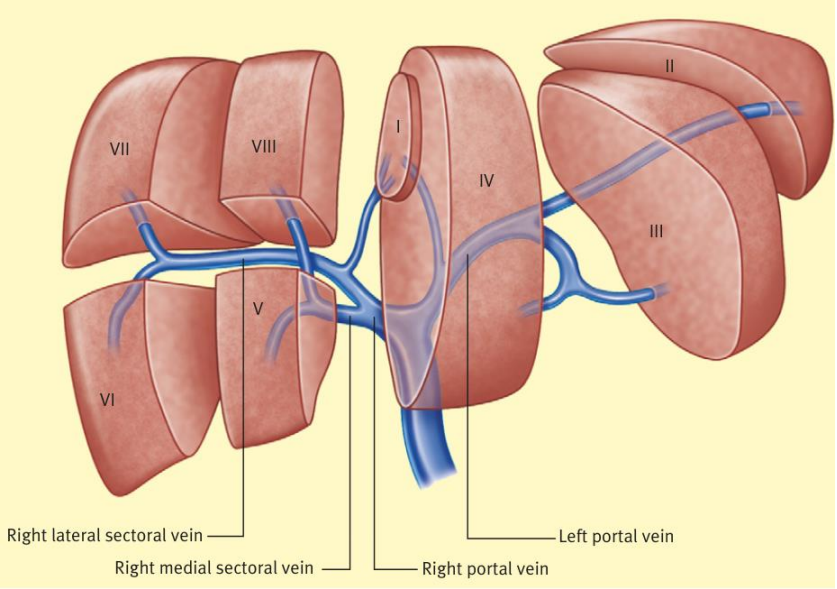

Figure 1. Subdivisions of liver

Source: Ellis, (2011).

Each segment except segment I is subdivided into superior and inferior subsegments by a transverse plane drawn through the right and left main portal branches. Segment I is defined by the three vertical scissurae and one transverse scissura. The numbering of the segments is in a clockwise manner on a frontal view of the liver. Segment I is caudate lobe and process, is situated on the posteroinferior surface of the liver posterior to the hilar plate. Its inflow is from the hepatic pedicle and outflow into the inferior vena cava (IVC) that is independent of the hepatic veins (Lafortune et al., 1991). Segment II is superior left lateral sector that is bounded medially by falciform ligament and inferiorly by plane of main portal vein (MPV). It lies between the left margin of the liver on the left and between the portoumbilical fissure superoanteriorly and the fissure for the ligament venosum posteroinferiorly on the right. It receives blood from branches of the vessels of the hepatic pedicle (portal triad) that arise from the posterolateral aspect of its left division as the latter turns into the portoumbilical fissure (Soyer et al., 1994).

Segment III is inferior left lateral sector, which is bounded medially by the falciform ligament and superiorly by the plane of the MPV bifurcation. It receives blood from the vessels of the left division of the hepatic pedicle shortly before the latter is joined by the round ligament. Segment IV lies between the portoumbilical and median fissures anterosuperiorly. It extends up to the hilar plate, which separates it from the caudate lobe and process

(segment I). It is supplied by the branches of the left branch of the hepatic pedicle (portal triad) that curve medially in a rightward direction. This segment is divided into segment IVA that is superior left medial sector and segment IVB that is inferior left medial sector. Both of these segments are bounded laterally by falciform ligament and medially by Cantlie's line (Bismuth, 1982).

Segment V is inferior left medial sector that is bounded anteriorly by the gallbladder fossa and posteriorly by the plane of the right hepatic vein, superiorly bounded by the plane of MPV bifurcation. Its blood is supplied by descending branches of the anterior division of the right branch of the hepatic pedicle. Segment VI lies to the right of the right fissure and is limited posteriorly by a plane passing through the hilum. Its blood supply is from the descending branches of the posterior branch of the vessels of the right hepatic pedicle. Segment VII presents on the superior and posterior surface and is delineated by the right fissure and the hilar plane. The blood supply is derived from the ascending branches of the posterior branch of the right hepatic pedicle (Leslie et al., 2017). Segment VIII is superior right anterior sector that is bounded anteriorly by the plane of the gallbladder fossa and middle hepatic vein, posteriorly bounded by the plane of the right hepatic vein and inferiorly by the plane of the MPV bifurcation (Rutkauskas et al., 2006).

