Morphology, Histometry, Histochemistry and Haemopoietic Activity of the Liver of the Foetus of the Dromedary (*Camelus dromedarius*)

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Dedication

To my mother, father, brothers and sisters

To my small family:

My husband, my son and my daughters,

With love

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First of all I thank Allah for providing me with health and strength to conduct this work.

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Morphology, Histometry, Histochemistry and Haemopoietic Activity of the Liver of the Foetus of the Dromedary (*Camelus dromedarius*)

Ph.D in Anatomy

Fatima Abakar Hussein Adam

Abstract: The objectives of this study were to investigate the morphology, histometry,histochemistry and haemopoietic activity of the liver of the foetus of the dromedary. Ninety threefoetuses of Butana breed and the breed bred by Nomadic Sudanease Arab tribes in South Darfur state were collected from Tamboul andNyala slaughter points and were classified into three groups: First trimester (31 foetuses) ranging between 71 and 130 days of age, second trimester (41foetuses)ranging between 135 and 251 days of age and third trimester (21foetuses) ranging between 257 and 426 days of age. The age of the foetuses was estimated according to the curved crown-rump length (CVRL) method by using the equation: Y= 0.366X – 23.99. Standard international techniques were used. The hepatic primordium appeared in the peritoneal cavity beneath the mesenchyme in a foetus of 71 days of age. The size of the liver increased and occupied most of the abdominal and pelvic cavities in foetuses between 76 and 92 days of age. The shape of the liver varied between quadrilateral, irregular and trianglular during the first, second and third trimesters, respectively. The liver was first developed as right and left lobes while the quadrate and caudate lobes completed their development at the second and the third trimesters, respectively. The average length of the liver was 8, 14.6 and 22.3cm during the first, second and the third trimesters, respectively. The average width of the narrow part of the liver was 2.6, 5 and 7.2cm during the first, second and the third trimesters, respectively. The

average width of the broad part of the liver was 4, 9 and 13cm during the first, second and the third trimesters, respectively. The hepatic primordium consisted of hepatocytes and haemopoietic cells. The portal vein and the central vein were developed in a foetus of 76 days of age. The cytoplasm of the hepatocytes possessed large amount of cytoplasmic vacuoles in a foetus of 85 days of age. The s capsule appeared in a foetus of 74 days of age. The ’primordium of Glisson interlobular hepatic cords appeared in a foetus of 229 days of age and disappeared in a foetus of 339 days of age and onward.The development of intrahepatic bile ducts started and was completed in foetuses of 85 and 107 days of age, respectively. The mean diameter of the hepatocytes was 6.4, 7.3 and 6.2µm during the first, second and third trimesters, respectively. The mean diameter of megakaryocytes was 17.4, 18.3 and 24µm during the first, second and third trimesters, respectively. Round and rod mitochondria and rouph endoplasmic reticulum were found in a foetus of 183 days of age and onward. Large lipid droplets and multivesicular bodies appeared in the cytoplasm of hepatocytes. The central vein was lined with continuous layer of fenestrated endothelium in a foetus of 183 days of age and onward. The hepatic sinusoids were lined with complete layer of both fenestrated and unfenestrated endothelium, and Kupffer cells and Hepatic stellate cells were found in a foetus of 278 days of age and onward. Intercellular bile canaliculi appeared in a foetus of 156 days of age and onward. The hepatocytes showed negative reaction for PAS resistant material during the first trimester while reacted positively during the second and third trimesters. The hepatocytes revealed negative reaction for PAS diastase digested material, alkaline phosphatase and acid phosphatase enzymes during the three trimesters. The important information included in this study is vital for the understanding of any malformation of the liver and consequently will provide a better knowledge about the physiological disturbance and pathological change due to malformation.

المورفولوجيا، القياسات النسيجية، الكيمياء النسيجية ونشاط تكون الدم للكبد فى جنين الإبل وحيدة السنام

درجة الدكتوراه في علم التشريح

فاطمة ابكر حسين آدم

المستخلص: أهداف الدراسة هى دراسة الخصائص الشكلية والقياسات النسيجية والكيمياء النسيجية ونشاط تكو ن الدم للكبد في جنين الإبل ذات السنام الواحد. أجريت ه ذه الدراسة على 93جنين من سلالة البطانة والسلالة المرباه بواسطة القبائل السودانية العربية الرعوية بولاية جنوب دارفورتم جمعها من نقاط الذبح بمدينتتمبول ونيالا وصنفت إلى ثلاثة مجموعات: الثلث الأول من الحمل (31 جنين) تراوحت أعمارهم بين 71 و 130 يوم، الثلث الثانى من الحمل (41 جنين) تراوحت أعمارهم بين 135 و 251 يوم والثلث ال ثالث من الحمل (21 جنين) تراوحت أعمارهم بين 257 و426 يوم. قُدر عمر الأجنة حسب طريقة قياس طول المنحنى من التاج الى قمة الذيل بإستخدام المعادلة: $Y= 0.366X -23.99$. تم إستخدام التقنيات العالمية القياسية. ظهر المكون البدائى للكبد في التجويف ال صفاقى خلف اللحمة المتوسطة فى الجنين عمر71 يوم. إزداد حجم الكبد وإحتلت معظم تجويفى البطن والحوض فى الأجنة التى تراوحت أعمارها بين 76 و 92 يوم. إختلف شكل الكبد بين رباعى الجوانب، غير المنتظم و ثلاثي الأضلاع خلال الثلث الأول، الثاني والثالث من الحمل على التوالى. بلغ متوسط طول الكبد 8.0، 14.6، 22.3 سم خلال الثلث الأول، الثانى والثالث من الحمل على التوالى. بلغ متوسط عرض الجزء الرفيع من الكبد 2.6، 7.2،5 سم خلال الثلث الأول، الثانى والثالث من الحمل على التوالى.بلغ متوسط الجزء العريض من الكبد 4، 9، 13 سم خلال الثلث الأول، الثانى والثالث من الحمل على التوالى. إحتوى المكون البدائى للكبد على الخلايا الكبدية والخلايا المكونة للدم. الحبال الكبدية بسمك خليتين والخلايا الكبدية مكعبة الشكل فى الجنين عمر 74 يوم ثم تحولت إلى شكل متعدد الرؤوس فى الجنين عمر 85 يوم فأكثر. تطور الوريد البابى والوريد

المركزى فى الجنين عمر 76 يوم. أظهر سيتوبلازم الخلايا الكبدية كمية كبيرة منالفجوات السيتوبلازمية فى الجنين عمر 85 يوم. ظهر المكون البدائى لمحفظة جليسون فى الجنين عمر 74 يوم. ظهرت حبال كبدية بين الفصيصات في الجنين عمر 229 يوم و إختفت فى الجنين عمر 339 يوم. ظهرت خلايا الدم الحمراء و خلايا الدم البيضاء الناضجة فى الأجنة عمر 92 و 112 يوم على التوالى. إختفى نشاط تكوين الدم فى الجنين عمر 372 يوم فأكثر.بدأ تطور القنوات الصفراوية داخل الكبد وإكتمل النمو فى الأجنة عمر 85 و 107 يوم على التوالى. بلغ متوسط قطر الخلايا الكبدية 6.4، 7.3، 6.2 ميكرون خلال الثلث الأول، الثانى والثالث من الحمل على التوالى. بلغ متوسط قطرالنوْاء 17.4، 18.3، 24 ميكرون خلال الثلث الأول، الثانى والثالث من الحمل على التوالى. وجدت المتقدرات الدائرية والعصوية والشبكة الهيولية الباطنة الخشنة فى الجنين عمر 183 يوم فأكثر. ظهرت قطيرات دهنية كبيرة وأجسام حويصلية متعددة فى سيتوبلازم الخلايا الكبدية. بُطن الوريد المركزى بطبقة متواصلة من خلايا بطانية مثقبة فى الجنين عمر 183 يوم فأكثر. بُطنت الجيبانيات الكبدية بطبقة مكتملة من خلايا بطانية مثقبة أو غير مثقبة ووجدت خلايا كوبفروخلايا الكبد النجمية فى الجنين عمر 278 يوم فأكثر. ظهرت القنيات الصفراوية بين الخلوية فى الجنين عمر 156 يوم فأكثر. أظهرت الخلايا الكبدية تفاعلاً سالباً لمادة عديد السكريد المخاطى المقاومة لخميرة الدياستيزخلال الثلث الأول من الحمل بينما تفاعلت إيجابياً خلال الثلثين الثانى والثالث. أظهرت الخلايا الكبدية تفاعلاً سالباً لمادة عديد السكريد المخاطى المهضومة بواسطة خميرة الدياستيز و إنزيمى الفوسفاتيز القلوى والحمضى خلال فترة الحمل. المعلومات المهمة التى ضمنت فى هذه الدراسة يمكن الإستفادة منها فى فهم التطور غير السوى للكبد وبالتالى الإستفادة منها فى معرفة الإضطرابات الوظيفية والتغيرات المرضية التى تحدث نتيجة للتطور غير السوى.

Table of Contents

Introduction

The camel, an important and multipurpose animal, is well adapted to live in wide zones in Africa and Asia. It represents an important source of meat and milk for a large group of population in these areas (Liona, 2009). Moreover, they are used for riding, transport and a source of prestige for their owners (Dirie and Abdurahman, 2003). The family camelidae is divided into three genera: The old world camels (genus Camelus) and the new world camels (genus Lama with the species L. glama, L. guanicoe, L. pacos and genus Vicugna with the species V. vicugna) (Wilson and Reeder, 2005).There are two species in the genus camilus: the dromedary or one-humped camel(*Camelus dromedarius)* and the bacterian or two-humped camel(*Camelus bacterianus)*(Rao, Gupta and Dastur. 1970;Higgins, Allen, Mayhew and Snow, 1992; Fowler, 1998).

Dromedaries were originally domesticated in central and southern Arabia and from there they were gradually dispersed to North Africa and eastwards to the desert and semi desert areas of the Middle East (Vidal-Rioja, Zambelli and Semorile, 1994, Tibary, 1997; Nowak, 1999).

In Sudan, the only species in the genus camilus is the one humped camel (*Camilus dromedarius*). The estimated total number of camels in Sudan is about 3,000,000 (Schwartz and Dioli, 1992). More than 80 percent of camel population is found in western and eastern states of Sudan (Musa, 2004).

The liver is a vital organ because it is the site of metabolic processes of all nutrients consumed by the animal. A great capacity of regeneration and compensation are found in the hepatic tissue due to the increased metabolic demands (Jones and Spring-Mills, 1977).

The anatomy of the adult camel liver was studied by Abdalla, Arnutovic and Fahmy (1971), Smuts and Bezuidenhout (1987), Lalla and Drommer (1997), Endo, Gui-Fang, Dugarsuren, Erdemtu, Manglai and Hayashi (2000), Abdalla, Vauthey and Couinaud (2002), Ahmed, Abdalla and Ali (2014). Bahgat, Mustafa, suliman and Elmrousi (1964), Shahien, Fahmy and Sokkar (1977), Ahmed (2002) and Ahmed, Abdalla and Ismail (2015) investigated some histochemical substances.

The prenatal development of the liver was studied in some species including the rat (Bankston and Pino, 1980; Daimon, David, VonZglinicki and Marx, 1982; Barbera-Guillem, Arrue, Ballesteros and Vanaclocha, 1986; Vassy, Kraemer, Chalumeau and Foucrier, 1988; Godlewski, Gaubert-Cristol, Rouy and Prudhomme, 1997), chick (Stephens and Bils, 1967; Sandström and Westman, 1971) and human (Godlewski, Gaubert-Cristol, Rouy and Prudhomme, 1997; Albay, Malas, Cetin, Cankara and Karahan, 2005). The role of the liver as a haemopoietic organ was carried out in the mouse (Jones, 1970; Iwatsuki, Sasaki, Suda, Itano, 1997; Cardier and Barbera-Guillem, 1997; Sasaki and Iwatsuki, 1997; Sasaki and Sonoda, 2000), human (Slayton, Juul, Calhoun, Liy, Braylan, Christensen, 1998; Lee, Erm, Kim, Becker, 1999; Taviana and Peauit, 2005) and bovine (Li and Congote, 1995).

The foetal liver is an important centre of blood formation (haemopoiesis) during considerable period of the mouse, human and mammalian prenatal development (Cardier and Barbera-Guillem, 1997; Slayton ***et al.*** 1998; Olga, 2012) respectively.

McGeady, Quinn, Fitz Patrick and Ryan (2006) reported that the blood forming role of the embryonic mammalian liver begins during the second month of gestation and causes a rapid increase in the size of the liver during early embryological development.

The prenatal development of the camel liver was briefly studied by Abd EL-Hafez (2009). It was therefore decided to study the foetal liver of the camel with the following objectives.

General objective: to study the prenatal development of the liver and its role as a haemopoietic organ.

The specific objectives include the investigation of the following parameters in the liver during prenatal life of camel foetus:

1. The gross anatomy.
2. The histological development.
3. The fine structure of the hepatic cells.
4. To determine the age of the foetus at which the liver can be considered as a haemopoietic organ.
5. Histometry of some components of the camel liver during prenatal life.
6. To investigate some histochemical components of the liver.

CHAPTER ONE
LITERATURE REVIEW

1.1.Morphology

1.1.1. Growth anatomy

1.1.1.1. Differentiation & Topography

Bloom (1926) reported that, the human liver was developed as a hollow diverticulum from the duodenum. Bradley (1948) reported that, the hepatic diverticulum could be identified extending ventrally from the duodenal portion of the gut in 4mm CVRL of the pig embryo and became clearly differentiated into a mass of branching and anastomosing cell cords grows out of it ventrally and cephalically between 5 and 6mm CVRL. Bradley (1964) stated that the liver in some vertebrates was developed as a diverticulum from the ventral wall of the gut immediately caudal to the stomach. This information has been confirmed by McGeady ***et al*** (2006) who repored that the mammalian liver develops as a hollow ventral diverticulum from the caudal region of the fore gut. More details were added by Roskams and Desmet (2008) that the first analage of the bile ducts and the liver in human is the hepatic diverticulum or liver bud, which started as a thickening of the endoblastic epithelium in the ventral wall of the cephalad portion of the fore gut in 2.5mm CVRL (18 days of gestation). In a foetus of 3mm CVRL (22 days of gestation-19 somite embryo) the diverticulum was formed then appeared as a well defined hollow structure when the embryo reached 22 somite stage. Taviana and Peauit (2005) also reported that the hepatic plate of human embryo has been identified as an endodermal thickening at the rosteral intestinal end, caudal to the heart at around 22 days of gestation (10 somite stage).

Bradley (1964) stated that, the hepatic primordium of the chick embryo was first recognized at about 22 somite stage. Burke and Tosh (2012) noted that, the liver arises from the developing endoderm together with the pancreas, and both tissues arise from the neighboring regions. Bradley (1964) reported that the mammalian hepatic diverticulum consisted of a considerable mass of branching cords of endodermal cells which are the primordia of the glandular tubules of the liver in a foetus of 5mm CVRL. These cell cords which constitue the main mass of the growing liver, soon spread out aganist the dorso-caudal face of the septum transversum.

During the prenatal development of the human embryo, short sprouts of endodermal cells from the ventral and lateral surface of the diverticulum, on which the endoderm is in contact with the bulk of the mesoderm of the septum transversum, extend into the latter to form the earliest analage of the liver (Severn, 1972; Kessler, 2007). Sasaki and Sonoda (2000) noted that, the liver analage could be observed in the septum transversum beneath the pericardial cavity at 10 days of gestation in the foetus of the mouse and by 11 days, lobes of the liver analage protruded into the embryonic peritoneal cavity and showed rapid increase in volume after 12 days of gestation. The hepatic primordium of the mammalian embryos grows cranio-ventrally into the ventral mesogasterium and extends into the septum transversum (McGeady ***et al.,*** 2006). However, Godlewski ***et al***. (1997) reported that in the mouse embryo at 4-5 weeks of gestation, the septum transversum differentiates to form the hepatic diverticulum and the hepatic primordium and the two develop to form the different components of the liver and gall bladder in the adult mouse.

At 8 weeks of gestation, the liver of the mouse embryo develops rapidly and forms a visible bulge on the surface of the embryo directly under the heart bulge and occupies the ventral body cavity together with

parts of the gastrointestinal tract and urinary system (Godlewski ***et al***., 1997).

McGeady ***et al.*** (2006) stated that, the final position and orientation of the liver in the abdominal cavity are influenced by the development and rotation of the other abdominal organs.

1.1.1.2. Shape and lobulation

Albay ***et al***. (2005) observed that, the square shape is the most common shape of the human foetal liver. However, Christoph, Carla and Maciej (1976) stated that, the normal human liver is pyramidal in shape.

McGeady ***et al***. (2006) stated that, during prenatal life of mammals, the liver develops right and left lobes; subsequently two outgrowths from the right lobe give rise to the caudate and quadrate lobes. Moreover, subdivisions of the left and right lobes may occur in some species. However, Guang, Hee, Hyung-Sun, Jang, Jeong, Jin, and Baik. (2008) described three lobes in the early stage of human hepatic formation.

1.1.1.3.The attachments

McGeady ***et al***. (2006) stated that, in mammalian foetus the mesoderm of the septum transversum which surrounds the expanding liver, gives rise to the hepatic capsule and associated peritoneal covering; cranially the liver remains attached to the tendonus centre of the diaphragm by the coronary ligament, and laterally to the body wall by the lateral ligament. The mesoderm of the septum +transversum and the ventral mesogasterium between the liver and the lesser curvature of the stomach form the lesser omentum, while the mesoderm between the liver and the ventral abdominal wall forms the falciform ligament. The round ligament starts from the umbilicus and passes through the falciform ligament and

the ligamentum venosum (Carlson, 1981). In the adult ox, sheep and goat, the falciform and round ligaments are abscent (Nickel, Schumer and Seiferl, 1973, Getty, 1975) while the round ligament is also abscent in the dog (Sleight and Thomford, 1970) and the pig (Getty, 1975). All ligaments are present in the horse (Bradley, 1946; Getty, 1975) and man (Snell, 2000).

1.1.1.4.Blood supply

The liver of the foetus receives the oxygenated blood via the umbilical vein. In the horse, the umbilical vein forms a single large trunk which is separated from the other constituents of the umbilical cord on entering the abdomen and passes forward along the abdominal floor in the free border of the falciform ligament (Sisson, 1953).

The umbilical vein enters the liver at the umbilical fissure and joins the portal vein, so that the blood conveyed by it passes through the capillary of the liver before entering the posterior vena cava (Sisson, 1953). Two umbilical veins pass through most of the length of the umbilical cord of carnivores and ruminants and they join to form the left umbilical vein before entering the body of the embryo (Noden and de Lahunta, 1985). In the ox and dog, some of the blood in the umbilical vein is conveyed directly to the posterior vena cava by the ductus venosus. In the horse and pig, the umbilical veins fuse within the amniotic part of the cord, while in other specieses they fuse on entering the abdominal cavity (McGeady ***et al***.,2006).

In a human foetus between 5 and 10 weeks of gestation, only precursors of the portal veins are visible and the vessels retain their primitive uniform characteristics. The vascular architecture of the human foetal liver is acquired through development of the intra-hepatic arteries and

growth and differentiation of the portal vein and hepatic sinusoids between 10 and 25 weeks of gestation. This process is mainly controlled by the vascular endothelial growth factor exhibiting the maximal expression from week 10 to week 25. After that time, minimal changes are observed in the vascular architecture and differentiation (Kissler, 2007). However, Godlewski ***et al***. (1997) observed that, in the mouse foetus between 4 and 5 weeks of gestation, large vascular channels can be noticed coursing through the liver primordium, and a large ductus venosus is also observed.

In the foetuses of the one-humped camel, the two umbilical veins emerge from the placenta and proceed together untill they enter the abdominal cavity and unite in a venous sinus near the liver. After passing through the liver, the umbilical vein unites with the left main portal vein to form straight tubular duct known as the ductus venosus, and the later joins the posterior vena cava at its ventral surface (Elgazouli, 2010).

