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Histological and Structural Development of the Liver of Rats from the Embryonic Stage to Adulthood

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ABSTRACT

This study was conducted in the animal house of the College of Veterinary Medicine/Tikrit University. The study included (24) white rats and 4 male rats used for mating purposes only. They were divided into four equal groups, each group containing 6 samples of the liver of white rats (embryonic stage, one day old after birth, 7 days old after birth and adulthood stage). The study of the liver using the microscope showed that there was a gradual growth between the embryonic liver and the mature liver at the level of liver cells, blood sinuses, bile ducts, and liver lobes. The embryonic liver had simple squamous endothelium of the central vein, scattered hepatocytes, and hepatocyte aggregates of hematopoietic cell types, such as lymphocytes, red blood cells, and at times megakaryocytes. The hepatocyte packing associated with eosinophilic cytoplasm and lipid droplets, dilated sinusoids containing hematopoietic cells, white blood cell infiltration in the peripheral connective tissue. Seven days after birth, columns of hepatocytes were formed, branches of the portal vein and bile ducts were seen with the infiltration of white blood cells, and the isolated foci of hematopoietic cells and primitive bile ductules were identified.

Polygonal hepatocytes in the adult liver were radially organized around the central vein, and a well-integrated sinusoidal network was present, which harbored Kupffer cells, and this indicated structural and functional maturity. These data demonstrate the process of hepatic maturation of embryonic hematopoiesis into postnatal differentiation and vascular maturation, which leads to a functional structure with parenchymal architecture.

1. Introduction

The liver is regarded as one of the most crucial organs in the body because of its crucial functions in the metabolism processes, bile secretion, detoxification, and synthesis of plasma proteins; thus, it is considered the major organ that provides metabolic homeostasis [1]. The liver is a unique organ, and it has a major reorganization of structures and functions as it passes through various stages of development, which is supported by progressive specialization of the liver and the formation of a complete organ with combined metabolic and immunological functions [2].

The primitive gut tube forms the hepatocytes in the hepatic lobules to which blood channels are formed which later form hepatic sinusoids. The first apparent hepatic parenchymal tissue is known to occur on the tenth day of fertilization and is comprised of epithelial cord buds that can be found embedded in the visceral mesoderm [3].

The liver is an important part of the fetus since it serves as the major hematopoietic location during this time, that is, it serves as a supportive tissue microenvironment to which the hematopoietic stem cell proliferates and develops prior to the full maturation of the bone marrow. This period is distinguished by broad blood sinuoids, a high density of the vascular system, and high concentration aggregates of blood cells, and hepatocytes are simple and not yet differentiated [4,5].

The liver starts to experience some of the basic structural and functional changes as birth is nearing and the baby enters the extrauterine life. In the initial neonatal period, the hematopoietic activity is decreasing in parallel with the activation of the hepatic metabolic processes, in particular, lipid and energy metabolism. This phase is defined by a more high-density of hepatocytes, the presence of lipid droplets in the cytoplasm, and the alteration in the width and structure of the hepatic sinuoids [6].

The liver keeps to restructure its histological structure in the first days and weeks of birth. The forerunners of the bile canaliculism and a significant regression of a hematopoietic foci are accompanied by a gradual plate formation of hepatocytes, and a further development of the vascular and biliary architectures. Recent findings also show that this is a critical period of development of the normal lobular architecture of the adult liver [7].

The liver is fully structurally and functionally matured in adulthood. The hepatocytes are organized radially around the central vein and an integrated sinuoidal network comprising Kupffer cells is formed. These cells are the key to the immune surveillance and the blood clearance. This is the exact structure that is indicative of the functional stability of the adult liver and its ability to conduct its essential physiological processes in a highly efficient way [8].

Purposes of the Study

Despite the large number of studies conducted to analyze the liver development during a certain age stages, there are few studies focusing on correlating the sequential histological changes in the fetal stage to the early neonatal stage all the way to adulthood. Thus, the current research will focus on the analysis of histological and developmental alterations of the liver at various age-related stages.