9. Conclusions

Imaging of the liver, such as ultrasonography, computerized tomography (CT), magnetic resonance imaging (MRI), etc. help the anatomists, surgeons, and radiologists for successful liver surgery. Proper knowledge of the liver anatomy is of critical importance for the safe and successful surgical procedures of the liver. Growing more knowledge on vascular anatomy with advancement of technologies has made the liver surgery safer and effective. As a result, false reports will be decreased that will help surgeons to reduce morbidity and mortality during surgical procedures.

References

Abdel-Misih, S. R. H., Bloomston and M. M., (2010). Liver Anatomy. *Surgical Clinics of North America, 90*(4), 643-653.

Augusto, D. L. C., Fernandez and J. R. D., (2021). Anatomy of the Human Liver, Role of the Segmentary Portal Branch V. *Journal of Morphology and Anatomy*, *5*, S3.

Bismuth, H., (1982). Surgical Anatomy and Anatomical Surgery of the Liver. *World Journal of Surgery*, *6*(1), 3-9.

Cholongitas, E. et al., (2005). Systematic Review: the Model for End-Stage Liver Disease: Should It Replace Child–Pugh's Classification for Assessing Prognosis in Cirrhosis? *Alimentary Pharmacology & Therapeutics*, *22*(11-12), 1079-1089.

Couinaud, C., (1954). Anatomic Principles of Left and Right Regulated Hepatectomy: Technics. *Journal of Chiropractic (Paris*), *70*(12), 933-966.

Couinaud, C., (1999). Liver Anatomy: Portal (and Suprahepatic) or Biliary Segmentation. *Digestive Surgery*, *16*(6), 459-467.

Creswell, J. W., (2007). *Qualitative Inquiry and Research Design: Choosing Among Five Approaches*. Thousand Oaks, CA: Sage Publications.

Elias, H., (1955). Liver Morphology. *Biological Reviews, 30*(3), 263-310.

Ellis, H., (2011). Anatomy of the Liver. *Surgery*, *19*(12), 589-592.

Elobu, A. E., et al., (2021). Surgical Anatomy of the Liver. *Anatomical Science, 4*(1), 1-3.

Emma, O., (2022). Anatomical Description and Functions of Liver in Human Body. *Journal of Liver*, *11*(3), 1000137.

Frixione, E., (2006). Albrecht von Haller (1708-1777). *Journal of Neurology*, *253*(2), 265-266.

Healey, J. E. Jr., Schroy and P. C., (1953). Anatomy of the Biliary Ducts within the Human Liver; Analysis of the Prevailing Pattern of Branchings and the Major Variations of the Biliary Ducts. *AMA Archive of Surgery*, *66*(5), 599-616.

Hettiaratchi, L., (2022). A Case Study of Physiotherapy on a Patient After Liver Transplantation. Bachelor Thesis, Physiotherapy Department, Faculty of Physical Education and Sport, Charles University.

Juza, R. M., Pauli and E. M., (2014). Clinical and Surgical Anatomy of the Liver: A Review for Clinicians. *Clinical Anatomy*, *27*(5), 764-769.

Kalra, A., et al., (2023). *Physiology, Liver*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

Kothari, C. R., (2008). *Research Methodology: Methods and Techniques (2nd Ed.)*. New Delhi: New Age

International (P) Ltd.

Krishna, M., (2013). Microscopic Anatomy of the Liver. *Clinical Liver Disease*, *2*(Suppl 1), S4-S7.

Lafortune, M., et al., (1991). Segmental Anatomy of the Liver: A Sonographic Approach to the Couinaud Nomenclature. *Radiology*, *181*(2), 443-448.

Legesse, B., (2014). Research Methods in Agribusiness and Value Chains. School of Agricultural Economics and Agribusiness, Haramaya University.

Leslie, H., et al., (2017). Surgical and Radiologic Anatomy of the Liver, Biliary Tract, and Pancreas. *In Blumgart's Surgery of the Liver, Biliarytract and Pancreas*. W.R. Jarnagin (Ed.), Elsevier, 2-59.

Liu, R., et al., (2021). Revisiting Human Liver Anatomy: Dynamic Watershed Theory. *HepatoBiliary Surgery and Nutrition*, *10*(1), 139-141.

McIndoe, A. H., Counseller and V. X., (1927). The Bilaterality of the Liver. *Archives of Surgery*, *15*(4), 589-612.

Mohajan, D., Mohajan and H. K. (2024a). Visceral Fat Increases Cardiometabolic Risk Factors among Type 2 Diabetes Patients. Unpublished Manuscript.

Mohajan, D., Mohajan and H. K., (2023a). Obesity and Its Related Diseases: A New Escalating Alarming in Global Health. *Journal of Innovations in Medical Research*, *2*(3), 12-23.