The gross anatomy of the liver of the one-humped camel foetus was studied during early stages (7- 185 mm CVRL) by Abd El-Hafez (2009)

The primordium of the foetal liver appeared as a mass between the pericardium cranio-ventrally and the mesonephros caudo-dorsally in a foetus of camel at 7-9mm CVRL but still the septum transversum could not been distinguished. Moreover, when the foetus reaches between 12 and 19 mm CVRL, the liver is related cranially to the septum transversum and heart, caudally to the primitive spleen, mesogasterium, primitive stomach and the lesser omentum, dorsally to the mesonephros and ventrally to the floor of the abdominal cavity (Abd El-Hafez, 2009).

Abdalla ***et al***(1971) and Abdel-Moniem, Alam Edin, Abdel-Rahman and El-Nady (2000) suggested that, the liver occupies most of the abdominal

cavity in the one-humed camel foetus. Abd El-Hafez (2009) added that the enlargement of the liver starts in the camel foetus at 50-75mm CVRL and extends from the diaphragm cranially to the pelvic inlet caudally and occupies this area until the foetus reaches 185mm CVRL.

Abdalla ***et al***. (1971), Ahmed (2002) and Ahmed ***etal.*** (2014) demonstrated the irregular shape of the camel liver. During the prenatal development of the one-humped camel foetus, the liver lobulation begins to appear when the foetus ranges between 50 and 75mm CVRL. Three lobes are distinguished, the left lobe is found on the left side of the umbilical vein, the intermediate lobe is medial to the umbilical vein while the right basic lobe is separated from the intermediate one by a deep fissure (Abd El-Hafez, 2009).

Abdalla ***et al***. (1971) reported that, the round ligament is noticeable in the neonate and at full term one-humped camel foetus and is reduced to a cord in the adult camel.

1.1.2. Histology

Jones (1970)examined the hepatic tissue at 12 days of gestation and noticed that it forms a loose mass of cells with little apparent grouping of the different cell types in the mouse foetus while hepatocytes appear much more cohesive with the development of the liver cords at 13 days of gestation and thereafter. Haemopoietic cells appear as groups within and between the hepatocytes.

The hepatic cords consisted of one or three cells in thickness radiating from the central vein at 18 days of gestation in the foetus of the mouse (Khalid, Tahir, Mumtaz and Sami, 2009).

Sasaki and Sonoda (2000) reported that the hepatocytes of the foetus of the mouse are cuboidal in shape between 17 and 19 days of gestation. However, Khalid ***et al***. (2009) stated that the hepatic cells that form the hepatic cords are polyhedral in shape with central nucleus, distinct nuclear envelope and one or two prominent nucleoli at 18 days of gestation in the same species.

Daimon ***et al.*** (1982) observed that the hepatocytes are irregular in shape in the rat foetus at 15 days of gestation. HoweverVassy ***et al***., (1988) stated that the hepatocytes change during the prenatal development from potato-like on days 12,13 and 14 of gestation to cuboidal on day 20 of gestation with an intermediate more spheric stage on day 18 of gestation in the same species.

At 10 days of gestation in the foetus of the mouse and rat and 5 weeks of gestation in human foetus, the hepatic cords grow into the mesenchymal tissue of the septum transversum, and primitive sinusoid-like structure is simultaneously observed between the liver cell cords and develops the basic structure of the sinusoids between 12 and 14 days of gestation in the mouse and rat and at 8 weeks of gestation in human foetus (Enzan, Himeno, Hiroi, Kiyoku, Saibara and Onishi., 1997).

The development of the intrahepatic bile ducts during the intrauterine period was studied in human (Bloom, 1926; Koga, 1971; Severn, 1972; Vijayana and Tan, 1999; Libbrecht, Cassiman, Desmet, Roskams, 2002).

The time for the first appearance of the intrahepatic bile duct system in human embryo is at 22mm CVRL (Bloom, 1926) and at 7 weeks of gestation (Blankenberg, Lund and Reubner, 1991).

The ductal plate is a primitive billiary epithelium which develops in the mesenchyme adjacent to the branches of the portal vein during the liver development and it is extensively reorganised to form the intrahepatic bile ducts in the human foetus (Koga, 1971; Godlewski ***et al***., 1997; Vijayana and Tan, 1999). The adult system of the tubular anastomosing bile ducts develops at around 11weeks of gestation in the human foetus (Koga, 1971; Vijayan and Tan, 1999).

The intrahepatic bile ducts of human develop around the portal vein as plates of epithelial cells separated from each other by primitive connective tissue and then they are changed into a complex network of bile ducts. The formation of the intrahepatic bile ducts is completed during the third month of gestation (Koga, 1971).

Libbrecht ***et al.*** (2002) observed that, the mesenchyme of the portal tracts in the ductal plate stage in the human foetus is devoid of a branch of the hepatic artery and contains numerous and diffusely scattered portal myofibroblasts. However, when the portal tracts become large and contains branch of the hepatic artery, the myofibroblasts are restricted to the periductal mesenchyme until it disappears after the full incorporation of the bile duct.

Abd El-Hafez (2009) reported that the histology of the liver of the one-humped camel during prenatal life consists of hepatocytes which are polyhedral in shape with large round nuclei and arranged in the form of anastomosing cords separated by irregular blood spaces in 12-19mm CVRL one-humped camel foetus. A well developed hepatic laminae arranged in radiating rows around the central vein is a characteristic feature of the foetal liver between 140 and 185 mm CVRL and the hepatocytes are large in size and show high mitotic activity.

Abd El-Hafez (2009) mentioned that the primordium of Glissons's capsule starts to cover the liver of the one-humped camel foetus between 50 and 75mm CVRL and it consists of one layer of flattened cells with oval nuclei and condensed very fine collagen fibres.

Tavassoli (1991) stated that, the haemopoietic activity of the liver begins at the 10th day of gestation in the foetus of the mouse and continues during foetal life until the first postnatal week. During early organogenesis, the foetal liver is populated by haemopoietic stem cells which are the source of a number of blood cells including nucleated erythrocytes (Lee, William, Geremy, Hongzu, Beena, Barbara, Karen, Seth and Christopher. 2012).

Trowell (1965) noticed that the mouse foetal liver contains hepatocytes, endothelial cells, erythropoietic cells, megakaryocytes, granulocytes and possibly stem cells which show non of the characteristic features of other cell types. Moreover, Olga (2012) found that the mammalian foetal liver contains epitheliocytes, macrophages, various stromal elements of hepatic stellate cells, fibroblasts, myofibroblasts, vascular smooth muscle fibres, endothelial cells and mesenchymal stromal cells. Li and Congote (1995) reported that, the stromal cells are one of the components of the haemopoietic microinviroments which play an important role in bovine foetal erythropoiesis.

Sasaki and Sonoda (2000) studied the distribution of the haemopoietic compartments from 11 to 19 days of gestation in the liver of the foetus of the mouse. They reported that, at 11 days the haemopoietic cells in the primitive hepatic cell cords are scattered signally and in small groups either on the sinusoidal wall or among the hepatoblasts. Thereafter, the areas of the haemopoietic compartments rapidly enlarge by fusing to form

haemopoietic foci. At 13 days, the liver is almost entirely filled with ellipsoidal haemopoietic foci surrounded by hepatoblasts. At 15 days, the arrangement of hepatocytes become prominent in section profile and the haemopoietic foci are relatively decreased, while between 17 and 19 days, it contains small solitary haemopoietic foci diffusely scattered through the hepatic cell cords.

The erythroblasts proliferate within the haematopoietic foci between 11 and 12 days of gestation in the foetal mouse and some erythroids are anucleated (Sasaki and Sonoda, 2000).

Primitive macrophages arise in the yolk sac and then differentiate into foetal macrophages and these enter the blood and migrate into the developing liver (Makoto Naito, Hasegawa Go, Yusuke Ebe, Takashi Yamamoto, 2004). Macrophages are present within the lumina of the primitive sinusoids between 11 and 12 days of gestation in the mouse embryo. Thereafter, macrophages are found in the primitive hepatic cell cords and could be observed within the haemopoietic foci, which are surrounded by a ring of erythroid cells in various stages of maturation forming cell clusters designated as erythroblastic islands (Sasaki and Iwatsuki, 1997; Sasaki and Sonoda, 2000). Iwatsuki ***et al.*** (1997) reported that, at 11 days of gestation in the mouse embryo, the primitive sinusoidal macrophages are considered as the possible precursors of the central cells in hepatic erythroblastic islands. According to the upper reports, two kinds of macrophages could be identified in the mouse foetal liver: sinusoidal macrophages and central macrophages of the erythroblastic islands (Sasaki and Iwatsuki, 1997). However, Jones (1970) stated that macrophages are not observed in the mouse foetal liver.

Megakaryocytic lineage cells among hepatocytes are observed in human foetal liver (Emura, Sekiva, Ohnishi., 1984). At 12, 13 and 14 days of gestation in the mouse foetal liver, megakaryocytes are usually observed in a close position to the hepatocytes, rarely with erythroid cells and usually in pairs or in groups of four cells early in development, although they are observed singly at a later stage (Jones, 1970). At the end of gestation, the blood forming activity of the liver ceased in the foetus of the rat and only the space of Disse separated the epithelium lining the sinusoids from the parenchymal cells (Bankston and Pino, 1980). However, Cardier and Barbera-Guillem (1997) reported that liver haemopoiesis ceases after birth in the mouse.

Abd El-Hafez (2009) observed that the haemopoietic cells are dispersed inside the liver parenchyma between 12 and 19mm CVRL one-humped camel foetus and these cells are round in shape with deeply stained centrally located and relatively large round nuclei. Megakaryocytes with lobulated nuclei are observed among haemopoietic cells in the liver between 25 and 38mm CVRL one-humped camel foetus.

1.1.3. Ultrastructure

The ultrastructural features of the liver during prenatal life were studied in the rat (Stephens and Bils, 1967; Jones, 1970; Sandström and Westman, 1971; Daimon ***et al***., 1982; Vassy ***et al***., 1988). The nucleus of the hepatocytes remains large and ovoid and the mitochondria round between 12, 13 and 14 days of gestation in the mouse embryo (Jones, 1970).

Vassy ***et al***. (1988) observed small and round mitochondria in the cytoplasm of hepatocytes at 12, 13 and 14 days of gestation in the foetal rat and they become oblong from day 18 of gestation and onwards. In the

chick embryo from 4 days old until before hatching, the mitochondria of the hepatocytes increase in size and number during development with conspicuous changes from round toward more rod shape and elongated forms (Sandström and Westman, 1971). Abd El-Hafez (2009) described the hepatocytes in 125mm CVRL one-humped camel foetus as large cells with large nuclei and many mitochondria.

The Golgi apparatus of the hepatocytes of 12 and 13 days of gestation in the rat foetus is well developed (Vassy ***et al***., 1988). Stephens and Bils (1967) reported that the activation of the hepatocytes Golgi complex takes place on the fourth and fifth days in incubated chick embryo as judged by its expansion and the formation of variety of vesicles. However, Sandström and Westman (1971) claimed that, the Golgi apparatus does not assume its adult appearance until about the 8th day of incubation in the chick embryo.

The rouph endoplasmic reticulum is very sparse in the cytoplasm of the hepatocytes on the third day of incubation in the chick embryo and first appears mainly in a vesicular form which eventually changes into a cisternal form and becomes closely associated with the plasma membrane and mitochondria (Stephens and Bils, 1967).

A well developed rough endoplasmic reticulum is reported in the cytoplasm of hepatocytes at 12 and 13 days of gestation in the rat embryo (Vassy ***et al***., 1988). While Daimon ***etal***. (1982) observed a well developed rouph endoplasmic reticulum in the hepatocytes of the rat at 15 days of gestation but the smooth endoplasmic reticulum is not differentiated yet.

Extensive rough endoplasmic reticulum is observed in the cytoplasm of hepatocytes in 125mm CVRL of the one-humped camel foetus (Abd El-Hafez, 2009).

Glycogen is first observed in the cytoplasm of hepatocytes in 6 days old incubated chick embryo and then continuously increased in amount throughout development (Standström and Westman, 1971). On the other hand, the cytoplasm of hepatocytes possesses large spaces which are rapidly filled with glycogen from 16 days of gestation and onward in the mouse embryo (Jones, 1970). However, Daimon ***etal***. (1982) stated that, glycogen is not observed within the cytoplasm of the hepatocytes of the rat at 15 days of gestation, until on the 18^{th} day the accumulation of glycogen is observed and then decreased rapidly at birth. A variable appearance of the glycogen is found in the cytoplasm of hepatocytes at 6 days incubated chick embryo and It is often seen as distinct granules but in other cases these granules become indistinct (Karrer, 1961). Cytoplasmic glycogen is found in the cytoplasm of hepatocytes at 185mm CVRL one-humped camel foetus (Abd El-Hafez, 2009).

The hepatocytes possess several large lipid droplets in their cytoplasm on 15 days of gestation in the rat embryo (Daimon ***et al***., 1982).

At 10 days of gestation in the mouse and rat embryos and 5 weeks of gestation in human embryo, the hepatic sinusoids are usually lined by a continuous endothelium but without a basement membrane. Incompletely fenestrated sinusoids appear at the middle stage of gestation (Enzan ***et al***., 1997).

Kupffer cells are a population of fixed tissue macrophages found in the lumen of the hepatic sinusoids and their role is endocytic aganist blood-borne materials entering the liver (Makoto ***et al***., 2004). Kupffer

cells are easily identified as early as 13 days of gestation in the rat foetal liver (Bankston and Pino, 1980). Lee ***et al.*** (1999) observed an emperipolesis of erythroblasts within Kupffer cells in the liver of the human foetus (Emperipolesis is defined as cells which can inhabit other cells without damage).

Sandström and Westman (1971) suggested that, subsinusoidal space of Disse is not present in the liver until about 16 days of incubation in the chick embryo.

Hepatic stellate cells are located in the space of Disse between the sinusoidal endothelial cells and hepatic epithelial cells and play vital roles in liver physiology and fibrogenesis and contain vitamin A and numerous lipid droplets (Chunyue, Kimberley, Kinji and Didier., 2013)

Barbera-Guillem ***et al***. (1986) observed a highly fenestrated endothelium that characterized the central veins of the foetal rat liver.

Abd El-Hafez (2009) stated also that, the blood sinusoids of the liver in 185mm CVRL one- humped camel foetus are lined by incomplete layer of flat endothelial cells that bulge into their lumina

1.2. Histochemistry

The histochemistery of the liver during prenatal life is poorly investigated.

Abd El-Hafez (2009) investigated the PAS positive material in the liver of the one-humped camel foetus between 7 and 185mm CVRL. The megakaryocytes show PAS- positive material while the surrounding hepatocytes are faintly stained during all stages of development.

No information is found in the available literature to the author about the activities of alkaline phosphatase and acid phosphatase in the liver during prenatal development of all animal species.

1.3. Anatomy of the liver of adult camel

In the camel, the liver is in the intrathoracic part of the abdominal cavity occupying most of the right hypochondriac and epigastric regions. The long axis of the organ extended cranioventrally from the second lumber vertebrum to the caudal border of the fifth rib. The cranial part of the organ curves ventromedially and caudally to the left side at the level of the caudal border of the fifth rib (Abdalla ***et al***. 1971). Higazi (1945) observed that the liver is extended caudally to the level of 11^{th} rib. However, Abdel-Moniem ***etal.*** (2000) stated that the long axis of the liver extends from the level of the 5^{th} rib to the 12^{th} rib in the same species.

The colour of the liver is dark brown in the dromedary camel (Abdalla ***et al***., 1971; Smuts and Bezuidenhout, 1987; Ahmed, 2002; Ahmed ***etal***., 2014). The shape of the liver is triangular in the two-humped camel (Endo ***et al***., 2000) and irregular in the dromedary camel (Abdalla ***et al***., 1971; Ahmed, 2002; Ahmed ***etal***. 2014). The lobes in the dromedary camel are cranial, caudal, quadrate and caudate lobes (Abdalla ***et al***., 1971; Ahmed, 2002; Ahmed ***etal***. 2014). In the two-humped camel, the left (cranial) lobe was known as left lateral and left medial (Endo ***et al***., 2000).

Abdalla ***et al***. (1971) and Lalla and Drommer (1997) stated that the liver of the dromedary is covered with a thick connective tissue capsule consisting mainly of collagenous bundles which send off trabeculae

dividing the liver parenchyma into hepatic lobules. Adibomoradi, Asadi, Ferdosi and Rezakhani (2008) and Ahmed and Abdalla (2015) added also, that the dromedary camel has a reconizable interlobular connective tissue.

The hepatic lobules of the dromedary consist of hepatic cords one cell thick radiating irregulary from the central vein. The hepatocytes are large with centrally situiated spherical nuclei and some of hepatocytes were binucleated (Abdalla ***et al***., 1971; Lalla and Drommer, 1997). Lalla and Drommer (1997) observed that the portal tracts and the central veins are surrounded by a variable amount of fibrous tissue. Moreover, Abdalla ***et al***. (1971) described the central veins being surrounded by reticular fibres and longitudinally arranged collagenous bundles of variable thickness.

Lalla and Drommer (1997) noticedthat, the endothelial cells lining the sinusoids show multiple fenestrations and are surrounded by a discontinuous basal lamina in the dromedary camel and the collagen fibres form dense three dimensional network around the sinusoids.

Glycogen and lipid could be demonstrated in the cytoplasm of hepatocytes depending on the functional state of the liver (Nickel ***etal.*** 1973). The content of these materials in the liver might therefore vary greatly with the diet (Bloom and Fawcett, 1986). Lalla and Drommer, (1997) observed that, in hepatocytes containing lipid droplets, the glycogen is concentrated mainly around these droplets.

In healthy liver of camel, Bahgat, Mustafa and Suliman (1965), stated that glycogen granules were evently distributed throughout the lobules. However, Shahien ***etal.*** (1977) claimed that, in some lobules, glycogen was concentrated more in the hepatocytes at the peripheral and central zones while in other lobules, glycogen is evenlly distributed.

Moreover, Ahmed (2002) and Ahmed ***etal.*** (2015) found that, the glycogen content of the liver varied from animal to animal and among lobes and lobules within the same liver. The left and quadrate lobes contained more glycogen than the right and caudate lobes. In some lobes, the lobules adjacent to subcapsular region of the liver, contain more glycogen compared to the lobules located far from the capsule. Morerover, the cells located directly under the capsule showed intensely stained masses of glycogen (Ahmed ***et al***., 2015)

In all mammals, lipid droplets were few in normal hepatocytes but may increase in disease after consumption of alcohol, or toxic substance (Bloom and Fawcett, 1986). Abdalla ***etal*** (1971) observed large fat cells in the liver of the camel. Shahien ***etal***(1977) demonstrated small to medium-sized lipid droplets concentrated in the peripheral part of the cells along the sinusoids. Lalla and Drommer (1997) described mild to moderate fatty infiltration in the hepatocytes of the same species. MoreoverAhmed (2002) and Ahmed ***et al*** (2015) observed moderate to large amount of lipid droplets in the hepatocytes of dromedary liver and distributed all over the lobule but they are more concentrated in cells at the periportal zone than in the central cells. On the other hand, Khatim, Bou-Resli, Bishay and Gumaa (1985) stated that, the hepatocytes of camel were characterized by the presence of numerous cytopplasmic inclusions (vesicles, vacuoles) that might occupy most of the cell, and appeared larger than the nuclei, although their significance was unknown.

CHAPTER TWO

MATERIALAND METHODS

2.1.Material:

The livers of the one-humped camel foetuses of both sexes were used in this investigation. The foetuses, at different stages of development, were obtained from pregnant she camels slaughtered in Nyala and Tamboul slaughter points. The foetuses were removed shortly after slaughter of the mother. The age of the foetus was estimated according to the curved vertebral crown-rump length (CVRL) by using the following equation:

Y = 0.366X - 23.99

The equation of the chest circumference (CC) **Y = 0.214 x – 16.24**was also measured in a large number of foetuses to calculate the mean difference in days between the two equations.