Materials and Methods

Study animals: This was done on a total of 24 white rats (albino Rats), divided into four equal groups of 6 rats each namely Group 1: Fetal stage (prenatal 18 day befor birth) , Group 2: Neonatal stage (one day after birth), Group 3: Early postnatal stage (seven days after birth), and Group 4: Adult rats. Late-stage embryo was used to collect fetal liver samples, neonatal liver samples and early postnatal liver samples were collected at one day and seven days, respectively. The liver samples of the adults were obtained from fully mature animals. All the procedures involved in the collection of samples followed the ethical guidelines of care and use of laboratory animals and were done under sterile conditions.

Tissue Fixation and Processing

Collected samples were immediately fixed in 10% formalin for 24–48 hours. After fixation, the samples were gradually dehydrated through a series of ethanol concentrations: 70%, 80%, 95%, and 100%, followed by clearing with xylene, and then embedded in paraffin wax. Paraffin-embedded samples were sectioned at a thickness of 4–5 µm using a rotary microtome, and the sections were mounted on glass slides.The slides were stained with hematoxylin and eosin (H&E) to evaluate General tissue architecture and Hepatocyte morphology [9].

Results and Discussion

Histological examination of the embryonic liver demonstrated the presence of a central vein lined with simple squamous endothelial cells, with variability in its blood content among different sections. Scattered hepatocytes were observed, along with dilated blood sinusoids containing aggregates of hematopoietic cells, particularly

lymphocytes and red blood cells (Fig. 1). The hepatic tissue was surrounded by a thin capsule composed of fine collagen fibers, and the blood sinusoids appeared as wide channels arranged within an organized vascular network. Hepatocytes were poorly defined morphologically and irregularly distributed, with scattered primitive hepatic cells present within the liver tissue (Fig. 2). The hepatic sinusoids of the embryonic liver consisted of uniformly dilated channels forming a network of blood vessels, whose lumina contained foci of embryonic hematopoietic activity and chains of leukopoietic cells (Fig. 3). The liver is among the essential vital body organs as it plays a central role in controlling the metabolic processes as well as the various other vital body functions without which the body cannot survive since the fetus stage until adulthood. The hepatic functions change significantly in the course of the developmental stages; during the period before birth, the liver plays a major role in hematopoiesis, which gradually change after birth to a higher metabolic involvement finally attaining complete integrated metabolic functions in adulthood.

Histological study of the fetal liver in rats demonstrated that the liver had a central vein lining with simple squamous endothelium, and that the level of blood content within the various sections varied. Moreover, there were hepatic sinusoids of dilated sinusoids with high content of hematopoietic cells especially of erythrocytes and lymphocytes as well as limited supply of large megakaryocytes. These results are aligned with those of [10] and [11] who found strong dilated sinusoids, dense clusters of hematopoietic cells, and incomplete and poorly-differentiated hepatocytes in the fetal liver. These observations also support the principle role of the fetal liver as a hematopoietic organ of significance in late gestation period before the bone marrow has fully matured.

On the contrary, the current research showed that the liver experiences unique histological changes due to gradual invasion of a hematopoietic organ in fetal life to a mature organ in adult life, which has integrated metabolic and immune functions. It is interesting to note that hepatic sinusoids were arranged in an easily recognizable vascular network even though hepatocytes were primitive at this stage. These results are consistent with the findings of studies made by [12] and [13]. Nevertheless, the existing findings suggest that it has a greater level of vascularization compared to a number of past investigations, which claimed the fetal hepatic tissue to be less organized. These inconsistencies can be explained by the age of the fetus, study design.

The histological examinations of the liver of a neonate one day after delivery showed significant structural alterations. Loose connective tissue with high density of white blood cells was present in the periphery of the liver which is an indication of an active peripheral immune action. Hepatic parenchyma was also filled with hepatocytes characterized by eosinophilic cytoplasm and spherical and euchromatic nuclei with cytoplasmic lipid droplets observed. Fig. 4 shows that the sinsuoid of blood in particular locations were enlarged (and a narrowed peripheral sinsuoid) with hematopoietic cell clusters. In general, neonatal liver was characterized by high packing of hepatocytes, sinusoidal dilation, lipid droplets, hematopoietic cells and white blood cells perivascular invasion (Fig. 5). These results indicate the early postnatal hepatic developmental stage which entails active metabolic and hematopoietic preparation.