Mohajan, D., Mohajan and H. K., (2023b). Basic Concepts of Diabetics Mellitus for the Welfare of General Patients. *Studies in Social Science & Humanities*, *2*(6), 23-31.

Mohajan, D., Mohajan and H. K., (2023c). Body Mass Index (BMI) is a Popular Anthropometric Tool to Measure Obesity among Adults. *Journal of Innovations in Medical Research*, *2*(4), 25-33.

Mohajan, D., Mohajan and H. K., (2023d). A Study on Body Fat Percentage for Physical Fitness and Prevention of Obesity: A Two Compartment Model. *Journal of Innovations in Medical Research*, *2*(4), 1-10.

Mohajan, D., Mohajan and H. K., (2023e). Long-Term Regular Exercise Increases $\dot{V}O_2$max for Cardiorespiratory Fitness. *Innovation in Science and Technology*, *2*(2), 38-43.

Mohajan, H. K., (2017). Two Criteria for Good Measurements in Research: Validity and Reliability. *Annals of Spiru Haret University Economic Series*, *17*(3), 58-82.

Mohajan, H. K., (2018). Aspects of Mathematical Economics, Social Choice and Game Theory. PhD Dissertation, Jamal Nazrul Islam Research Centre for Mathematical and Physical Sciences (JNIRCMPS), University of Chittagong, Chittagong, Bangladesh.

Mohajan, H. K., (2020). Quantitative Research: A Successful Investigation in Natural and Social Sciences. *Journal of Economic Development, Environment and People*, *9*(4), 50-79.

Mohajan, H. K., (2024a). Alcoholic Liver Disease: Diagnosis and Treatment Strategies. Unpublished Manuscript.

Mohajan, H. K., (2024b). Alcoholic Hepatitis: Diagnosis and Management Procedures. Unpublished Manuscript.

Mohajan, H. K., (2024c). A Study on Functions of Liver to Sustain a Healthy Liver. Unpublished Manuscript.

Mohajan, H. K., (2024d). Alcoholic Liver Cirrhosis: A Chronic Liver Failure Due to Alcohol Abuse. Unpublished Manuscript.

Nguyen-Lefebvre, A. T., Horuzsko and A., (2015). Kupffer Cell Metabolism and Function. *Journal of Enzymology and Metabolism*, *1*(1), 101.

Pandey, P., Pandey and M. M., (2015). *Research Methodology: Tools and Techniques*. Bridge Center, Romania, European Union.

Polit, D. F., Hungler and B. P., (2013). *Essentials of Nursing Research: Methods, Appraisal, and Utilization (8th Ed.)*. Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins.

Ramachandran, K., Kumar and R. D., (2019). A Study on the morphological Variations of the Liver and Its Clinical Significance. *Indian Journal of Anatomy and Surgery of Head, Neck and Brain*, *5*(4), 110-113.

Ramazanoglu, C., Holland and J., (2002). *Feminist Methodology: Challenges and Choices*. Sage Publications, London.

Rocca, J., (2003). Galen on the Brain: Anatomical Knowledge and Physiological Speculation in the Second Century CE. *Studies in Ancient Medicine*, *26*, 1-313.

Rutkauskas, S., et al., (2006). Clinical and Anatomical Basis for the Classification of the Structural Parts of Liver. *Medicina (Kaunas)*, *42*(2), 98-106.

Singh, H. R., Rabi and S., (2019). Study of Morphological Variations of Liver in Human. *Translational Research in Anatomy*, *14*(2019), 1-5.

Skandalakis, J.E., et al., (2004). Hepatic Surgical Anatomy. *Surgical Clinics of North America*, *84*(2), 413-435.

Soyer, P. et al., (1994). Surgical Segmental Anatomy of the Liver: Demonstration with Spiral CT during Arterial Portography and Multiplanar Reconstruction. *American Journal of Roentgenology*, *163*(1), 99-103.

Sumadewi, K. T., (2023). Embryology, Anatomy and Physiology of the Liver: Review. *Indian Journal of Clinical Anatomy and Physiology*, *10*(4), 138-144.

Tie, C. Y, Birks, M, Francis and K., (2019). Grounded Theory Research: A Design Framework for Novice Researchers. *Sage Open Medicine*, *7*, 1-8.

van Gulik, T. M., (2022). Liver Anatomy by Francis Glisson. *Hepatobiliary Surgery and Nutrition*, *11*(4), 502-503.