X: unknown foetal age in days.

Y: known foetal dimensions (Elwishy, Hemeida, Omer, Mobarak and Elsyed, 1981).

A tape meter was used to take the measurements of the foetal dimensions.

93 foetuses were collected and divided into three groups according to the method described and adopted by Eisa (2008).

Group 1: (31 foetuses) first trimester: ranging between 2cm and 23.5 cm CVRL (between 71 and 130 days of age).

Group 2: (41 foetuses) second trimester: ranging between 28cm and 67cm CVRL (between 142 and 249 days of age).

Group 3: (21 foetuses) third trimester: ranging between 70cm and 132cm CVRL (between 257 and 426 days of age).

The number of foetuses in each trimester to gether with their CVRL and their age in days and months were shown in table 1.

2.2.Methods:

2.2.1. Morphology

2.2.1.1. Growth anatomy

The anatomical study demonstrated in this investigation was carried out in 47 foetuses during the three trimesters. The specimens were dissected either in fresh state or after fixation in 10% formalin. The investigation included the degree of differentiation, topography, colour, shape, dimensions, lobation, attachments, and blood supply.

To investigate the topography of the liver, the foetus was first laid on its left side and by using scalpel and forceps a mid ventral incision was made extending from the end of the neck to the inlet of the pelvic cavity. Two cephalad incisions extending from the two ends of the mid ventral incision dorsal to the mid line were conducted and then the skin covered these areas was dissected and removed. In some specimens, the muscles that attached the fore limb were cut and the fore limb was pushed cranially for a short distance. The abdominal muscles with associated subjacent parietal layer of the peritoneum and the muscles covering the lateral side of the thoracic cavity were also removed. In some foetuses, some of the ribs and their intercostal muscles were cut at their cartilaginous ends and parts of the diaphragm attached to the medial part of the cartilaginous ends of the ribs were excised. Then the ribs were pushed up to the dorsal surface of the foetus to illustrate the cranial extermity of the liver. Finally, all the ribs that covered the liver were cut and pushed up dorsally to expose the dorsal, ventral and caudal aspects of the liver and their relation with the other adjacent developing organs in the abdominal cavity. After completing the investigation at the right side, the foetus was laid on the right side and the same procedure was repeated to determine the size and topography of the

liver on the left side. In some foetuses only the intercostal muscles were removed.

Foetuses at very early stage of development up to 7 cm CVRL, (85 days of age) were prepared according to the paraffin wax embedding technique and stained with H&E stain (Drury and Wallington, 1980). Then the position of the liver and its topography to the other developing organs were investigated.

After exposingthe liver, its colour was noted and documented and then the liver was carefully removed from the foetal carcass after severing the attachments that fixed the liver and then its shape was observed.

By using a thread and a ruler, the length, and width of the liver at both the narrow and broad parts of the liver were measured.

The lobation and lobulation of the liver during the three trimesters were investigated. The ligaments that attached the liver to the adjacent structures were studied.

To investigate the blood supply of the liver, corrosion casts were prepared from 3 livers to study the fine blood vessels within the liver. Vinyl acetate injection technique was used. The idea of this technique, in general, is to fill the blood vessels with a plastic injected mass. The liver receives blood from the placenta via the umbilical veins which were washed thoroughly with normal saline and then with acetone untill all blood was removed. Then the liver was injected with vinyl acetate via the umbilical vein, and the specimen was immersed in cold water and left for 24 hours to allow the plastic material to harden. Finally, the specimen was immersed in concentrated hydrochloric acid in a glass jar to corrode the soft tissue in the specimen. This usually takes between 2 and 4 days to allow the injected mass to be exposed. After full corrosion of the specimen, it was removed gentelly from

the glass jar and washed carefully by means of a fine jet of water, cleaned, and placed in a suitable jar and covered (Tompsett, 1970)

2.2.1.2. Histology

A total of 52 specimens were obtained from the liver of foetuses and their age ranged between 2 cm CVRL (71 days) and 132 cm CVRL (426 days) were used to study the development of the microscopic structures of the liver.

Fixatives including 10% buffered neutral formalin, formal saline, Bouin′s fluid and Gender fluid were used to fix the small embryos and the liver of the large foetuses. After proper fixation, small pieces from the livers were dehydrated with ascending grade of ethanol (70%, 90% and 100%) for 2 minutes in each grade, cleared with chloroform (maximum for 18 hours). The specimens were impregnated in melted paraffin wax (its melting point was about 50-55c˚) in three different changes (one hour for each change), and then blocked in the same melted paraffin wax. Sections, 5-7 µm thick were cut in a rotary microtome and stained with different histological stains as follows:

1. Haematoxylene and Eosin (H&E) was used for studying the general histological structure of the liver (Drury and Wallington, 1980).
2. Masson′s trichrome and Van Gieson stains were used to differentiate between collagen fibres and smooth muscle fibres (Culling, 1974).
3. Gordon and Sweets's stain was used for demonstration of reticular fibres (collagen fibres type II) (Bancroft and Steven, 1990).
4. Orcein stain was used for detection of elastic fibres (Drury and Wallington, 1980).

2.2.1.3. Histometry

20 stained sections were selected from the three trimesters and used to conduct some histometrical measurements in some components of the hepatic

tissue during the three trimesters by using ocular micrometer lens. The objective lens X40 was used to determining the measurements after calibrating the ocular scale of microscope (Thienpont, Rochette and Vanparijs, 1986)The components which were measured included:

.The diameter of hepatocytes/µm.

.The diameter of megakaryocytes/µm.

2.2.1.4. Electron microscopy

12 liver specimens were used to conduct the electron microscopical investigation. The specimens were cut into small pieces (approximately 2mm in thickness), and fixed in 2.5% gluteraldehde in 0.1m sodium cacodylate buffer, at PH 7.4. The fixed tissues were rinsed several times in cacodylate buffer, postfixed in 1% osmium tetraoxide, rinsed several time in cacodylate buffer, dehydrated in ascending grades of ethanol (50, 70, 90 and 100%), cleared in acetone, and thenempregnated and embedded in Epon resin. Semithin sections were cut and stained with toluidine blue and ultrathin sections, from the desired areas were cut with diamond knife usingultramicrotome. The thin sections were mounted on copper grids, stained with 5% aqueous solution of uranyl acetate for 30 minutes, washed with distilled water and then stained with Reynold′s lead citrate for 10 minutes. A transmission electron microscopeJEM100CXII was used to examine the sections for studying the intracellular components (Bancroft and Stevens, 1996).

2.2.2. Histochemistry:

2.2.2.1. PAS positive materials: The most important PAS positive materials in tissues are polysaccharide (glycogen), neutral mucopolysaccharide, mucoprotein and glycolipids (Drury and Wallington, 1980). PAS positive

diastase resistant material and PAS positive diastase digested material (glycogen) were investigated.

Specimens from 30 livers representing the three trimesters (10 from each trimester) were used to investigate the carbohydrates.

The specimens were fixed in Bouin′s fluid or Gender′s fluids. After processing, paraffin sections were stained according to the Periodic Acid Schiff (PAS) method with diastase control (sections were incubated in 1% diastase solution or saliva at 37c˚for one hour) for the differentiation between glycogen and mucopolysachrides (Drury and Wallington, 1980).

2.2.2.2. Enzymes

Specimens from 21 livers were used to investigate the alkaline and acid phosphatase enzymes. Small pieces of tissue, up to 3mm thick, were fixed in acetone at 4c˚ for 24 hours, dehydrated with acetone, cleared in chloroform for 1/2-1 hour, and then infiltrated with paraffin wax at 56c˚ for 15-30 minutes in the oven. Sections were cut at 5µm., flattened on lukewarm water path, mounted in albumenized slides and then stained according to the following methods:

a-Calcium phosphatase (Lillie, 1954) for the detection of alkaline phosphatases (Drury and wallington, 1980).This method depends upon the action of the enzyme on a substrate containing organic phosphate. The working substrate consisted of two solutions. Solution A: was composed of 6.1g. sodium barbitone, 1.2g. calcium chloride, 0.5g. Magnesium sulphate and 1000ml. distilled water. Solution B: composed of one percent Sodium B-glycerophosphate in distilled water. The working solution was made up of 50ml. of solution A and 30ml. of solution B. control sections were treated in solution in which the substrate was omitted.

b- Lead nitrate (Gomori, 1950) for the detection of acid phosphatases (Drury and wallington, 1980). The working solution consisted of 500ml. of 0.05 M. acetate buffer (PH. 5.o) added to 1.5g. sodium B-glycerophophate and 0.7g. of lead nitrate . The solution was incubated at 36c˚. for 24 hours and then filtered. Control sections were treated similarly but the solution did not contain the substrate.

Table (1): Showing the number of foetuses, their CVRL and their age in days and months.

A N	CVRL in cm	Age in days	Age in months	Gestation periods
1	2	71	2.4	First trimester
2	2.5	72	2.4	First trimester
3	3	74	2.4	First trimester
4	3.3	74.6	2.5	First trimester
5	3.5	75	2.5	First trimester
6	3.7	76	2.5	First trimester
7	4	76.5	2.5	First trimester
8	4.8	79	2.6	First trimester
9	5.3	80	2.7	First trimester
10	5.6	80.8	2.7	First trimester
11	7	85	2.8	First trimester
12	9.5	92	3	First trimester
13	10.5	94	3	First trimester
14	13.5	102	3.4	First trimester
15	13.5	102	3.4	First trimester
16	14.5	105	3.5	First trimester
17	15.2	107	3.6	First trimester
18	17	112	3.7	First trimester

19	17	112	3.7	First trimester
20	17	112	3.7	First trimester
21	17.5	113	3.7	First trimester
22	20.5	122	4	First trimester
23	21.5	124	4.1	First trimester
24	22.5	127	4.2	First trimester
25	22.5	127	4.2	First trimester
26	22.5	127	4.2	First trimester
27	22.5	127	4.2	First trimester
28	23.5	130	4.3	First trimester
29	23.5	130	4.3	First trimester
30	23.5	130	4.3	First trimester
31	23.5	130	4.3	First trimester
32	25.5	135	4.5	Second trimester
33	28	142	4.7	Second trimester
34	32	153	5.1	Second trimester
35	32	153	5.1	Second trimester
36	33	156	5.2	Second trimester
37	34	158	5.3	Second trimester
38	34	158	5.3	Second trimester
39	34.5	160	5.3	Second trimester
40	34.5	160	5.3	Second trimester
41	35.5	162	5.4	Second trimester
42	36	164	5.5	Second trimester
43	37	167	5.6	Second trimester
44	37	167	5.6	Second trimester
45	37.5	168	5.6	Second trimester
46	37.5	168	5.6	Second trimester

47	38	169	5.6	Second trimester
48	40	175	5.8	Second trimester
49	40.5	176	5.9	Second trimester
50	43	183	6.1	Second trimester
51	44	186	6.2	Second trimester
52	45	188	6.2	Second trimester
53	45	188	6.2	Second trimester
54	47	194	6.5	Second trimester
55	47	194	6.5	Second trimester
56	48.5	198	6.6	Second trimester
57	48.5	198	6.6	Second trimester
58	50	202	6.7	Second trimester
59	51	205	6.8	Second trimester
60	51	205	6.8	Second trimester
61	54	213	7.1	Second trimester
62	54.5	214	7.2	Second trimester
63	57	221	7.4	Second trimester
64	57	221	7.4	Second trimester
65	57.5	223	7.4	Second trimester
66	60	229	7.6	Second trimester
67	61	232	7.7	Second trimester
68	63	238	7.9	Second trimester
69	66	246	8.2	Second trimester
70	66.5	247	8.2	Second trimester
71	67	249	8.3	Second trimester
72	68	251	8.3	Second trimester
73	70	257	8.6	Third trimester
74	70	257	8.6	Third trimester

75	74	267	8.9	Third trimester
76	74	267	8.9	Third trimester
77	75.5	271	9	Third trimester
78	78	278	9.2	Third trimester
79	78	278	9.2	Third trimester
80	84	295	9.8	Third trimester
81	87	303	10.1	Third trimester
82	88	306	10.2	Third trimester
83	89	3.9	10.3	Third trimester
84	92	317	10.6	Third trimester
85	100	339	11.3	Third trimester
86	100	339	11.3	Third trimester
87	101	342	11.4	Third trimester
88	104	350	11.7	Third trimester
89	108	361	12	Third trimester
90	112	372	12.4	Third trimester
91	113	374	12.4	Third trimester
92	129	418	13.9	Third trimester
93	132	426	14.2	Third trimester

AN = animal number.

CVRL= curved vertebral crown rump length

CHAPTER THREE

THE RESULTS

3.1.Morphology

3.1.1.Growth anatomy

3.1.1.1. Defferentiation and Topography

A. First trimester

During early stage of development in a foetus of 2cm CVRL (71 days of age), at the right side, the hepatic primordium appeared in the peritoneal cavity beneath the mesenchyme which will form the septum transversum. Caudal to the hepatic primordium was the mesonephros and ventrally it was related to the ventral mesoderm. Primitive blood vessels were found inside the hepatic primordium (fig.1).

In a foetus of 2.5cm CVRL (72 days of age), the hepatic primordium increased in size and the septum transversum was differentiated. A large space separated the primordium of the liver from the septum transversum. The mesonephros was located caudodorsal to the liver primordium and the latter was still releated ventrally to the ventral mesenchyme. The hepatic primordium was invested by many blood cells (fig. 2).

In a foetus of 3cm CVRL (74 days of age), the hepatic prrimordium moved toward the septum transvrsum which separated it from the pericardial cavity and the heart. The hepatic primordium was related to the concave surface of the mesonephros along the caudal side of the foetus (fig. 3).

In a foetus of 3.3cm CVRL (74.6 days of age), the hepatic primordium had the same relation mentioned in the previous age but ventrally it was related to the developing primitive stomach. A large ductus venosus occupied the middle part of the liver (fig. 4).

In a foetus of 3.5cm CVRL (75 days of age), the hepatic primordium extended dorsally and caudoventrally and the mesonephros moved dorsally. Alarge space

which measured 40 µm separated the hepatic primordium from the mesonephros (fig. 5a,b).

In a foetus of 3.7cm CVRL (76 days of age), the liver extended more dorsally and caudally toward the pelvic cavity of the foetus and at the same time the mesonephros also moved dorsally. The space which separated the hepatic primordium from the mesonephros decreased to 30 µm (figs. 6a,b).

In a foetus of 4cm CVRL (76.5 days of age), the caudal border of the liver was concave and became in contact with the developing right metanephros (fig. 7).

With advancing age, in foetuses of 4.8 and 5.3cm CVRL (79 and 80 days of age), the liver increased rapidly in size and occupied most of the abdominal cavity together with parts of the developing gastrointestinal tract and the metanephros (fig. 8).

In a foetus of 7cm CVRL (85 days of age), the liver increased in size and parts of the gastrointestinal tract were embedded within the visceral surface of the liver parenchyma. Microfissures were seen on the visceral surface of the liver (fig. 9).

In a female foetus of 9.5cm CVRL (92 days of age), the liver was greatly enlarged and occupied most of the abdominal cavity and extended into the pelvic cavity.

In a male and female foetuses of 22.5cm CVRL (127 days of age), at the right lateral view, the liver still occupied all the right side of the abdominal cavity, and extended cranially to the caudal border of the fifth or sixth ribs and caudally to the pelvic cavity. The caudodorsal region of the abdominal cavity was occupied by the right kidney and a small part of the intestine (figs. 10,11). The liver became more compact having a convex surface and three borders (cranial, dorsal and ventral). The cranial border extended along the convexity of the

diaphragm and the caudal border of the fifth or sixth rib. The dorsal border was short and thick and in contact caudally with the right kidney and medially to the right adrenal gland (fig. 12). The ventral border was thin and related to the floor of the abdominal cavity. At the left lateral view, the liver curved cranially, and this was due to the continuous development of parts of the gastrointestinal tract specially the rumen, so that the liver at this side was pushed laterally and ventrally up to the level of the last rib. The liver at this age was related to the cranioventral sac of the rumen, reticulm and omasoabomasal complex viscerally, the caudodorsal sac of the rumen dorsally, and the jejunum, colon, spleen and the left kidney caudodorsally (fig. 13). The gall bladder was abscent in the liver of all foetuses studied during the first trimester.

B. Second trimester:

The liver in male foetuses of 35.5, 37 and 37.5cm CVRL (162,167 and 168 days of age) increased in size and still had the same topography mentioned previously (fig. 14).

With advancing age, in female foetuses of 48.5, 54.5, 57 and 66.5cm CVRL (198, 214, 221 and 248 days of age) and a male foetus of 66 cm CVRL (247 days of age), the liver at the right lateral side became more thick and convex and related cranially to the caudal border of the fifth rib (fig.15). At the left lateral view, the liver was pushed more laterally and ventrally due to the pressure of the cranioventral sac of the rumen and displaced to the level opposite to the ninth intercostal space and related caudally to the spiral loop of the ascending colon and the jejunum (figs. 16,17& 18).

C. Third trimester:

During the third trimester, in a male foetus of 70cm CVRL (257 days of age) the liver had the same topography as in the previous age in the second trimester.

In male foetuses of 108 and 129cm CVRL (361 and 418 days of age), at the right lateral view, the liver became more convex and was pushed laterally due to the progressive enlargement of parts of the gastrointestinal tract. The caudoventral angle of the liver was moved dorsally and became opposite to the caudal end of the right kidney, and the intestine appeared dorsal, ventral and caudal to this angle. The caudal border of the liver was opposite to the last intercostal space (fig. 19). At the left lateral view and due to the enlargement of the rumen, the liver was pushed cranially and ventrally and was related viscerally only to the cranioventral sac of the rumen. The caudal end of the liver was opposite to the 8th intercostal space. Caudal to the liver was the enlarged spiral loop of the ascending colon separated from it by a narrow space (fig. 20). By the end of the third trimester the gall bladder was still absent.

3.1.1.2. Colour & Shape

During the prenatal life, the colour of the liver was bright brown in foetuses of 22.5 and 23.5cm CVRL (127 and 130 days of age) and varied between bright brown and dark brown in all foetuses older than 23.5 cm CVRL.

The shape of the liver also varied throughout the intrauterine period. It was quadrilateral and consisted of a narrow part and wide part during the first trimester in a foetus of 22.5cm CVRL (127 days of age). During the second trimester in foetuses of 37, 37.5, 54.5, 57 and 66cm CVRL (167, 168, 213, 221 and 246 days of age) and due to the development of quadrate lobe and subdivision of the left lobe in addition to the little expansion of the right lobe, the outline of the liver became irregular but still consisted of a narrow part and a wide part (figs. 24, 26&27). During the third trimester, with more development of the right lobe as compared with the other lobes (left and quadrate), the liver tended to take a trianglular shape in foetuses of 108 and 129cm CVRL (361 and

418 days of age). The expanded right lobe could be considered the base of the organ while the narrow left lobe was considered the apex (fig. 29).

3.1.1.3. Lobation and lobulation

A. First trimester

In foetuses of 4.8, 5.3, 7 and 9.2cm CVRL (79, 80, 85 and 92 days of age), the liver contained two main lobes referred to as the right and left lobes. The right lobe occupied the right side of the abdominal and pelvic cavities of the foetus and the left one occupied the left side of the two cavities.