Histological analysis showed a significant structural alteration, in which there was an augmentation in the density of hepatocytes, circular nuclei with nebulous chromatin and eosinophilic cytoplasm, and the gathering of lipid droplets in hepatocytes. Besides that, hepatic sinusoids dilation. These characteristics show the beginning of the functional shift of the liver as a hematopoietic organ to a more active metabolic organ. This result can be compared to the reports given by [14] and [15], who noted that the initial postnatal stage is a crucial transitional period in the development of the liver. Lipid droplets in hepatocytes at this stage is an arguably transient physiological process due to the partial maturation of lipid metabolism enzymes. Further, the extreme presence of leukocytes in the area of the liver indicates that hepatic immune functions were activated earlier after the birth.

Histological examination of the liver seven days postnatally revealed well-defined structural organization. Hepatocytes in the parenchyma were arranged predominantly in columns, each two cells thick, with eosinophilic cytoplasm and basophilic, spherical nuclei. The cells exhibited a polygonal shape. Sinusoids contained few Kupffer cells, while branches of the portal vein were hyperemic and located adjacent to branches of the bile duct. These portal structures were infiltrated by white blood cells (Fig. 6). The central vein displayed a wide lumen lined by simple squamous endothelium. Hepatocytes were abundant, mostly organized in columns, and occasionally in

clusters, with spherical euchromatic nuclei. Blood sinusoids formed a narrow network of channels containing few Kupffer cells (Fig. 7). The liver periphery was covered by a delicate connective tissue capsule, with some white blood cells present in the subcapsular region. Hepatocytes were densely packed, surrounding multiple sinusoidal channels continuous with the periphery of the central vein. Isolated foci of hematopoietic cells were observed, and primitive bile ductules were evident (Fig. 8).

These findings indicate advanced postnatal hepatic organization, characterized by columnar hepatocyte arrangement, maturation of the vascular and biliary architecture, and ongoing hematopoietic activity, the results demonstrated a more advanced level of histological organization. Hepatocytes began to acquire their characteristic polygonal shape and became arranged into hepatic plates, accompanied by narrowing of the hepatic sinusoids and the appearance of Kupffer cells within them, in addition to the clear identification of portal triad components. These findings are in agreement with the studies of [13] and [16], who reported that the first postnatal week is characterized by pronounced structural maturation of the hepatic parenchyma, including closely packed polygonal hepatocytes with round nuclei of variable chromatin density, eosinophilic cytoplasm, and the persistence of binucleated cells, along with the progressive development of the vascular and biliary architecture. Moreover, the persistence of small foci of hematopoietic is evidence that the process of hematopoietic activity would be gradual and not sudden, confirming the idea of a functional progression of the liver.

Adult liver tissue showed the well-organized polygonal hepatocytes with each having a spherical nucleus of basophilic chromatin in the parenchyma. A network of channels with a low concentration of Kupffer cells was produced by the blood sinusoids (Fig. 9). The liver lobule had a central vein and the channels around the lobule had a sinuous channel which was filled with Kupffer cells. Hepatocytes were polygonal and had spherical euchromatic nuclei and distinct nucleoli (Fig. 10). The network of channels that developed in the blood due to sinusoids of blood consisted of hypertrophic Kupffer cells, with an extension of the periphery of the central vein that had a small number of red blood cells. The hepatocytes were polygonal cells, which were radially oriented around the central vein (Fig. 11). These findings indicate structural maturity of the adult liver with a radial structure of hepatocytes around the central vein, integrated sinusoidal network with a small number of Kupffer cells, and little hematopoietic phenotype. These data strongly coincide with the recent research that has characterized the adult liver as a structurally and functionally stable organ that is at the core of metabolism, detoxification, and control of immune processes [2].

Overall, these results confirm that liver development proceeds through a precise structural and functional sequence, beginning with prominent fetal hematopoietic activity, followed by a transitional postnatal phase characterized by extensive histological reorganization, and culminating in complete structural and functional maturation during adulthood.