In a foetus of 22.5cm CVRL (127 days of age), the left lobe was separated from the right lobe by a deep fissure. This fissure extended from the cranioventral side of the liver and caudally to join the umbilical fissure where the umbilical vein entered the liver (figs. 21, 22). The visceral surface of the right lobe contained the porta hepatis. Three outgrowths projected from the visceral surface of the right lobe. The first outgrowth was cranioventral to the porta hepatis and gave rise to the quadrate lobe later on. The second outgrowth was craniodorsal to the porta hepatis and gave rise to the papillary process, while the third outgrowth was caudodorsal to the porta hepatis (medial to the renal depression) and gave rise to the caudate process which together with the papillary process formed the caudate lobe (fig. 23).

B. Second trimester

In foetuses of 37 and 37.5cm CVRL (167 and 168 days of age), the quadrate lobe was clearly identified. The papillary process was clearly developed as a circular process while the caudate process was poorly developed. The ventral side of the visceral surface of the liver possessed many microfissures (fig. 24). The caudoventral part of the left lobe was gradually subdivided from the left lobe by a small fissure (fig. 25).

In foetuses of 54.5, 57, 66 and 66.5cm CVRL (214, 221, 246 and 248 days of age), the left lobe consisted of two parts after it completed its subdivision (fig 26, 27). The caudate process was moderately developed. In most cases, the quadrate lobe was tongue- shaped but heart shape was also observed in a few cases.

C. Third trimester

In foetuses of 88, 92, 108 and 129cm CVRL (306, 317, 361 and 418 days of age), the right lobe was greatly enlarged and the caudate process was well developed and the porta hepatis was caudal to the circular and concave papillary process. The microfissures found at the ventral side of the liver increased in number especially in the right and left lobes (fig. 28, 29).

3.1.1.4.Dimensions

A. First trimester:

During the first trimester, the length of the liver varied between 6cm in a foetus of 20.5 cm CVRL (122 days of age) and 9cm in a foetus of 23.5cm CVRL (130 days of age) with an average of 8cm. The width of the narrow part of the liver varied between 1.7cm in a foetus of 20.5cm CVRL(122 days of age) and 3.1cm in a foetus of 23.5cm CVRL(130 days of age) with an average of 2.6 cm, while the broad part varied between 2.3cm and 5cm with an average of 4.5cm (Table 3).

B. Second trimester:

Throughout the second trimester the length of the liver varied between 10cm in a foetus of 28cm CVRL (158 days of age) and 22cm in a foetus of 67cm CVRL (249 days of age) with an average of 14.6cm. The width of the narrow part of the liver varied between 4cm in a foetus of 28cm CVRL(158 days of age) and 8cm in a foetus of 67cm CVRL (249 days of age) with an average of 5cm. The

width of the broad part of the liver varied between 5.8cm in a foetus of 28cm CVRL(158 days of age) and 14cm in a foetus of 66.5cm CVRL (247 days of age) with an average of 9cm (Table 4).

C. Third trimester:

During the third trimester, the length of the liver varied between 17.5 cm in a foetus of 70cm CVRL (256 days of age) and 33cm in a foetus of 129cm CVRL (418 days of age) with an average of 22.3cm. The width of the liver at the narrow part (apex) varied between 6cm in a foetus of 70cm CVRL(256 days of age) and 10cm in a foetus of 129cm CVRL(418 days of age) with an average of 7.2 cm. The width of the broad part (base) of the liver varied between 10cm in a foetus of 70cm CVRL(256 days of age) and 20cm in a foetus of 129cm CVRL(418 days of age) with an average of 13cm (Table 5).

Table (2): showing the dimensions of the developing liver.

AN	CVRL In cm	Age in days	Length In cm	Width in cm narrow part_ broad part (apex)	(base)
1	20.5	122	6	1.7	2.3
2	22	126	7.5	2.3	3
3	22.5	127	8	3	4.3
4	22.5	127	8	3	4.2
5	22.5	127	7.8	2	4.5
6	23	128	7.8	2.8	4.5
7	23.5	130	9	3.1	5
8	28	142	10	4	5.8
9	34	158	12	4.4	7
10	34.5	160	12	4.2	9

11	37	167	10.4	4.4	6.5
12	37.5	168	12	4	6.5
13	48.5	198	14	4	7.5
14	48.5	198	13.5	4	8.5
15	51	205	15.5	5	11
16	54.5	214	15.5	5.5	8.5
17	57.5	223	16	5.5	9.2
18	66	246	18	7	11
19	66.5	248	19	6	14
20	67	249	22	8	12.5
21	70	257	17.5	6	10
22	72	262	18.5	6	11
23	75	270	18	6	11
24	81	287	23	7	13.5
25	84	295	21	7	11.5
26	88	306	22	7.4	12.5
27	88.5	307	23	8	14
28	108	361	25	8.2	14
29	129	418	33	10	20

AN= Animal number

Table (3): Showing the liver dimensions during the first trimester.

Measurements	**Minimum in cm**	**Maximum in cm**	**Average in cm**
Length	6	9	8
narrow part	1.7	3.1	2.6

Width broad part	2.3	5	4

Table (4): Showing the liver dimensions during the second trimester.

Measurements	**Minimum in cm**	**Maximum in cm**	**Average in cm**
Length	10	22	14.6
narrow part	4	8	5
Width broad part	5.8	14	9

Table (5): Showing the liver dimensions during the third trimester.

Measurements	**Minimum in cm**	**Maximum in cm**	**Average in cm**
Length	17.5	33	22.3
Apex	6	10	7.2
Width Base	10	20	13

3.1.1.5.The attachments of the liver of foetuses

The mesoderm of both the septum transversum and the mesogastrium gave rise to the peritoneum covering the liver. From the peritoneum, group of attachments together with the developing neighbouring organs fixed the liver. These attachments could be divided into two groups according to the side of attachment of the liver (visceral and parietal).

(a) Visceral group

This group attached the liver at its visceral surface and includes:

1- Hepatorenal ligament: this ligament attached the convex surface of the right kidney to the concave border of the renal depression on the surface of the liver (fig. 30).
2- Lesser omentum: an extensive peritoneal fold originated along a curved line and extended between the liver and the concavity of the omasoabomasal complex (fig. 31).

(b) Parietal group

This group attached the liver at its parietal surface and includes:

1- Coronary ligament: this ligament consisted of a thick lamina closely attached the diaphragm to the border of the groove of the caudal vena cava inside the liver (fig. 32).
2- Round ligament: an extensive fold that surrounded the umbilical vein at the umbilical fissure of the liver (fig. 33).
3- Falciform ligament: this ligament extended from the floor of the abdominal cavity and was attached to the liver along a vertical line started from the umbilical fissure and joined the round ligament to the free border of the coronary ligament (figs. 32, 33). The falciform ligament could be considered as the clear demarcation between the left and right lobes.
4- The right triangular (lateral) ligament: this ligament attached the liver along a large triangular area (fig. 34) and consisted of three strong laminae: the first one was attached to the muscular part of the diaphragm, the second one fused with the corresponding part of the hepatorenal ligament to be attached to the lateral border of the renal depression, while the third one was attached to the sublumber region and the right crura of the diaphragm (figs. 35, 36).

3.1.1.6. Blood supply

The liver of the one-humped camel foetus was supplied by:

- The umbilical veins: two umbilical veins which entered the abdominal cavity and united in a venous sinus near the liver. The united umbilical vein passed through the liver and then united with the left main portal vein to form tubular duct known as the ductus venosus and the latter joins the posterior vena cava.
- The portal vein: The foetal liver receives also venous blood from the splanchnic circulation via the portal vein. The portal vein was formed by the union of cranial mesenteric vein and splenic vein. At the porta, the portal vein divided into three main branches named right dorsal, right ventral and left branch. The left branch was the largest one which joined the umbilical vein insid the liver to form the ductus venosus.
- The hepatic artery: the foetal liver supplies also by the hepatic artery which arose as one of the three primary branches of the celiac artery (the splenic, the left gastric and the hepatic). The hepatic artery enters the liver through porta hepatis dorsally to the portal vein and then divided into right dorsal, right ventral and left branches (fig. 37).

3.1.2. Histology

A. First trimester

At the early stages of development in a foetus of 2cm CVRL (71 days of age), the primordium of the liver consisted of two types of cells: hepatocytes and haemopoietic cells. The hepatocytes were large cells with large lightly stained nuclei and prominent nucleoli. The haemopoietic cells consisted of original

haemopoietic cells, precursers of erythrocytes and megakaryocytes. Original haemopoietic cells were small cells arranged in groups and some of them were scattered between the hepatic cords and their nuclei were deeply stained and occupied most of the cell cytoplasm. The precursers of the erythrocytes were large oval or round cells with large nuclei. The megakaryocytes were very large cells with large nuclei and some of them contained more than one nucleus. The hepatocytes were arranged in the form of thick laminae and solid cords and some of these laminae and cords anastomosed together leaving large round or irregular spaces between them. Some of the hepatic cords were arranged into follicular shape. The haemopoietic cells were dispersed among the cords and laminae of hepatocytes or inside the spaces between them. Large number of haemopoietic cells and a few hepatocytes showed mitotic figures. Large spaces were observed (fig. 38).

In a foetus of 2.5cm CVRL (72 days of age), the haemopoietic cells extensively proliferated so that the primordium of the liver was invested by many haemopoietic elements and infilterated throughout the hepatic cords and laminae and inside the spaces between them. Blood vessels coursed through the liver primordium, and the spaces between the hepatic cords developed primitive endothelium forming a continuous layer of flat cells with elongated nuclei but a basement membrane was abscent. These spaces constituted the basic structures of the hepatic sinusoids. Most of the haemopoietic elements that filled the blood vessels and the spaces were mostly the precursor of erythrocytes. Megakaryocytes increased in number and some of them were seen inside the spaces.

In a foetus of 3cm CVRL (74 days of age), the haemopoietic cells (precurser of erythrocytes) constituted the largest component of the liver parenchyma. The proliferation of the haemopoietic cells was more extensive along the cranial part opposite the septum transversum than the middle and caudal parts of the liver.

At the part of the liver opposite the septum transversum, the liver parenchyma consisted mainly of haemopoietic cells (precorser of erythrocytes) and a few hepatic cords (fig. 39). At the middle part of the liver, the haemopoietic cells accumolated in the spaces between the interlacing hepatic cords and hepatic follicles (fig. 40). At the caudal part of the hepatic parenchyma, opposite the mesonephros, the haemopoietic cells accumulated in groups of different size and each group was called haemopoietic focus which was surrounded by hepatocytes and the haemopoietic foci were round or irregular in shape. Most of the hepatic cords at this age of development were two cells thick and the hepatocytes were cuboidal in shape and their nuclei were large and round and possessed prominent nucleoli and peripheralheterochromatin (fig. 41). The hepatocytes and the haemopoietic cells still showed mitotic figures. The liver was surrounded by a thin continuous layer of mesothelium which constituted the primordium of Glisson′s capsule (fig. 42).

In foetuses of 3.5 and 4cm CVRL (75 and 76.5 days of age), the liver had a similar structure to that mentioned in the previous age but there was an increase in the size of the haemopoietic foci. The haemopoietic cells were still the precursors of erythrocytes.

In a foetus of 4.8cm CVRL (79 days of age), the liver possessed more but less compact cellular elements, and developed small vein- like structures without clear endothelium; they developed into the central and portal veins which were scattered throughout the liver but without a definite arrangement (fig. 43). Megakaryocytes with one to three nuclei were frequently singly dispersed. Macrophages were seen within the haemopoietic foci. At this age of development, a large number of immature erythrocytes appeared within the erythrocyte series and they were ovoid cells and contained nuclei. Granulocyte precursors appeared for the first time and these were large cells and their cytoplasm contained large number of granules. Reticular fibres were formed

along the developing capsule and extended to support the hepatic cords and haemopoietic cells (fig. 44).

In a foetus of 5.3cm CVRL (80 days of age), the hepatic sinusoids became wider, irregular and continuous with the developing central veins through openings. Immature erythrocytes increased in number. Haemopoietic cells constituted the largest component of the liver parenchyma but the haemopoietic foci were fragmented into small irregular groups of cells. Macrophages were found in close contact with the haemopoietic foci. The developed central veins were still without clear endothelium.

In a foetus of 5.6cm CVRL (80.6 days of age), all vessels in the liver (subcapsular veins, central veins and hepatic sinusoids) were filled with immature erythrocytes together with granulocyte series. The subcapsular veins acquired a thin layer of endothelium.

In a foetus of 7cm CVRL (85 days of age), the liver was covered with a serous membrane (peritoneum) and part of it extended inside the liver forming the ligaments (fig. 45).The developmental changes occured at this age led to the formation of typical hepatic lobules but interlobular connective tissue was not clear. The liver appeared more compact, and the hepatic cords were arranged around the central veins in radiating rows. The hepatocytes were relatively large polyhedral cells with large round nuclei and prominent nucleoli and their cytoplasm was finely granular and contained discrete cytoplasmic vacuoles (fig. 46). The central veins were lined with discontinuous layer of flattened cells. The hepatic sinusoids were irregularly arranged between the hepatic cords and some of them were continuous with the central veins with slit-like openings (fig. 47). The haemopoietic cells and hepatocytes increased in number and they still showed high mitotic figures. Megakaryocytes also increased in number so that some of them were grouped in the same area. A few fine collagenous fibres

were developed subjacent to the mesothelium covering the liver .The branches of the portal vein were surrounded with primitive billiary epithelium forming the ductal plate stage during the development of the intrahepatic bile ducts (figs. 48,49).

In a foetus of 9.5cm CVRL (92 days of age), the arrangement of the hepatic cords around the central veins was disrupted due to the extensive proliferation of the haemopoietic cells within the haemopoietic foci specially the granulocyte series. The nucleated erythrocytes completed their differentiation and were transformed into mature erythrocytes (RBCs). Mature erythrocytes filled the central veins and were infiltrated throughout the liver parenchyma (fig. 50). Granulocyte series increased in number but mature granulocytes didn′t appear yet.

In a foetus of 10.5cm CVRL (94 days of age), the hepatic cords were still irregular. Vacuoles were dispersed within the cytoplasm of all hepatocytes. Some vacuoles were small in size, while others were large. The amount of reticular fibres supporting the hepatic cords and haemopoietic cells was increased and extended to surround the central veins (fig. 51).

In a foetus of 13.5cm CVRL (102 days of age), the surface of the liver showed shallow invaginations and these constituted the first step for the formation of microfissures later on. Periportal areas were still not developed (fig. 52).

In foetuses of 14.5 and 15.2cm CVRL (105 and 107 days of age), the liver developed large microfissures which separated the surface of the liver into small parts. The fissures were lined with the mesothelium of the capsule. Periportal areas of loose mesenchymal tissue surrounded the portal veins. The periportal mesenchymal tissue consisted of fine collagenous fibres, fibroblasts and mesenchymal cells (fig. 53). The primitive billiary epithelium which surrounded the portal area was reorganized in bile ductules. At the beginning, the periportal

areas contained only branches of the portal vein and a bile ductule but with advancing age branches of the hepatic artery were found. The branch of the portal vein was lined with a layer of endothelium, while the bile ductule was lined with a single layer of cuboidal cells (fig. 54). Macrophages and megakaryocytes were frequently observed inside the haemopoietic foci. Hepatic sinusoids were filled with blood.

In foetuses of 17 and 17.5 cm CVRL (112 days of age), hepatic sinusoids were irregularly inserted between the hepatic cords and haemopoietic foci (fig. 55). The central vein was still lined with incomplete layer of endothelium. Lipid droplets increased in size (figs. 56,57) Mature granulocytes (eosinophils) appeared and the erythrocyte series decreased in number when compared with the granulocyte series. Megakaryocytes with more than four nuclei were observed inside the hepatic sinusoids. Haemopoietic foci were accumulated more in the subcapsular area than in the entire liver parenchyma. The capsule contained moderate amount of collagenous fibres covered with alayer of mesothelium.

In foetuses of 20.5 and 21.5cm CVRL (122 and 124 days of age), the liver parenchyma consisted mainly of haemopoietic foci. Mature RBCs extensively infilterated the liver. Hepatic arteries increased in size and lined with a single layer of flattened cells Large macrophages were seen inside the haemopoietic foci surrounded with immature and mature erythrocytes.

In a foetus of 23.5cm CVRL (130 days of age), the central veins together with the hepatic sinusoids were filled with blood (fig. 58).

B. Second trimester

In a foetus of 32cm CVRL (153 days of age), hepatocytes accumulatd more cytoplasmic vacuoles. In some hepatocytes, the vacuoles were fused to produce large vacuole which occupied most of the cell cytoplasm and pushed the

nucleus to one side of the cell. The endothelium lining the Hepatic sinusoids rested on a fine layer of connective tissue fibres (fig. 59)

In foetuses of 33, 34 and 34.5cm CVRL (156, 158 and 160 days of age), small groups of hepatocytes were formed at the area under the capsule. Most of the hepatic sinusoids between the irregular hepatic cords were filled with mature RBCs while a few of them were empty. The endothelium lining the sinusoids was in close contact with the hepatocytes. Megakaryocytes were also observed (figs. 60,61&62).

In a foetus of 36cm CVRL (164 days of age), mature RBCs were extensively differentiated and let to the enlargement of the sinusoids.

In foetuses of 37.5 and 38cm CVRL (168 and 169 days of age), most of the blood was drained so that the sinusoids contained less blood than in the previous age.the spaces of Disse were developed and appeared as narrow spaces separating the endothelium lining the sinusoids from the hepatocytes (fig. 63). Some of the central veins were lined with continuous layer of endothelial cells and were continuous with the sinusoids through slits. Haemopoietic cells proliferated so that the erythrocyte series and granulocyte series reappeared. Megakaryoctes were still found in large number.

In a foetus of 40cm CVRL (175 days of age), the sinusoids were empty but the haemopoietic cells were still extensively proliferated and differentiated so that the haemopoietic foci constituted the dominant appearance of the liver and consisted mainly of small lymphocytes with deeply stained nuclei. Hepatocytes contained large cytoplasmic vacuoles andperipheral nuclei due to the increasing amount and size of thesevacuoles. Immature erythrocytes and granulocytes were observed (fig. 64).

In a foetus of 44cm CVRL (186 days of age), the Glisson′s capsule consisted of a thick layer of collagenous fibres. A large subcapsular vein was formed inside

the liver parenchyma subjacent to the capsule. The subcapsular area consi**sted mainly of groups of hepatocytes and a few haemopoietic foci. The central vein and the hepatic sinusoids were empty (fig. 65)

In foetuses of 47 and 48.5cm CVRL (194 and 198 days of age), branches of the portal vein, hepatic artery,central veins and hepatic sinusoids were well developed. The hepatocytes were regularly arranged around the central veins and the hepatic sinusoids were empty (fig. 66). The accumulation of cytoplasmic vacuoles inside the hepatocytes varied quite considerably; in some areas the hepatocytes showed many cytoplasmic vacuoles while in other areas the cytoplasmic vacuoles were few or abscent. The hepatocytes in the subcapsular area contained many cytoplasmic vacuoles. The haemopoietic cells were found in small and large groups and the megakaryocytes were usually found in groups of two cells.

In foetuses of 50 and 51cm CVRL (202 and 205 days of age), the arrangement of hepatocytes was interrupted due to extensive proliferation of the haemopoietic foci and mature RBCs were extensively differentiated and were observed also in groups of different size along the wall of the subcapsular vein (fig. 67).

In a foetus of 54cm CVRL (213 days of age), all mature RBCs were found inside the blood vessels of the liver and only the megakaryocytes were still found between the hepatocytes. The connective tissue of the portal area contained large amount of reticular fibres.

In foetuses of 57 and 57.5cm CVRL (221 and 223 days of age), the hepatic cords wereregularly arranged around the central veins forming the hepatic lobules but without clear demarcation. The endothelium lining the central veins rested on a layer of connective tissue fibres. The hepatic sinusoids were empty. The reticular fibres formed a network supporting all components of the liver

parenchyma (hepatic cords, group of hepatocytes, haemopoietic foci, central veins and hepatic sinusoids) (fig. 68).

In foetuses of 60, 61and 63 cm CVRL (229, 232 and 238 days of age), the hepatocytes were arranged in two different types of hepatic cords: intralobular and interlobular hepatic cords.The hepatic lobules were separated from each other by interlobular hepatic cords which coursed along the periphery of the lobules. The cytoplasm of the hepatocytes of the interlobular hepatic cords was more acidic than the cytoplasm of the hepatocytes of the intralobular hepatic cords (fig. 69). The portal areas contained lymphatic vessels in addition to branches of the portal vein and hepatic artery and a bile ductule. Large number of hepatic sinusoids was developed between the interlobular hepatic cords which separated the lobules. The interlobular hepatic cords separating the lobules were one cell thick and the hepatocytes were smaller (4.5 µm) than the hepatocytes of the intralobular hepatic cords (7 µm). The hepatic sinusoids contained a few number of megakaryocytes (fig. 70)

In a foetus of 67cm CVRL (249 days of age), at the end of the second trimester, the haemopoietic foci were still dispersed in a large number and the hepatic sinusoids were empty.

C.Third trimester

In foetuses of 74 and 75.5cm CVRL (267 and 271 days of age), the cytoplasm of the hepatocytes of both the interlobular and intralobular hepatic cords had the same stainability.. Hepatic sinusoids were large and irregularly dispersed between the branching hepatic cords and most of them were empty. Haemopoietic foci were dispersed within the liver parenchyma but fewer than in the second trimester. Megakaryocytes also decreased in number.The reticular fibres increased in amount and supported the branching hepatic cords and surrounded the sinusoids between them.

In a foetus of 78cm CVRL (278 days of age),the hepatic lobules were still separated from each other by interlobular hepatic cords coursing along the periphery of the lobules. Each lobule contained a small central vein and the hepatic cords were arranged around it in a radiating manner but the arrangement of the dilated hepatic sinusoids and the distribution of some of the haemopoietic foci between the hepatic cords caused irregularty of the hepatic cords around the central vein. The hepatocytes of the interlobular hepatic cords were still smaller than that of the intralobular hepatic cords but the hepatic sinusoids between the interlobular hepatic cordswere wider than those between the intralobular hepatic cords.haemopoietic foci decreased in number (fig. 71).

In foetuses of 84, 88 and 92 cm CVRL (295, 306 and 317 days of age), the lobulation of the liver parenchyma was clearly observed. The haemopoietic foci decreased dramatically in size and number. The hepatic sinusoids, specially thosedirectly under the capsule contained mature RBCs. Megakaryocytes were rarely seen.

In foetuses of 100 and101 cm CVRL (339 and 342 days of age), the hepatic cords were regularly arranged around the central veins. The interlobular hepatic cords separating the lobules disappeared so that the intralobular hepatic cords of neigbouring lobules extended without clear demarcation. The important change at this age of development was the enlargement of the portal areas and their vessels were well developed (figs. 72,73). Lipid still appeared in large droplets within the cytoplasm of hepatocytes (fig. 74).

In a foetus of 104cm CVRL (350 days of age), septa of connective tissue extended from the connective tissue of the capsule and trabeculae into the liver parenchyma andreplaced the interlobular hepatic cords separating the lobules.The hepatic sinusoids near the capsule contained blood more than the hepatic sinusoids inside the liver parenchyma (figs. 75,76).

In a foetus of 112cm CVRL (372 days of age), the hepatic cords branched and anastomosed to form a three dimentional structure like sponge.the hepatocytes decreased in size and the cytoplasmic vacuoles dispersed throughout the cytoplasm of the hepatocytes. The haemopoietic foci disappearedcompletely and the hepatic sinusoids were empty. The trabeculae surrounding the liver lobules contained large amount of reticular fibres which also supported the hepatic cords and hepatic sinusoids (fig. 77).

In a foetus of 129cm CVRL (418 days of age), large trabeculae of connective tissue fibres separated the hepatic lobules from each other and the lobules displayed the typical appearance of distinct hepatic lobulation as in the adult camel. Hepatic sinusoids were filled with mature RBCs (fig. 78). All the liver components were supported with dense reticular fibres.

In a foetus of 132cm CVRL (426 days of age), the typical arrangement of hepatocytes within the hepatic lobule was observed: the central vein was in the centre of the lobule, the hepatic cords were irregularly branched around the central vein and the empty hepatic sinusoids were arranged between the branched hepatic cords.

3.1.3.Histometry

During the first trimester, the mean diameter of the hepatocytes varied between 5 µm in a foetus of 2 cm CVRL and 10 µm in a foetus of 7 cm CVRL with an average of 6.4 µm. The mean diameter of megakaryocytes varied between 12 µm in a foetus15.2 cm CVRL and 25 µm in a foetus of 7 cm CVRL with an average of 17.4 µm (Table 6).

During the second trimester, the mean diameter of the hepatocytes varied between 5 µm in a foetus of 48.5 cm CVRL and 10 µm in a foetus of 37.5 cm CVRL with an average of 7.3 µm. The mean diameter of megakaryocytes varied between 15 µm in a foetus of 48.5 cm CVRL and 20 µm in a foetus of 36 cm CVRL with an average of 18.3 µm (Table 7).

During the third trimester, the mean diameter of the hepatocytes varied between 5 µm in foetuses of 104 and 132 cm CVRL and 8 µm in a foetus of 112 cm CVRL with an average of 6.2 µm. The mean diameter of megakaryocytes was 24 µm in a foetus of 78 cm CVRL (Table 8).

Table 6: Mean diameter of hepatocytes and megakaryocytes during the first trimester.

CVRL/cm	**Mean diameter/µm**	
	Hepatocytes-	**Megakaryocytes**
2	5	17
3	7	-
7	10	25
10.5	6	-
15.2	6	12
17	6	20
20.5	6	15
21.5	7	13
23.5	5	20
Total	58	122
Mean	6.4	17.4

Table 7: Mean diameter of hepatocytes and megakaryocytes during the second trimester.

CVRL/cm	**Mean diameter/µm**	
	Hepatocytes-	**Megakaryocytes**
32	8	20
34	7	-
36	7	20
37.5	10	-
48.5	5	15
54	7	18
67	7	-
Total	51	73

Mean	7.3	18.3

Table 8:Mean diameter of hepatocytes and megakaryocytes during the third trimester.

CVRL/cm	Mean diameter/µm	
	Hepatocytes	**Megakaryocytes**
78	7	24
104	5	-
112	8	-
132	5	-
Total	25	24
Mean	6.2	24

3.1.4. Ultrastructure

A. First trimester:

Ultrastructural examination revealed that in foetuses of 17 and 17.5 cm CVRL (112 and 113 days of age), the liver parenchyma consisted of hepatocytes and haemopoietic cells. Haemopoietic cells were aggregated into haemopoietic foci scattered among hepatocytes or inside hepatic sinusoids (figs.79,80). The hepatocytes were large cells and their nuclei were large and round and containing euchromatin and peripheral heterochromatin. Their cytoplasm contained round mitochondria with sparse cristae, a few rough endoplasmic reticulum mainly in a vesicular form closely associated with mitochondria at the begining and then scattered throughout the cytoplasm. Several large lipid droplets of varying size were also found and some of them

pressed the nucleus and pushed it to one side of the cell. Lipofuschin pigments were frequently observed while glycogen particles were not observed (figs. 81, 82). Hepatocytes and haemopoietic elements showed proliferative activity as judged by many mitotic figures followed by a period of maturation. During maturation the cytoplasm of hepatocytes was filled with free ribosomes followed by the development of small mitochondria, rough endoplasmic reticulum (fig. 83). The central vein was lined with discontinuous layer of endothelial cells resting on a thin basal lamina. Large number of erythrocytes appeared inside the lumen of the central vein. The hepatic sinusoids were lined with incomplete layer of endothelial cells and filled with immature and mature erythrocytes. The extruded nuclei of mature erythrocytes and blood platelets were observed within the cytoplasm of endothelial cells lining the sinusoids. In the region where the sinusoids were devoid of lining endothelium, the haemopoietic elements were in intimate contact with the surrounding hepatocytes. The space of Disse was not developed (fig. 84).The hepatocytes were attached to each other by desmosomes. The plasma membrane between adjacent hepatocytes was not clear except at the regions of desmosomal connection which appeared more electron dense (fig. 85).

B. Second trimester:

In a foetus of 25.5 cm CVRL (135 days of age), the structure of the liver was similar to that of first trimester and the megakaryocytes were observed within the haemopoietic foci and inside the hepatic sinusoids. Platelets are anucleated blood elements were observed near the megakaryocytes (fig. 86). Mature megakaryocyte is large cell with folded cytoplasmic membrane which forms long cytoplasmic processes or proplatelets projections. The proplatelets projections fragmented into circulating particles.

In a foetus of 33 cm CVRL (156 days of age), haemopoietic elements were extensively proliferated within the haemopoietic foci (fig. 87) and inside the connective tissue of the portal area in addition to adipocytes (figs. 88, 89). The cytoplasm of the newly formed granulocytes in the haemopoietic foci contained free ribosomes and azor granules and the nucleus was excentric and contained masses of heterochromatin extended from the periphery of the nucleus toward the centre. The plasma membrane of neighbouring hepatocytes became gradually clear and separated from each other and at the same time intercellular bile canaliculi were developed (fig. 90).

In a foetus of 43 cm CVRL (183 days of age), the cytoplasm of the hepatocytes contained round or rod shape numerous mitochondria, rough endoplasmic reticulum well developed in the form of cisternae and large lipid droplets. Glycogen particles were still not observed. Intercellular bile canaliculi were frequently observed between neighbouring hepatocytes (fig. 91). These intercellular bile canaliculi appeared between three to four adjoining hepatocytes and possessed long and short stuby microvilli. Accumulation of fine filaments were observed within the hepatocytes parallel to the intercellular canaliculi (fig. 92). The central vein was lined with fenestrated endothelium which accumulated more cytoplasm in the middle of the cell where the nucleus is found while the two ends of the cell were very narrow with very fine fenestrae. The space of Disse was still not developed (figs. 93,94). In some central veins large spaces appeared subiacent to the basal lamina and filled with the haemopoietic elements. The surface of the hepatocytes parallel to these areas showed fine plasmalemal folds. Fibroblasts appeared subjacent to the lining endothelium.

In a foetus of 45 cm CVRL (188 days of age), the fibroblasts subjacent to the endothelium lining the central vein produced considerable amount of collagen fibres longitudinally caursing along the basal lamina (fig. 95). The Glisson's

capsule consisted of two distinct layers: the surface one was a single layer of fibroblasts which possessed interdiggitation connection while the internal layer consisted of a large amount of collagen bundles and haemopoietic elements (Fig. 96). Bundles of collagen fibres extended to surround the haemopoietic elements.

In a foetus of 57 cm CVRL (221 days of age), the cytoplasm of the hepatocytes contained multivesicular bodies, long cisternae of rough endoplasmic reticulum, lipid droplets and many lipofushin pigments. Intercellular bile canaliculi were also observed (fig. 97). Large number of erythrocytes in varying degree of developmentand immature granulocytes appeared within the haemopoietic foci and hepatic sinusoids. Hepatocytes were also extensively proliferated (figs. 98,99).

In a foetus of 68 cm CVRL (251 days of age), collagen fibres subjacent to the endothelium lining the central vein were increased in number but they were abscent where fenestration existed. The cytoplasm of hepatocytes of the interlobular hepatic cords contained large amount of lipid droplets of varying size and each droplet was surrounded by many vesicles (figs. 100,101).

C.Third trimester:

In a foetus of 78 cm CVRL (278 days of age), considerable number of haemopoietic elements were scattered among the hepatocytes or inside the sinusoids. Some of the hepatic sinusoids were lined with highly fenestrated endothelium while others were lined with nonfenestrated endothelium. Kupffer cells were clearly identified between the lining endothelium of the sinusoids. Some platelets were observed inside the cytoplasm of the kupffer cells. In some sinusoids, kupffer cells were larged and occupied most of the lumen of the sinusoid or even occluded the lumen. Megakaryocytes were observed at this stage of development (figs.102, 103). Hepatic stellate cells were observed in the

perisinusoidal space of Disse and sometimes associated with haemopoietic elements. These cells increased in number with advancing age. The nucleus of the hepatic stellate cell was large as compared with their cytoplasm (figs. 104). Well developed rough endoplasmic reticulum characterized the cytoplasm of the hepatic stellate cells and sometimes appeared dilated and surrounded the mitochondria. Small lipid droplets were also observed in the cytoplasm of the hepatic stellate cells. In some sinusoids, the spaces of Disse were enlarged and showed bundles of collagen fibres (figs. 105, 106, 107& 108).

In a foetus of 87 cm CVRL (303 days of age), the hepatocytes contained more multivesicular bodies in their cytoplasma. The cisternal form of rough endoplasmic reticulum became closely associated with the plasma membrane and mitochondria and sometimes a single cisternum surrounded almost each mitochondrion. A large number of mature erythrocytes and erythrocyte fragments appeared inside the hepatic sinusoid (fig. 109). The bile duct was lined with a single layer of cuboidal cells with large rounded nuclei and showed fine microvilli at their apical surface (fig. 110). The connective tissue of the portal areas contained large number of collagen bundles in addition to a few scattered haemopoietic elements.

In a foetus of 90 cm CVRL (311 days of age), multivesicular bodies occupied most of the cytoplasm of hepatocytes and these vesicular bodies became larger and more prominent. Cisternae of rough endoplasmic reticulum surrounded groups of multivesiculr bodies (figs.111, 112). Mesenchymal stromal cells were found subjacent to the wall of the central vein. At the area of the central vein where the mesenchymal cells were found, three types of cells separated the lumen of the central vein from the hepatic sinusoid or the hepatocytes. These cells were: endothelium of the central vein, mesenchymal stromal cells and hepatic stellate cells. Apoptopsis of hepatocytes was observed during the course of hepatic

development and some apoptic bodies appeared inside the hepatic sinusoids and then phagocytosed by the kupffer cells.

In a foetus of 100 cm CVRL (339 days of age), Large lipid droplets were still observed and pressed the nucleus in some hepatocytes. Intercellular bile canaliculi were found between the hepatocytes. Erythropoiesis was still observed and large amount of erythrocyte fragments were observed. Kupffer cells and hepatic stellate cells were also observed (figs. 113, 114& 115).

3.2. Histochemistry

3.2.1. PAS positive materials:

3.2.1. a- PAS positive diastase resistant material

A. First trimester:

In a foetus of 2 cm CVRL (71 days of age), the hepatic cords and laminae gave faint reaction for PAS technique. Original haemopoietic cells and erythrocyte series gave negative reaction while megakaryocytes reacted positively (fig. 116).

In foetuses of 17 and 20.5 cm CVRL (112 and 122 days of age) the hepatic cords still revealed faint reaction for PAS. megakaryocytes showed reaction strong than that mentioned in the previous age while haemopoietic cells and infiltrated erythrocytes showed negative reaction (fig. 117).

B.Second trimester:

In foetuses of 37.5 and 40 cm CVRL (168 and 175 days of age), the hepatic cords showed week reaction while megakaryocytes showed strong reaction. Haemopoietic cells and erythrocytes still revealed negatively (fig. 118).

In a foetus of 61 cm CVRL (232 days of age), the hepatic cords showed positive reaction. Groups of hepatocytes and large hamopoietic foci near and directly under the capsule revealed negative reaction. The connective tissue between the cords and the connective tissue of the capsule reacted positively (fig. 119).

C. Third trimester:

In foetuses of 72, 75.5 and 92 cm CVRL (262, 267 and 317 days of age), the hepatic cords and groups of hepatocytes directly under the capsule gave positive reaction and the reaction increased with advancing age. The connective tissue fibres of the interlobular spaces reacted positively. The small megakaryocytes showed reaation stronger than the large ones (figs. 120, 121).

In a foetus of 112 cm CVRL (372 days of age), the hepatic cords inside the parenchyma of the liver and the groups of hepatocytes near or directly under the capsule showed reaction stronger than that in the previous age. the connective tissue between them also showed positive reaction.

3.2.1. b- PAS positive diastase digested materialAll the specimens studied throughout the three trimesters revealed negative reaction.

3.2.2. Enzymes

3.2.2.1.Alkaline phoshatase

During the three trimesters of development, all liver specimens of the foetuses showed negative reacrion for alkaline phosphatase enzyme

3.2.2.2. Acid phosphatase

All components of the liver revealed negative reaction for acid phosphatase enzyme during the three trimesters of development.

CHAPTER FOUR

DISCUSSION

4.1. Morphology

4.1.1.Growth anatomy

4.1.1.1. Defferentiation & Topography

The liver was developed as a hollow diverticulum from the duodenum in human (Bloom, 1926) and the pig (Bradley, 1948), from the ventral wall of the gut immediately caudal to the stomach in some vertebrates (Bradley, 1964), from the caudal region of the foregut in some mammalian species (McGeady ***et al***., 2006). In human, the hepatic diverticulum started as a thickening of the endoplastic epithelium at 18

days of age (Roskams and Desmet, 2008) or at 22 days of age (Taviana and peauit, 2005). The hepatic primordium of the chick was first recognized at about 22 somite stage (Bradley, 1964).The earliest analage of the liver in human embryo was formed from the endodermal cells that contacted with the bulk of the mesoderm of the septum transversum (Severn, 1972; Kessler, 2007).The liver analage of the mouse could be observed in the septum transversum beneath the pericardial cavity at 10 days of gestation and then the liver analage protruded into the embryonic peritoneal cavity at 11 days (Sasaki and Sonoda, 2000). In the present investigation, the hepatic primordium appeared at the right side in the peritoneal cavity beneath the mesenchyme which will form the septum transversum in 2 cm CVRL (71 days of age) foetus. The hepatic primordium in 2.5 cm CVRL (72 days of age) foetus in the present investigation increased in size and was related ventral to the mesogastrium. The septum transversum was also differentiated. This observation is in agreement with McGeady ***etal***. (2006) in some mammalian species but disagree with Godlewski ***et al***. (1997) in the mouse.

The liver of the mouse embryo was developed rapidly at 8 weeks of gestation and occupied the ventral body cavity together with part of the gastrointestinal tract and urinary system (Godlewski ***et al***., 1997). The same observation was noticed in the present investigation in a foetus of 3.3 cm CVRL (74.6 days of age). In the present study, parts of the gastrointestinal tract embedded within the visceral surface of the liver parenchyma in foetuses of 5.3 and 7 cm CVRL (80 and 85 days of age). Microfissures are present within the visceral surface of the liver in a foetus of 7 cm CVRL (85 days of age). With advancing age the liver was greatly enlarged and occupied most of the abdominal cavity and extended

into the pelvic cavity in a foetus of 9.5 cm CVRL (92 days of age). This finding is in agreement with the findings of Abdalla ***etal***. (1971) and Abdel- Moniem ***etal***.(2000). They suggested that the liver occupied most of the abdominal cavity in the foetus of the one-humped camel.

Abd EI-Hafez (2009) observed that the enlargement of the liver started in the camel foetus between 50 and 75 mm CVRL and extended from the diaphragm cranially to the pelvic inlet caudally and occupied this area until the foetus reached 185 mm CVRL. The same extention is noticed in the present investigation.

In the present investigation, during the first trimester, the primordium of the liver is related cranially to the mesenchyme which will form the septum transversum, caudally to the mesonephros and ventrally to the ventral mesoderm in a foetus of 2 cm CVRL (71 days of age). Later on, the septum transversum is differentiated and the liver is related to it cranioventrally in a foetus of 2.5 cm CVRL (72days of age). This result dis agreed with that of Abd El- Hafez (2009) who stated that the septum transversum could be distinguished and the liver is related to it cranioventrally in one-humped camel foetuses between 12 and 19 mm CVRL.

The Topography of the liver in the camel foetus is changeable throughout the gestation period.The topogragphy of the liver at the full term foetus in the present study is still different from the topography of the liver in the adult camel that mentioned by Higazi (1945), Abdalla ***etal.*** (1971), Abdel-Moniem ***etal.*** (2000) and Ahmed (2002).

McGeady ***etal***. (2006) stated that the final position and orientation of the liver in the abdominal cavity are influenced by the development and rotation of the other abdominal organs in some mammalian species.

The result in the present study is in conformity with the above mentioned observation.

4.1.1.2. Colour and Shape

The liver is substantially heavier in the young animal than in the adult and is usually brownish-red in colour (Dyce, Sack and Wensing, 1987). Abdalla ***etal***. (1971), Smuts and Bezuidenhout, (1987) and Ahmed (2002) mentioned that the liver of the dromedary was dark brown in colour and similar to human (Gray, 1918). In the present investigation, the liver of the foetus is bright brown in colour at the first trimester in foetuses of 22.5 and 23.5 cm CVRL (127 and 130 days of age) and varied between bright brown and dark brown in all foetuses older than 23.5 cm CVRL during the second and third trimesters.

The shape of the liver of human foetus was pyramidal (Christoph ***etal***., 1976) or square (Albay ***etal***., 2005), while in the dromedary, the shape of the liver was irregular (Abdalla ***etal***., 1971; Ahmed, 2002) and triangular intwo- humped camel (Endo ***etal***., 2000). In the present study, the liver of the one-humped camel foetus takes different shapes during the intrauterine period; it's quadrilateral and consists of a narrow part and wide part during the first trimester in a foetus of 22.5 cm CVRL (127 days of age) and irregular during the second trimester in foetuses of 37, 37.5, 54.5, 57 and 66 cm CVRL (167, 168, 213, 221and 246 days of age). The change in shape of the liver is due to the development of the quadrate lobe, subdivision of the left lobe and enlargement of the right lobe. During the third trimester, the liver becomes triangular in shape in foetuses of 108 and 129 cm CVRL (361 and 418 days of age) due to more development and enlargment of the right lobe as compared with the other

lobes. The enlarged right lobe could be considered the base of the liver while the narrow left lobe is considered the apex.

4.1.1.3. Lobation and lobulation

In the present investigation, during the first trimester, the liver develops right and left lobes in foetuses of 4.8, 5.3, 7 and 9.5 cm CVRL (79, 80, 85 and 92 days of age).This result confirmed the observation of McGeady ***etal***. (2006) in some mammalian species and Farag (1990) who stated that the liver of the adult dromedary consists of two lobes, but disagreed with Guang ***etal***. (2008) in human foetus. Near the end of the first trimester in a foetus of 22.5 cm CVRL (127 days of age), three outgrowths from the right lobe give rise to the quadrate and caudate lobes. This observation is in agreement with McGeady ***etal***. (2006) in some mammalian species.

In the present investigation, the quadrate lobe is clearly identified during the second trimester in foetuses of 37 and 37.5 cm CVRL (167 and 168 days of age). With advancing age in foetuses of 54.5, 57, 66 and 66.5 cm CVRL (214, 221, 246 and 248 days of age), the quadrate lobe is tongue shaped in most cases but heart shape is also observed in a few cases. This finding confirmed the observation of Ahmed (2002) and Ahmed ***etal.*** (2014) in the adult dromedary camel. The papillary process is clearly developed as circular process during the second trimester in foetuses of 37 and 37. 5 cm CVRL (167 and 168 days of age) and become concave during the third trimester in foetuses of 88, 92, 108 and 129 cm CVRL (306, 317, 361 and 418 days of age). The concave circular shape of the papillary process in the present study is similar to the finding of Farag (1990); Ahmed (2002) and Ahmed ***etal.*** (2014) in the dromedary camel. In the present investigation, the caudate process is poorly

developed during the second trimester in foetuses of 37 and 37.5 cm CVRL (167 and 168 days of age) while moderate development occurred in foetuses of 54.5, 57, 66 and 66.5 cm CVRL (214, 221, 246 and 248 days of age) . During the third trimester in foetuses of 88, 92, 108 and 129 cm CVRL (306, 314, 361 and 418 days of age), the caudate process is well developed. The caudoventral part of the left lobe is subdivided gradually from the left lobe by small fissure during the second trimester in foetuses of 37 and 37.5 cm CVRL (167 and 168 days of age). The subdivision is completed and the left lobe consisted of two parts in foetuses of 54.5, 57, 66 and 66.5 cm CVRL (214, 221, 246 and 248 days of age). The right lobe is gradually enlarged during the second and third trimesters and reached their greatest enlargement in a foetus of 129 cm CVRL (418 days of age). The ventral side of the visceral surface of the liver possessed many microfissures during the second trimester in foetuses of 37 and 37.5 cm CVRL and gradually increased in number specially in the right and left lobes during the third trimester in foetuses of 88, 92, 108 and 129 cm CVRL. The observation of microfissures in the present study is in agreement with Abdalla ***etal***. (1971), Ahmed (2002) and Ahmed ***etal***. (2014) in the adult dromedary camel.

4.1.1.4.Dimensions

In the present investigation, a clear relationship was noticed between the dimension of the liver and the age of the foetus. The average length of the liver during the third trimester was 22. 3 cm which is higher than the average length of the liver during the second trimester (14.6 cm) and first trimester (8 cm). The average length of the liver during the third trimester (22.3 cm) was very low as compared with the average length of the liver in the adult: 70 cm (Droandi, 1936; Hegazi, 1954), 60 cm (Abdalla ***etal***. 1971) and 67 cm (Ahmed, 2002; Ahmed ***etal.***, 2014).

The average width of the liver at the narrow part during the third trimester (7.2 cm) is higher than the average width of the liver at the narrow part during the second trimester (5 cm) and first trimester (2.6 cm) .This average is much lower than the average width of the narrow part (apex) of the adult camel liver (18 cm)**(**Abdalla ***etal***., 1971). The average width of the liver at the broad part (base) during the third trimester (13 cm) is higher than the average width of the liver at wide part during the second trimester (9 cm) and first trimester (4.5 cm). The average width of the broad part of the liver during the third trimester (13 cm) is lower than that in the adult camel liver: 50-60 cm (Droandi, 1936), 34 cm (Higazi, 1954), 42 cm (Abdulla ***etal***., 1971) and 48 cm (Ahmed, 2002; Ahmed ***etal.***, 2014).

4.1.1.5. Attachments

The attachments which fixed the liver of the foetus of the dromedary camel arose from the peritoneum that covered the liver and could be divided into two groups (visceral and parietal) according to their attachment to the surface of the liver.

Visceral group:

- Hepatorenal ligament: in the present investigation this ligament connected the convex border of the kidney to the border of the renal depression in the liver.This observation is in agreement with Ahmed (2002) and Ahmed ***etal.*** (2014) in 85.81 and 96.79 cm CVRL dromedary camel fotuses and Abdalla ***etal***. (1971) in the adult camel.

- Lesser omentum: Ahmed (2002) and Ahmed ***etal.*** (2014) described this ligament in the camel foetuses of 85.81 and 96.79 cm CVRL. Moreover, Abdalla ***etal***. (1971) and Farag (1990) demonstrated this ligament in the liver of the adult camel. This ligament extends along the visceral surface

of the liver and convexity of the omasoabomasal complex similar to result in the present investigation.

Parietal group:

- Coronary ligament: in the present investigation, the coronary ligament consisted of a thick lamina extending between the diaphragm and the border of the groove where the caudal vena cava was embedded in the liver. This result is similar to that of Ahmed (2002) and Ahmed ***etal.*** (2014) in the camel foetuses of 85.81 and 96.79 cm CVRL and Abdalla ***etal***. (1971) in the adult dromedary camel.

- Round ligament: This ligament was abscent in the adult ox, sheep and goat (Nickel ***et al***, 1973; Getty, 1975), the dog (Sleight and Thomford, 1970) and the pig (Getty, 1975). However, Bradley (1946), Getty (1975) and Snell (2000) demonstrated this ligament in the horse and man respectively. Ahmed (2002) and Ahmed ***etal.*** (2014) also described this ligament in the foetuses of 85.81 and 96.79 cm CVRL and in the adult camel. Carlson (1981) added that this ligament starts from the umbilicus and passes through the falciform ligament and ligamentum venosum. In the present study, this ligament is found as an extensive fold that surrounded the umbilical vein at the umbilical fissure.

- Falciform ligament: This ligament was not found in the adult ox, sheep and goat (Nickel ***etal***., 1973; Getty, 1975), while Bradley (1946), Getty (1975) and (Snell, 2000) demonstrated it in the liver of the horse and man respectively. Ahmed (2002) and Ahmed ***etal.*** (2014) also demonstrated this ligament in the foetuses of 85.81 and 96. 79 cm CVRL and in the adult dromedary camel. In the present study, the falciform ligament extended from the floor of the abdominal cavity and was attached to the liver along a vertical line between the umbilical fissure and the free

border of the coronary ligament. This observation is similar to that of McGeady ***etal***. (2006) in some mammalian foetuses.

- The right triangular (lateral) ligament: Ahmed (2002) and Ahmed ***etal.*** (2014) found this ligament in camel foetuses of 85.81 and 96.79 cm CVRL. Abdalla ***etal***. (1971) demonstrated the right triangular ligament in the liver of the camel and consists of two strong laminae which are fused with the corresponding part of the hepatorenal ligament to be attached to the lateral border of the renal depression, the sublumber region and the right crura of the diaphragm. In the present investigation, the relation is similar to that of Abdalla ***etal***. (1971) but there is a third lamina which is attached to the muscular part of the diaphragm.

-The left triangular (lateral) ligament: This ligament is abscent and this result is in agreement with the observation of Abdalla ***etal***. (1971)in the dromedary camel and disagrees with Ahmed (2002) and Ahmed ***etal.*** (2014) who reported that the left triangular ligament is present in the liver of camel foetuses of 85.81 and 96.79 cm CVRL and in the adult camel.

4.1.1.6. Blood supply

In agreement with the finding of Elgazoli (2010) the present study showed that the two umbilical veins of the one-humped camel foetus entered the abdominal cavity and united in a venous sinus near the liver. The united umbilical vein passed through the liver and then united with the left main portal vein to form tubular duct known as the ductus venosus and the latter joins the posterior vena cava.

The division of the portal vein into right dorsal, right ventral and left branches within the porta hepatis as observed in this study was in agreement with that given by Farag (1990) and Ahmed ***etal***. (2014). in the dromedary camel.

In agreement with the findings of Eisa (2008) and Ahmed ***etal***. (2014), the present study showed that the hepatic artery arose as one of three pimary branches of the coeliac.However Smuts and Benzuidenhout (1987) reported that the hepatic artery of the camel arose by common trunk with the splenic artery.

In the present investigation, the liver of the foetus lacks a gall bladder during the three trimesters and this observation confirmed the result ofAbdel El-Hafez (2009) in the one-humped camel foetus at 185 mm CVRL and Smuts and Bezuidenhout (1987), Abdel-Moniem ***etal***. (2000), Ahmed (2002), Ahmed ***etal.*** (2014) in the adult camel. The equine species also lack a gall bladder (Rooney, Sack and Hobel., 1967 and Nickel ***etal.,*** 1973) but it is found in ruminant species (Habel, 1989).

4.1.2.Histology

The hepatic tissue at 12 days of gestation in a foetus of the mouse forms a loose mass of cells with little apparent grouping of the different cell types. Hepatocytes appear much more cohesive with the development of the liver cords at 13 days of gestation and thereafter (Jones, 1970). The liver of the one-humped camel consists of hepatocytes arranged in the form of anastomosing cords separated by irregular blood spaces between 12 and 19 mm CVRL (Abd El-Hafez, 2009). In the present investigation, the hepatic primordium consists of two types of cells:hepatocytes and haemopoietic cells in a foetus of 2 cm CVRL (71 days of age). The hepatocytes are arranged in thick laminae and solid cords and anastomosed together leaving large spaces between them. Haemopoietic cells consist of original haemopoietic cells, erythrocytic series and megakaryocytes.

The hepatic cords of the foetus of the mouse consist of one or three cells in thickness radiating from the central vein at 18 days of gestation and the hepatocytes are polyhedral in shape with central nucleus, distinct nuclear envelope and one or two prominent nucleoli (Khalid ***etal***., 2009).However, Sasaki and Sonoda (2000) stated that the hepatocytes of the foetus of the mouse are cuboidal in shape between 17 and 19 days of gestation. During the prenatal development of the rat, the hepatocytes change their shape from potato- like on days 12, 13 and 14 of gestation to cuboidal on day 20 of gestation with an intermediate spheric stage on day 18 of gestation (Vassy ***etal***., 1988). The liver of the one-humped camel consists of hepatocytes which are polyhedral in shape with large round nuclei between 12 and 19 mm CVRL (Abd El-Hafez, 2009). In the present investigation, the hepatic cords are two cells thick in a foetus of 3 cm CVRL (74 days of age) and the hepatocytes are cuboidal in shape with large round nuclei and prominent nucleoli and are transformed into polyhedral in shape in a foetus of 7 cm CVRL. In the liver of the one-humped camel foetus the hepatocytes are arranged in the form of anastomosing cords separated by irregular blood spaces between 12 and 19 cm CVRL. A well developed hepatic laminae arranged in radiating rows around the central vein and the hepatocytes are large in size and showed high mitotic activity, characteristic features of the liver of the foetus between 140 and 185 cm CVRL (Abd El-Hafez, 2009). In the present investigation, the hepatic cords are arranged regularly around the central vein in a foetus of 7 cm CVRL (85 days of age) and then this arrangement is disrupted due to the extensive proliferation of the haemopoietic foci among and between the hepatic cords. The arrangement of hepatic cords is changable between irregular and regular in foetuses of 40, 47, 48.5, 57, 57.5 and 67 cm CVRL (175, 194, 198, 221and 223 days of age). The permenant regular arrangement of the

hepatic cords around the central vein is established toward the end of the third trimester in foetuses of 100 and 101cm CVRL (339 and 342 days of age) and thereafter concurrent with the decrease and then disappearance of haemopoietic foci.

In the present study, the cytoplasm of the hepatocytes contains cytoplasmic vacuoles in a foetus of 7 cm CVRL (85 days of age) and some of them become large in a foetus of 9.5 cm CVRL (92 days of age) and onward while the larger cytoplasmic vacuoles which push the nucleus to one side of the cell appear during the second trimester in a foetus of 32 cm CVRL (153 days of age).

The hepatic cords grow into the mesenchymal tissue of the septum transversum and primitive sinusoid-like structures appear between the hepatic cords at 10 days of gestation in the foetus of the mouse and rat, and at 5 weeks of gestation in the human foetus. The basic structures of the sinusoids develop between 12 and 14 days of gestation in the mouse and rat and at 8 weeks of gestation in human foetus (Enzan ***etal***., 1997). In the present study, the spaces between the hepatic cords develop flat cells with elongated nuclei in a foetus of 2.5 cm CVRL (72 days of age) and these constitute the basic structure of the hepatic sinusoids. During the three trimesters of pregnancy, the hepatic sinusoids were filled with blood in some foetuses while in others they were empty.

In the present study, the portal vein and central vein are developed as small vein-like structures without clear endothelium in a foetus of 4.8 cm CVRL (79 days of age). The central veins are still without clear endothelium in foetuses of 5.3 and 5.6 cm CVRL (80 and 80. 5 days of age) and lined with discontinuous layer of endothelium in a foetus of 7 cm CVRL (85 days of age). A continuous layer of endothelium lining the

central vein appears during the second trimester in a foetus of 37 cm CVRL (167 days of age).

In the present investigation, formation of microfissures begins during the first trimester in a foetus of 13.5 cm CVRL (102 days of age) and the surface of the liver showed shallow invaginations, and then, became deep and separated the surface of the liver into small parts lined with mesothelium of the capsule in foetuses of 14.5 and 15.2 cm CVRL (105 and 107 days of age) and onward. Such observations have not been reported.

The primordium of Glisson's capsule in the one-humped camel foetus started to cover the liver between 50 and 75 mm CVRL and it consisted of one layer of flat cells with oval nuclei and condensed fine collagen fibres (Abd El-Hafez, 2009). In the present investigation, the primordium of Glisson's capsule started to cover the liver early during the first trimester in a foetus of 3 cm CVRL (74 days of age) and consisted only of one layer of flattened cells while fine collagenous fibres appeared in a foetus of 7 cm CVRL (85 days of age). A moderate amount of fibres was found in a foetus of 17 cm CVRL (112 days of age) and a thick connective tissue capsule is developed during the third trimester in a foetus of 104 cm CVRL (350 days of age) and onward.

In the present investigation, the interlobular connective tissue is abscent during the first trimester and up to near the end of second trimester. the hepatic lobules are separated from each other by long interlobular hepatic cords in foetuses of 60, 61, 63 and 67 cm CVRL (229, 232, 238 and 249 days of age) and continued during the third trimester in foetuses of 74, 75.5 and 78 cm CVRL (267, 271 and 278 days of age). The interlobular hepatic cords disappeared and were replaced by

trabeculae of connective tissue extending from the capsule in a foetus of 104 cm CVRL (350 days of age) and onward. Abdalla ***etal***. (1971) stated that, the liver of the dromedary is covered with a thick connective tissue capsule which sends off trabeculae dividing the liver parenchyma into hepatic lobules. Near the end of the third trimester, the hepatic lobules showed large amount of connective tissue fibres between them and displayed the typical appearance of distinct hepatic lobulation as in the adult camel in a foetus of 129 cm CVRL (418 days of age). This result is in agreement with that of Higazi (1945), Abdalla ***etal***. (1971), Lalla and Drommer (1997) and Adibomoradi ***etal***. (2008) in the dromedary, Endo ***etal***. (2000) in the two-humped camel and Bradley (1948) and Adibomoradi ***etal***. (2008)in pig and bony horse respectively.

The cytoplasm of the hepatocytes of the interlobular hepatic cords is more acidic than the cytoplasm of the hepatocytes of the intralobular hepatic cords during the second trimester in foetuses of 60, 61 and 63cm CVRL (229, 232 and 238 days of age). During the third trimester, the stainability of the cytoplasm of the hepatocytes of the two types of hepatic cords is similar. The difference in the stainability between the hepatocytes of the two types of cords may be due to either the type of contents, the amount of contents or both. The interlobular hepatic cords are one cell in thickness and separated by large number of sinusoids which are continuous with the sinusoids between intralobular hepatic cords and with the central veins. The author could not be able to find a similar observation in the literature in any species.

The haemopoietic activity of the liver begins at the 10^{th} day of gestation in the foetus of the mouse (Tavassoli, 1991). During early organogenesis, the foetal liver is populated by haemopoietic stem cells which are the sourse of a number of blood cells including nucleated

erythrocytes (Lee ***etal***., 2012).The liver of the mouse foetus contains hepatocytes, endothelial cells, erythropoietic cells, megakaryocytes, granulocytes and stem cells which showed non of the characteristic features of other cell types (Trowell, 1965). The mammalian foetal liver contains epitheliocytes, macrophages, various stromal elements of stellate cells, fibroblasts, myofibroblasts, vascular smooth muscle fibres, endothelial cells and mesenchmal stromal cells (Olga, 2012). The stromal cells play an important role in bovine foetal erythropoiesis (Li and Congate, 1995). In the present study, the liver of the foetus contained hepatocytes, original haemopoietic cells, precursors of erythrocytes and megakaryocytes in a foetus of 2 cm CVRL (71 days of age). Mature erythrocytes and precursors of granulocytes were observed in a foetus of 9.5 cm CVRL (92 days of age), while fibroblasts and mesenchymal cells in foetuses of 14.5 and 15.2 cm CVRL (105 and 107 days of age) and mature granulocytes in a foetus of 17 cm CVRL (112 days of age) and onward.

At 12 days of gestation in a foetus of the mouse, the haemopoietic cells appear as groups within and between the hepatocytes (Jones, 1970).The haemopoietic cells in the foetus of the mouse were dispersed among the primitive hepatic cords singly, and in small groups in the sinusoidal wall and among the hepatoblasts at 11 days of age. Thereafter, the haemopoietic foci were formed after rapid enlargement of the haemopoietic compartment by fusion of the spaces. At 13 days, the liver is almost entirely filled with ellipsoidal haemopoietic foci surrounded by hepatoblasts. The arrangement of hepatocytes becomes prominent in section profile at 15 days and the haemopoietic foci are relatively decreased, while between 17 and 19 days, small solitary haemopoietic foci are diffusely scattered through the hepatic cell cords (Sasaki and

Sonoda, 2000). The haemopoietic cells in the liver of the one- humped camel foetus are dispersed inside the liver parenchyma between 12 and 19 mm CVRL and these cells are round in shape with deeply stained centrally located and relatively large round nuclei (Abd El-Hafez, 2009). In the present investigation, the haemopoietic cells are scattered singly and in small groups among the hepatic cords and laminae in a foetus of 2 cm CVRL (71 days of age). Round and irregularly shaped haemopoietic foci were formed in a foetus of 3 cm CVRL (74 days of age) by accumulation of haemopoietic cells in different size and surrounded by hepatocytes.The haemopoietic foci increased in size in foetuses of 3.5 and 4 cm CVRL (75 and 76.5 days of age).

Between 11 and 12 days of gestation in a foetus of the mouse, the erythroblasts proliferate within the haemopoietic foci and some of the erythroids are anucleated (Sasaki and Sonoda, 2000). In the present investigation, the nucleated erythrocytes are present in a foetus of 4.8 cm CVRL (79 days of age), while mature erythrocytes are present in a foetus of 9.5 cm CVRL (92 days of age) and onward.

In a foetus of the mouse, primitive macrophages arise in the yolk sac and then differentiate into foetal macrophages and these enter the blood stream and migrate into the developing liver (Godlewski ***et al***. 1997).There are two types of macrophages in the liver of the foetus of the mouse: sinusoidal macrophages and central macrophages of the erythroblastic island (Sasaki and Iwatsuki, 1997). Sinusoidal macrophages are present within the lumina of the primitive sinusoids between 11 and 12 days of gestation. Central macrophages of the erythroplastic islands are found at the beginning in the primitive hepatic cell cords after 12 days of gestation and could be observed within the haemopoetic foci which are surrounded by a ring of erythroid cells in

various stages of development (erythroblastic island) (Sasaki and Iwatsuki, 1997; Sasaki and Sonoda, 2000). At 11 days of gestation in the mouse embryo, the primitive sinusoidal macrophages are considered the possible precursors of the central cells of the hepatic erythroblastic islands (Iwatsuki ***etal***., 1997). However,Jones (1970) stated that macrophages were not observed in the mouse foetal liver. In the present study, macrophages are observed inside the haemopoietic foci in a foetus of 14.5 cm CVRL (105 days of age), while central macrophages of erythroblastic islands are present towards the end of the first trimester in a foetus of 20.5 cm CVRL (122 days of age) and onward.

Megakaryocytic lineage cells among hepatocytes were observed in human foetal liver by Emura ***etal***. (1984) and in buffalo foetal liver at 3.2 cm CVRL (Osman, Dougbag and Kassem, 1984). In the foetus of the mouse, megakaryocytes are usually observed at 12, 13 and 14 days of gestation in a close position to the hepatocytes, rarely with erythroid cells and usually in pairs or in groups of four cells early in development, although they are observed singly at a later stage (Jones, 1970). Mohamed, Baready, Ammar, Balah and Ewais. (1986) andKhalil, Mansour and Ibrahim. (1987) observed megakaryocytes in the foetus of the camel at 40 cm and at 3.8 cm CVRL respectively. Paone, Cutty and Krause. (1975) stated that the megakaryocytes had one to four nuclei and occasionally multi-lobed or polymorphous in the liver of the opossum (*Didelphis virogianana*) foetus. Megakaryocytes with lobulated nuclei were observed among haemopoietic cells in the liver between 25 and 30 mm CVRL one- humped camel foetus (Abd El-Hafez, 2009). In the present investigation, megakaryocytes are found early in a foetus of 2 cm CVRL (71 days of age) and increased in number during the first and second trimester but rarely seen during the third trimester in a foetus of

84cm CVRL (295 days of age) and onward. Also megakaryocytes are usually dispersed singly and the number of the nuclei is similar to that reported by (Paone ***etal***., 1975)

The haemopoietic activity of the liver begins at the 10th day of gestation in the foetus of the mouse and continues during prenatal life until the first postnatal week (Tavassoli, 1991).The liver haemopoiesis ceased after birth in the mouse (Cardier and Barbera-Guillem, 1997), and Dimon ***etal.,*** (1982) observed that, the haemopoietic cells decreased in number at birth in the foetus of the rat and were confined to perisinusoidal space. The blood forming activity of the liver ceased at the end of gestation in the foetus of the rat and only the space of Disse separates the endothelium of the sinusoids from the parenchymal cells (Bankston and Pino, 1980). In the present study, the haemopoietic activity of the liver begins early during the first trimester in a foetus of 2 cm CVRL (71 days of age) and continues during the second trimester and ceased towards the end of the third trimester in a foetus of 112 cm CVRL (372 days of age) and onward. The spaces of Disse appeared during the second trimester in a foetus of 37.5 cm CVRL (168 days of age). Cutts, Leeson and Krause. (1973) observed that the loss of granulocytes from the liver occurs earlier than loss of erythrocytes in the marsupial. In the present investigation, the result agreed with the above observation.

The intrahepatic bile duct system in human embryo was observed at 22 mm CVRL (Bloom, 1926) and at 7 weeks of gestation (Blankenberg ***etal.***1991). In the present investigation, the development of the intrahepatic bile ducts begins in a foetus of 7 cm CVRL (85 days of age) and this observation disagreed with that of Abd El-Hafez (2009) who stated that, the bile duct system is not developed in the one-humped

camel foetus between 140 and 185mm CVRL. The ductal plate is a primitive biliary epithelium which develops in the mesenchyme adjacent to the branches of the portal vein during the liver development and it is extensively reorganised to form the intrahepatic bile ducts in the human foetus (Koga, 1971; Vijayana and Tan, 1999). Moreover, Terada., Kitamura and Nakanuma (1997) stated that, the ductal plate first appears from primitive hepatocytes around 8 weeks of gestation in human foetus and gradually undergoes remodeling from 12 weeks of gestation. Then, the duct cells are transformed into immature bile duct around 20 weeks of gestation. Bile ducts cells are differentiated from immature hepatocytes in the mouse (Shiojiri, 1984). The formation of intrahepatic bile ducts in human foetus is completed during the third month of gestation (Koga, 1971). In the present study, the ductual plates completed their reorganisation and the ducts of the intrahepatic bile tubular system appeared during the first trimester in foetuses of 14. 5 and 15. 2 cm CVRL (105 and 107 days of age) at the same time of increasing amount of loose mesenchymal tissue in the periportal area.

The mesenchyme of the portal tract in the ductual plate stage in human foetus is devoid of a branch of the hepatic artery and contains numerous and diffusely scattered portal myofibroblasts. However, when the portal tract becomes large and contains branch of the hepatic artery, the myofibroblasts are restricted to the periductal mesenchyme until it disappears after the full corporation of the bile duct (Libbrecht ***etal***., 2002). In the present investigation, the result is generally in agreement with that of Libbrecht ***etal***.(2002) and the branch of the hepatic artery appears within the portal area during first trimester in a foetus of 15.2 cm CVRL (107 days of age) and onward.

4.1.3. Ultrastructure

Daimon ***et al***. (1982) observed that the hepatocytes were irregular in shape and possess several large lipid droplets in their cytoplasm at 15 days of age in the foetus of the rat. In the present study, the hepatocytes in foetuses of 17 and 17.5 cm CVRL (112 and 113 days of age) were similar to the above observation.

Jones (1970) stated that the nucleus of hepatocytes remains large and ovoid between 12, 13 and 14 days of gestation in the mouse embryo. Large hepatocytes with large nuclei were described in the one- humped camel foetus at 125 mm CVRL(Abd El-Hafez, 2009). In the present study, the nucleus of the hepatocytes was large and rounded in foetuses of 17, 17.5 and 25.5 cm CVRL (112, 113 and 135 days of age) and onward.

Large and round mitochondria were found in the foetus of the mouse between 12, 13 and 14 days of gestation (Jones, 1970). On the other hand, Vassy ***et al.*** (1988) observed small and round mitochondria between 12, 13 and 14 days of gestation in the foetus of the rat and became oblong from days 18 of gestation and onward. The mitochondria of the hepatocytes increase in size and number from 4 days old until before hatching in the chick embryo with conspicuous changes from round toward more rod shape and elongated form (Sandström and Westman, 1971). Many mitochondria were described in the cytoplasm of the hepatocytes in the one-humped camel foetus at 125 mm CVRL (Abd El-Hafez, 2009). In the present investigation, mitochondria were large and round in shape in foetuses of 17 and 17.5cm CVRL (112 and 113 days of age) and then became numerous and some of them were transformed into rod shape in a foetus of 43 cm CVRL (183 days of age).

A well developed Golgi apparatus in the hepatocytes appeared at 12 and 13 days of gestation in the foetus of the rat (Vassy ***et al.*** 1988). The

activation of Golgi complex of the hepatocytestakes place on the fourth and fifth days in an incubated chick embryo as judged by its expansion and formation of variety of vesicles (Stephens and Bils, 1967). However, Sandström and Westman (1971) stated that the Golgi apparatus does not assume its adult appearance until about the 8^{th} days of incubation in chick embryo. In the present investigation, Golgi apparatus is not well developed during prenatal life.

Very sparse endoplasmic reticulum appears in the cytoplasm of hepatocytes of the chick embryo on the third day of incubation and first appears mainly in a vesicular form which eventually changes into a cisternal form and become closely associated with the plasma membrane and mitochondria (Stephens and Bils, 1967). A well developed rough endoplasmic reticulum is reported in the cytoplasm of hepatocytes at 12 and 13 days of gestation (Vassy ***et al.*** 1988) and at 15 days of gestation (Daimon ***et al.*** 1982) in the foetus of the rat. Extensive rough endoplasmic reticulum was observed in the cytoplasm of hepatocytes of the one- humped camel foetus at 125 mm CVRL (Abd El-Hafez, 2009). In the present study, rough endoplasmic reticulum was very sparse and appeared mainly in a vesicular form in foetuses of 17 and 17.5 cm CVRL (112 and 113 days of age) while well developed rough endoplasmic reticulum with cisternal shape appeared in a foetus of 43 cm CVRL (183 days of age) and onward.

Glycogen was first observed in the cytoplasm of hepatocytes in 16 days old incubated chick embryo and then continuously increased in amount throughout development (Sandström and Westman, 1971). The cytoplasm of hepatocytes possesses large spaces which were rapidly filled with glycogen from 16 days of gestation and onward in the mouse embryo (Jones, 1970). Glycogen was not observed within the cytoplasm

of hepatocytes in the rat at 15 days of gestation until on the 18th day the accumulation of glycogen is observed and then decreased rapidly at birth (Daimon ***et al.*** 1982). Cytoplasmic glycogen was found in the cytoplasm of hepatocytes at 185 mm CVRL in the one- humped camel foetus (Abd El-Hafez, 2009).In the present investigation, glycogen granules were not observed in the liver of all foetuses studied.Khatim ***et al***. (1985) stated that, the hepatocytes of camel were characterized by the presence of numerous cytopplasmic inclusions (vesicles, vacuoles) that might occupy most of the cell, and appeared larger than the nuclei, although their significance was unknown. In the present investigation, multivesicular bodies appeared in the cytoplasm of hepatocytes in a foetus of 57 cm CVRL (221 days of age) and gradually increased with advancing age.

The central veins of the foetus of the rat liver are lined with highly fenestrated endothelium (Barbera-Guillum ***et al.*** 1986). In the present study, the central veins are lined with discontinuous layer of endothelial cells in foetuses of 17, 17.5 and 25.5 cm CVRL (112, 113 and 135 days of age) while continuous layer of fenestrated endothelium charactrized the central veins in a foetus of 43 cm CVRL (183 days of age) and onward.

The endothelium lining the central veins rested on a thin basal lamina in foetuses of 17 and 17.5cm CVRL (112 and 113 days of age); fibroblasts appeared subjacent to the basal lamina in a foetus of 43 cm CVRL (183 days of age) and produced large amount of collagen fibres in a foetus of 68cm CVRL (251 days of age) and onward.

Enzan ***et al***. (1997) observed that, the hepatic sinusoids are usually lined by continuous endothelium but without a basment membrane at 10 days of gestation in the mouse and rat embryos, while incompletely

fenestrated endothelium lining the sinusoids appear at the middle period of gestation. The blood sinusoids of the liver in 185 mm CVRL one-humped camel foetus are lined by incomplete layer of flat endothelial cells that bulge into their lumina (Abd EI-Hafez, 2009). In the present investigation, the hepatic sinusoids were lined with incomplete layer of endothelial cells and filled with immature and mature erythrocytes; the extruded nuclei of mature erythrocytes and blood platelets were found within the cytoplasm of endothelial cells lining the sinusoids.

In agreement with the result of Deutsch and Tomer (2006) and Machlus and Italiano (2013) the present investigation revealed that the cytoplasm of mature megakaryocytes formed long cytoplasmic processes named proplatelet projections

Bankston and Pino (1980) stated that Kupffer cells are easily identified as early as13 days of gestation in the liver of the foetus of the rat. Kupffer cells are a population of tissue macrophages found in the lumen of the hepatic sinusoids and their role is endocytic against blood-borne material entering the liver (Makoto ***et al***., 2004). Lee ***et al.*** (1999) observed an emperipolesis of erythroblasts within Kupffer cells in the liver of human foetus. In the present study, Kupffer cells were clearly identified between the lining endothelium of the hepatic sinusoids in a foetus of 78cm CVRL (278 days of age) and onward and some platelets were found within the cytoplasm of Kupffer cells. In some sinusoids, Kupffer cells were large and occupied most of the lumen of the sinusoids or even occluded the lumen.

Hepatic stellate cells are located in the perisinusoidal space of Disse and contained lipid droplets and aquire morphological and phenotypic feature characteristic of myofibroblasts (Ramadori and Saile, 2002).

During the foetal period, the hepatic stellate cells are associated with the haemopoietc cells (Kiassov, Van Eyken, Van Pelt, Erik, Johan, Valeer, Desmet and Yap, 1995). In the present investigation, hepatic stellate cells were observed in the perisinusoidal space of Disse and sometimes associated with haemopoietic elements in a foetus of 78cm CVRL (278 days of age) and onward. Villeneuve, Pelluard, Nehme, Combe, Carles, Ripoche, Balabaud, Bioulac-Sage, Lepreux. (2009) stated that the number of hepatic stellate cells increases during the course of development in human. In the present investigation, the result is in agreement with that of Villeneuve ***et al.*** (2009). In human foetal liver, fibroblasts are located in the region of portal traids (Ramadori and Saile, 2002; Villeneuve ***et al***., 2009), around central veins and in Glisson′s capsule (Guyot, Lepreux, Combe, Combe, Doudnikoff, Bioulac-Sage, Balabaud, Desmoulière. 2006). In the present study, the finding is similar to the observation of Ramadori and Saile (2002), Villeneuve ***et al***.(2009) and Guyot ***et al***. (2006).

In human and murine foetal liver, mesenchymal stroml cells are a probable source of stromal cells similar in their characteristics to smooth muscle cells (Dennis and Charbord, 2002). It is also not excluded that they can be differentiated into myofibroblasts (Russo, Alison, Kreisel, Bigger, Amofah, Florou, Amin, Bou-Gharios, Jeffery, Iredale and Forbes., 2006) and endothelial cells (Krupnick, Balsara, Kreisel, Riha, Gelman, Estives, Amin, Rosengard and Flake., 2004). In the present investigation, mesenchymal stromal cells were observed subjacent to the wall of the central veins in a foetus of 90cm CVRL (311 days of age).

4.2. Histochemistry

4.2.1. PAS positive material

4.2.1. a- PAS positive diastase resistant material

In the present investigation, during the first trimester of development, the hepatic cords revealed negative reaction. This finding is in agreement with that of Khalil ***etal***. (1987) and Abd El-Hafez (2009) who stated that, the hepatocytes of the one-humped camel showed a negative reaction for PAS in a foetus of 4.7 cm and in foetuses between 7 and 185 mm CVRL respectively. However, Osman ***etal.*** (1984) showed strong PAS positive material in the cytoplasm of hepatocytes in 3.2 cm CVRL buffalo foetuses. Abd El-Hafez (2009) observed that, the megakaryocytes showed positive reaction for PAS in foetuses between 7 and 185 mm CVRL. In the present investigation, megakaryocytes give positive reaction during the first, second and part of the third trimester. Haemopoietic foci and the erythrocytes showed negative reaction during the three trimesters of development. The connective tissue of the capsule and parenchyma reacted positively.

4.2.1. b- PAS positive diastase digested material

In the present investigation and during the three trimesters of development, the hepatocytes of the foetus revealed negative reaction.This result is quite different from that reported in the adult camel by Bahgat ***etal***. (1964), Bahgat ***etal.*** (1965), Shahien ***etal.***(1977), Ahmed (2002) and Ahmed ***etal.***(2015). Nickel ***etal***. (1973) suggested that, the glycogen could be demonstrated in the cytoplasm depending on the functional state of the liver. The result in the present study might be explained by the suggestion of Nickel ***etal***. (1973).

4.2. 2. Enzymes

4.2. 2.1. Alkaline phosphatase

In the present investigation, the hepatocytes revealed negative reaction for alkaline phosphatase enzyme during the three trimesters of development. This result is different from the result of Abdel-Aziz (1997) who demonstrated the activity of this enzyme in the nuclei of both hepatocytes and endothelial cells while their cytoplasm revealed negative reaction in the normal rat liver.

4.2. 2. 2. Acid phosphatase

In the present investigation, the hepatocytes revealed negative reaction for acid phosphatase enzyme during the three trimesters of development. This result is different from the result of Abdel-Aziz (1997) who demonstrated the activity of this enzyme in the nuclei of both hepatocytes and endothelial cells while their cytoplasm revealed negative reaction in the normal rat liver.

Summary

1. Morphology, histometry, histochemistry and haemopoietic activity were studied in the liver of 93 one-humped camel foetuses during the prenatal life.
2. The foetuses were collected from Tamboul and Nyala slaughter points and

   the age of the foetuses was stimated according to the method of curved crown- rump length (CVRL) by using the following equation: Y = 0.366X- 23.99.
3. The foetuses were classified into: first trimester ranging between 2 and 23.5 cm CVRL (71 and 130 days of age), second trimester ranging between 25.5 and 68 cm CVRL (135 and 251 days of age) and third

trimester ranging between 70 and 132 cm CVRL (257 and 426 days of age).

4. During the first trimester, the hepatic primordium was differentiated and appeared in the peritoneal cavity beneath the mesenchyme in a foetus of 2 cm CVRL (71 days of age).
5. The liver occupied most of the abdominal cavity together with parts of developing gastrointestinal tract in foetuses of 4.8 and 5.3cm CVRL (79 and 80 days of age.
6. The liver wasbright brown in colour during the first trimester and varied between bright brown and dark brown during the second and third trimesters.
7. The shape of the liver was quadrilateral during the first trimester and changed into irregular during the second trimester; while during the third trimester the liver tended to take triangular shape.
8. The liver contained two main lobes refered as the right and left lobes in foetuses of 4.8, 5.3, 7 and 9.5 cm CVRL (79, 80, 85 and 92 days of age).

9. Three outgrowths projected from the visceral surface of the right lobe in foetuses of 22.5 cm CVRL (127 days of age).The three outgrowths gave rise to the quadrate lobe, papillary process and caudate process which together with the papillary process formed the caudate lobe.
10. During the first trimester the length of the liver varied between 6 and 9 cm with an average of 8 cm and the width of the narrow part of the liver varied between 1.7 and 3.1cm with an average of 2.6 cm, while the width of the broad part of the liver varied between 2.3 and 5cm with an average of 4cm.
11. During the second trimester, the length of the liver varied between 10 and 22 cm with an average of 14.6 cm and the width of the narrow part of the liver varied between 4 and 8cm with an average of 5 cm, while the

width of the broad part of the liver varied between 5.8 and 14cm with an average of 9cm.

12. During the third trimester, the length of the liver varied between 17.5 and 33 cm with an average of 22.3 cm and the width of the narrow part of the liver varied between 6 to 10cm with an average of 7.2 cm, while the width of the broad part of the liver varied between 10 and 20cm with an average of 13cm.
13. The liver was attached by hepatorenal and lesser omentum ligaments were attached on its visceral surface, while coronary, round, falciform and right triangular ligaments attached the liver on its parietal surface and the left triangular ligament was abscent from all foetuses studied.
14. During the first trimester, the hepatic primordium consisted of two types of cells, hepatocytes and haemopoietic cells in a foetus of 2 cm CVRL (71 days of age).
15. The hepatocytes were arranged in the form of a thick laminae and solid cords and the spaces between them developed primitive endothelium in a foetus of 2.5cm CVRL (72 days of age).
16. The haemopoietic foci were formed by accumulation of haemopoietic cells in a foetus of 3 cm CVRL (74 days of age) during the first and second trimester but decreased dramatically in size and number during the third trimester in foetuses of 84, 88 and 92 cm CVRL (295, 306 and 317 days of age) until they disappeared completely in a foetus of 112cm CVRl (372 days of age) and thereafter.
17. The hepatocytes of the hepatic cords and plates were cuboidal in shape in foetuses of 2 and 3 cm CVRL (71 and 74 days of age) and transformed into polyhedral shape with large nuclei and prominent nucleoli and cytoplasmic vacuoles in a foetus of 7 cm CVRL (85 days of age).

18. The portal vein and central vein were developed as small vein-like structures without clear endothelium in a foetus of 4.8 cm CVRL (79 days of age).
19. The primordium of Glissons's capsule started to cover the liver early in a foetus of 3 cm CVRL (74 days of age) and consisted of one layer of flattened cells, while a thick layer of connective tissue capsule appeared during the third trimester in a foetus of 104 cm CVRL (350 days of age) and onward.
20. The hepatic lobules were separated from each other by long interlobular hepatic cords during the second trimesterin a foetus of 60cm CVRL (229 days of age) and continuous during part of the third trimester and then disappeared and replaced by interlobular connective tissue in a foetus of 104cm CVRL (350 days of age) and onward.
21. The cytoplasm of the hepatocytes of the interlobular hepatic cords was more acidic than the cytoplasm of the hepatocytes of the intralobular hepatic cords during the second trimester, while during the third trimester the stainability of the cytoplasm of the hepatocytes of the two types of the hepatic cords was similar.
22. The megakaryocytes increased in number during the first and second trimester and decreased at bigining of third trimester until rarely seen in foetuses of 84, 88 and 92 cm CVRL (295, 306 and 317 days of age) and onward
23. The nucleated erythrocytes were present in a foetus of 4.8 cm CVRL (79 days of age), while mature erythrocytes were present in a foetus of 9.5 cm CVRL (92 days of age) and onward.
24. Precurssors of granulocytes were observed in a foetus of 9.5 cm CVRL, while mature granulocytes appeared in a foetus of 17 cm CVRL (112 days of age) and onward.

25. The mean diameter of the hepatocytes was 6.4 µm during the first trimester, 7.3 µm during the second trimester and 6.2 µm during the third trimester.
26. The mean diameter of the megakaryocytes was 17.4 µm during the first trimester, 18.3 µm during the second trimester and 24 µm during the third trimester.
27. The development of intrahepatic bile ducts started in a foetus of 7 cm CVRL (85 days of age) and was completed in foetuses of 14.5 cm CVRL (105 days of age) and the branch of hepatic artery was observed within the portal area in a foetus of 15.2 cm CVRL.
28. The cytoplasm of hepatocytes possessed round mitochondria with sparse cristae in foetuses of 17 and 17.5 cm CVRL, then became numerous and some of them were transformed into rod shape in a foetus of 43 cm CVRL (183 days of age).
29. Rouph endoplasmic reticulum appeared as small vesicles in foetuses of 17 and 17.5 cm CVRL while well developed rough endoplasmic reticulum with cisternal shape appeared in a foetus of 43 cm CVRL.
30. Large lipid droplets appeared in the cytoplasm of hepatocytes in a foetus of 7 cm CVRL (85 days of age) and onward and multivesicular bodies were found in a foetus of 57 cm CVRL (221 days of age) and gradually increased in amount and sometimes appeared bounded by rough endoplasmic reticulum in a foetus of 90 cm CVRL (311 days of age).
31. The central vein was lined with discontinuous layer of endothelial cells in a foetus of 17 and 17.5 cm CVRL (112 and 113 days of age) while a continuous layer of fenestrated endothelium appeared in a foetus of 43 cm CVRL (183 days of age) and onward and rested on a basal lamina.
32. The hepatic sinusoids were lined with incomplete layer of endothelium in a foetus of 17 and 17.5 cm CVRL,and complete layer of both

fenestrated or unfenestrated endothelium were found in a foetus of 78 cm CVRL (278 days of age) and onward.

33. Intercellular bile canaliculi were developed in a foetus of 33 cm CVRL (156 days of age) and onward.
34. Hepatic Stellate cells appeared in perisinusoidal space of Disse in a foetus of 78 cm CVRL and onward.
35. The hepatic cords revealed negative reaction for PAS resistant material during the first trimester, while reacted positively during the second and third trimesters and groups of hepatocytes near or directly under the capsule gave negative reaction during the second trimester, while reacted positively during the third trimester.
36. Megakaryocytes gave positive reaction but, the original haemopoietic cells and the infiltrated erythrocytes reacted negatively during the three trimesters of development.
37. The connective tissue of the parenchyma and the connective tissue of the capsule gave positive reaction.
38. The hepatocytes of the foetus revealed negative reaction for PAS positive digested material (glycogen) throughout the three trimesters.
39. The liver of the foetus showed negative reaction for alkaline and acid phosphatase enzymes.

الملخص

1- تمت دراسة الخصائص الشكلية، القياسات النسيجية، الكيمياء النسيجية ونشاط تكون الدم للكبد فى 93 من الجمال وحيدة السنام خلال الفترة الجنينية.

2- جمعت الأجنة من مصاطب الذ بح بمدينتى تمبول ونيالاوقدرت أعمار الأجنة حسب طريقة قياسطولالمنحنىمن التاج الي قمة الذيل بالتعويض فى المعادلة التالية Y= 0.366X- 23.99.

3- صنفت الاجنة إلى: الثلث الاول من الحمل وتتراوح بين 2 و 23.CVRL5 (71 و 130 يوم)، الثلث الثاني من الحمل وتتراوح بين 25.5 و 68 سم CVRL (135 و 251 يوم) والثلث الثالث من الحمل وتتراوح بين 70 و 132 سم CVRL (257 و426 يوم).

4- خلال الثلث الأول للحمل تمايزالمكون البدائى الكبد وظهر في التجويف البريتونى خلف الميزنكايم في الجنين عمر 2 سم CVRL (71 يوم).

5- إحتلت الكبد معظم مساحة التجويف البطني مع الأجزاء النامية من المسلك المعدي المعوي في الأجنة عمر 4.8 و 5.3 سم CVRL (79 و80 يوم).

6- لون الكبد بني فاتح خلال الثلث الأول من الحمل بينما إختلف بين البنى الفاتح و البني الغامق خلال الثلثين الثاني والثالث من الحمل.

7- شكل الكبد رباعية الجوانب خلال الثلث الأول من الحمل ثم تغيرت الى شكل غير منتظم خلال اثلث الثاني بينما خلال الثلث الثالث مالت الكبد إلي أخد الشكل المثلثى.

8- إحتوت الكبد علي فصين رئيسيين يعرفان بالفصين الأيمن والأيسر فى الأجنة عمر 4.8، 5.3، 7 و9.5 سم CVRL (79، 80، 85 و92 يوم).

9- برزت ثلاثة نموءات من السطح الحشوي للفص الأيمن في الجنين عمر 22.5سم CVRL (127 يوم) وكونت المكونات البدائية للفص المربع، الشاخصة الحلمية والشاخصة المذيلة حيث تكون الأخيرتان الفص المذيل.

10-خلال الثلث الأول من الحمل تراوح طول الكبد من 6 إلى9 سم بمتوسط 8 سم وتراوح عرض الجزء الضيق من لكبد من 1.7 إلي 3.1 سم بمتوسط 2.6 سم بينما تراوح عرض الجزء العريض من 2.3 إلى 5 سم بمتوسط 4 سم.

11- خلال الثلث الثاني من الحمل تراوح طول الكبد من 10 إلي 22 سم بمتوسط 14.6 سم وتراوح عرض الجزء الضيق من الكبد من 4 إلى 8 سم بمتوسط 5 سم بينما تراوح عرض الجزء العريض من 5.8 إلى 14 سم بمتوسط 9 سم.

12- خلال الثلث الثالث من الحمل تراوح طول الكبد من 17.5 إلى 33 سم بمتوسط 22.3 سم وتراوح عرض الجزء الضيق من الكبد من 6 إلي 10 سم بمتوسط 7.2 سم بينما تراوح عرض الجزء العريض من 10 إلى 20 سم بمتوسط 13 سم.

13- إرتبطت الكبد بالرباطين الكبدى الكلوي والثرب الصغيرعند السطح الحشوى بينما إرتبطت بالأربطة التاجي، المدور، المنجلي والمثلثى الأيمن عند السطح الجدارى بينما الرباط المثلثي الأيسر غير موجود فى كل الأجنة التى درست.

14- خلال الثلث الأول من الحمل إحتوى المكون البدائى للكبد علي نوعين من الخلايا، الخلايا الكبدية و الخلايا المكونة للدم في الجنين عمر 2 سم CVRL (71 يوم).

15- إرتصت الخلايا الكبدية في شكل صفائح سميكة وحبال مصمتة وبطنت المساحات بينها ببطانية بدائية حيث تعتبر أساس الجيبانيات الكبدية في الجنين عمر 2.5 سم CVRL (72 يوم).

16- تكونت البؤر المكونة للدم بتجمع الخلايا المكونة للدم في الجنين عمر 3 سم CVRL (74 يوم) وإستمرت خلال الثلثين الأول والثاني من الحمل ثم تناقصت تدريجيا" في الحجم والعدد خلال الثلث الثالث من الحمل فى الجنين عمر 84، 88 و92 سم CVRL (295، 306 و 317 يوم) حتي إختفت نهائيا" في الجنين عمر 112 سم CVRL (372 يوم).

17- الخلايا الكبدية المكونة للصفائح والحبال الكبدية مكعبة الشكل فى الجنين عمر 2 إلي 3 سم CVRL (71 إلي 74 يوم) ثم تحولت إلي متعددة الرؤوس مع نواة كبيره ذات نوية واضحة وفجوات سيتوبلازمية بأحجام مختلفة في الجنين عمر 7 سم CVRL (85 يوم).

18- نشأ الوريد البابي والأوردة المركزية كتراكيب صغيرة تشبه الأورده ولكن بدون بطانة واضحة فى الجنين عند 4.8 سم CVRL (79 يوم).

19- بدأ المكون البدائى لمحفظة Glisson مبكرا"يغطي الكبد فى الجنين عمر 3 سم CVRL (74 يوم) ويحتوي على طبقة واحده من الخلايا المفلطحة بينما ظهرت الطبقة السميكة من النسيج الضام خلال الثلث الثالث من الحمل في الجنين عمر104 سم CVR (350 يوم) فأكثر.

20- إنفصلت الفصيصات الكبدية عن بعضها البعض بواسطة حبال كبدية طويلة فى الجنين عمر 60 سم CVRL (229 يوم) خلال الثلث الثانى وجزء من الثلث الثالث من الحمل ثم إختفت وأستبدلت بنسيج ضام إمتد من المحفظة في الجنين عمر 104 سم CVRL (350 يوم) فأكثر.

21- سيتوبلازم الخلايا الكبدية المكونة للحبال الكبدية بين الفصيصات أكثر حمضية من سيتوبلازم الخلايا الكبدية المكونة للحبال الكبدية داخل الفصيصات خلال الثلث الثاني من الحمل بينما خلال الثلث الثالث كانت قابلية الإصطباغ لسيتوبلازم الخلايا الكبدية المكونة لنوعي الحبال الكبدية متشابهة.

22- إزدادت الخلايا ضخمة النواة فى العدد خلال الثلثين الأول والثاني من الحمل وتناقصت مع بداية الثلث الثالث حتى أصبحت نادره الوجود فى الجنين عمر 84، 88 و92 سم CVRL (295، 306 و317 يوم) فأكثر.

23- ظهرت خلايا الدم الحمراء المحتوية علي النواة في الجنين عمر 4.8 سم CVRL (79 يوم) بينما ظهرت الخلايا الحمراء الناضجة في عمر 9.5 سم CVRL (92 يوم) فأكثر.

24- لوحظت قبليات خلايا الدم البيضاء المحببة في الجنين عمر 9.5 سم CVRL بينما ظهرت الخلايا الناضجة فى الجنين عمر 17 سم CVRL (112 يوم) فأكثر.

25- متوسطقطر الخلية الكبدية 6.4 ميكرون خلال اثلث الأول من الحمل، 7.3 ميكرون خلال الثلث الثاني و6.2 ميكرون خلال الثلث الثالث من الحمل.

26- متوسط قطر الخلية ضخمة النواة 17.4 ميكرون خلال الثلث الأول من الحمل، 18.3 ميكرون خلال الثلث الثاني و24 ميكرون خلال الثلث الثالث من الحمل.

27- بدأ تطور القنوات الصفراوية داخل الكبد فى الجنين عمر 7 سم CVRL (85 يوم) وإكتمل فى الجنين عمر 14.5 سم CVRL (105 يوم) فأكثر ولوحظ فرع الشريان الكبدي في المنطقة البابية في الجنينعمر 15.2 سم CVRL (107 يوم).

28- أظهرت سيتوبلازم الخلايا الكبدية ميتوكوندريا دائرية بأعراف مبعثرة في الجنين عمر 17 و17.5 سم CVRL (112 و 113 يوم) ثم إزدادت بعد ذلك و جزء منها تحول إلي الشكل العصوى فى الجنين عمر 43 سم CVRL (183 يوم).

28- ظهرت الشبكة الإندوبلازمية الخشنة كحويصلات صغيرة فى الجنين عمر 17 و 17.5 CVRL (112 و113 يوم) بينما ظهرت شبكة إندوبلازمية متطورة وبأشكال صهريجية فى الجنين عمر 43 سم CVRL (183 يوم).

29- ظهرت قطيرات دهنية كبيرة فى سيتوبلازم الخلايا الكبدية فى الجنين عمر 17 و 17.5 سم (112 و113 يوم) فأكثر ووجدت أجسام حويصلية متعددة في سيتوبلازم الخلايا الكبدية في الجنين عمر 57 سم CVRL (221 يوم) و إزدادت كميتها تدريجيا" وظهرت أحيانا" محاطة بالشبكة الإندوبلازمية الخشنة في الجنين عمر 90 سم CVRL (311 يوم).

30- بطن الوريد المركزى بطبقة بطانية غير متواصلة في الجنين عمر 17 و17.5 سم CVRL (112 و113 يوم) بينما ظهرت طبقة متواصلة من الخلايا البطانية المثقبة فى الجنين عمر 43 سم CVRL (183 يوم) فأكثر.

31- بطنت الجيبانيات الكبدية بطبقة بطانية غير مكتملة في الجنين عمر 17 و 17.5 سم CVRL بينما ظهرت طبقة مكتملة من خلايا بطانية مثقبة أوغير مثقبة فى الجنين عمر 78 سم CVRL (278 يوم) فأكثر.

32-ظهرت القتيات الصفراوية بين الخلايا الكبدية فى الجنين عمر33 سم CVRL (156 يوم).

33- ظهرت خلايا الكبد النجمية في مساحات Disse حول الجيبانيات في الجنين عمر 78سم) CVRL.

34- أظهر سيتوبلازم الخلايا الكبدية المكونة للحبال الكبدية تفاعلا" سالبا" لمادة عديد السكريد المخاطي المقاومة لخميرة الدياستيزخلال الثلث الأول من الحمل بينما أظهر تفاعلا" موجبا" إزداد تدريجيا" خلال الثلثين الثاني والثالث من الحمل.

35- أظهر سيتوبلازم الخلايا الكبدية المتجمعة في مجموعات تحت المحفظة تفاعلا" سالبا" لمادة عديد السكريد المخاطي المقاومة لخميرة الدياستيزخلال الثلث الثاني من الحمل بينما تفاعل إيجابيا" خلال الثلث الُثالث من الحمل.

36- أظهر سيتوبلازم الخلايا ضخمة النواة تفاعلا" إيجابيا" لمادة عديد السكريد المخاطي المقاومة لخميرة الدياستيزبينما أظهرت الخلايا الدموية الأصل وخلايا الدم الحمراء تفاعلا" سالبا" خلال فترة الحمل.

37- النسيج الضام للمتن والنسيج الضام للمحفظة أظهرت تفاعلا" إيجابيا".

38- أظهر سيتوبلازم الخلايا الكبدية تفاعلا" سالبا" لمادة عديد السكريد المخاطي المهضومة بواسطة خميرة الدياستيز (جليكوجين) خلال فترة الحمل.

39- أظهرت الخلايا الكبدية للجنين تفاعلا" سالبا" لإنزيمى الفوسفاتيز القلوي والحمضى خلال الحياة الجنينية.

CONCLUSIONS

1. The hepatic primordium was differentiated in the peritoneal cavity in 2 cm CVRL (71 days of age) foetus.
2. The size of the liver is increased during the first trimester until occupied most of the abdominal cavity.
3. The final position of the liver in the abdominal cavity was influenced by the development and rotation of the other abdominal organ.
4. The shape of the liver varied between quadrilateral, irregular and triangular during the prenatal life.
5. The liver started as a right and left lobes and then secondary quadrate and caudate lobes were developed.
6. The cytoplasm of the hepatocytes contained cytoplasmic vacuoles in different size in a foetus of 7 cm CVRL (85 days of age) and onward).
7. The portal and the central veins were developed as small vein-like structures without endothelium in a foetus of 4.8 cm CVRL (76 days of age).
8. The hepatic cords were regularly arranged around the central vein in radiating manner in a foetus of 7 cm CVRL.
9. The basic structures of the sinusoids appeared in a foetus of 2.5 cm CVRL (72 days of age).
10. The haemopoietic foci were formed in a foetus of 3 cm CVRL (74 days of age) and disappeared in a foetus of 112 cm CVRL (372 days of age) and onward.
11. Mature erythrocytes appeared in a foetus of 9.5 cm CVRL (92 days of age).
12. The haemopoietic activity ceased toward the end of the third trimester in a foetus of 112 cm CVRL (372 days of age) and onward.

13. The development of the intrahepatic bile ducts was noted in a foetus of 7 cm CVRL (85 days of age) and completed in a foetus of 14.5 cm CVRL (105 days of age) and onward.
14. The histochemical finding revealed that the component of the liver parenchyma showed variable reaction for PAS technique and negative reaction for both alkaline and acid phosphatases.

Recommendations

Further studies are needed to:

- More histochemical tests and immunohistochemical investigation to evaluate the functions of the hepatocytes and some of the haemopoietic cells during prenatal life.
- To compare the blood constituents of the liver with those of the blood circulation during the three trimesters of pregnancy
- Ultrastructural analysis of hepatic haempoiesis during the three trimester.

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