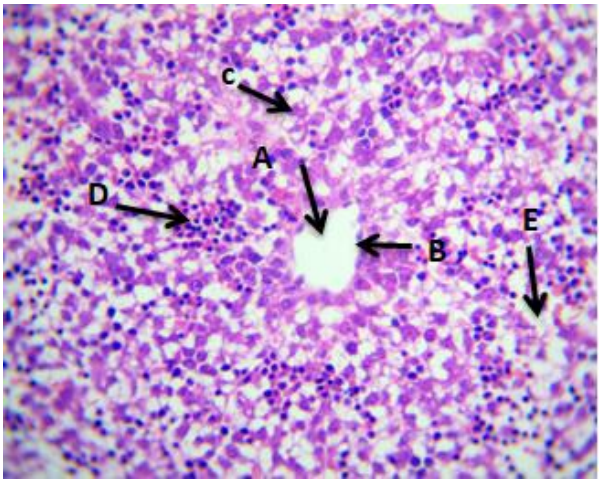

Figure 1: Liver embryo, central vein(A), Endothelium(B), Scattered of liver cells (C), Foci of hematopoietic cells (D), Blood sinusoid (E). (H&E X40).

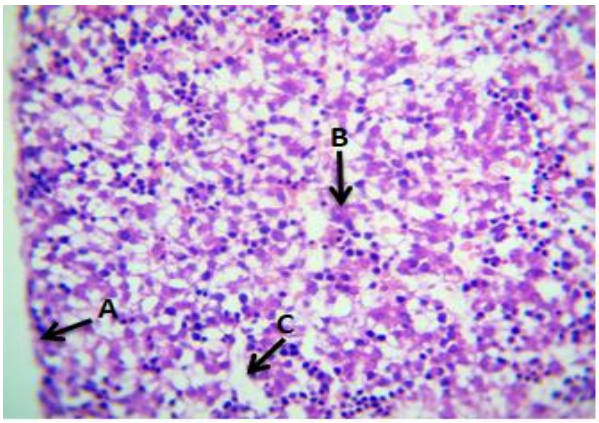

Figure 2: liver tissue of embryo, capsule of delicate C.T.(A), Scattered liver cells (B), Dilated blood sinusoid (C). (H&E X40).

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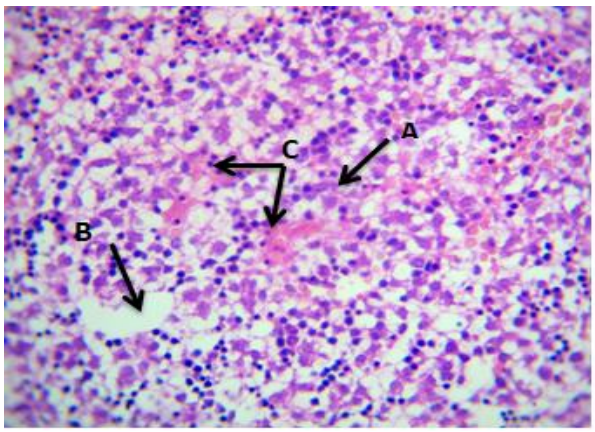

Figure 3:parenchyma of the liver tissue of embryo, ill- defined liver cells (A), Dilated blood sinuosoids (B), foci of blood hemapiotic cells of RBCs & WBCs(C). (H&E X40).

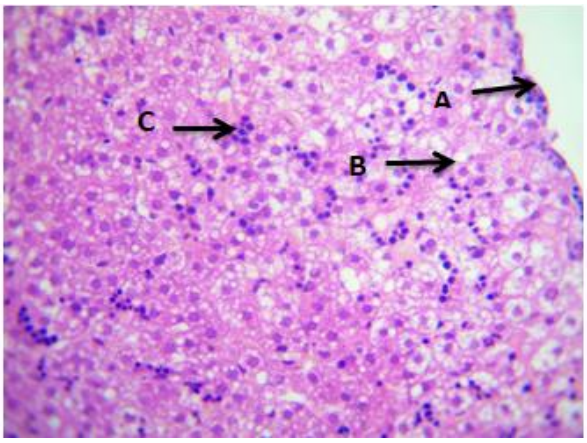

Figure 4: capsule of delicate C.T. of one day postnatally (A), liver cells with vacuoles containing fat droplets (B), hematopoietic foci of cells (C),. (H&E X40).

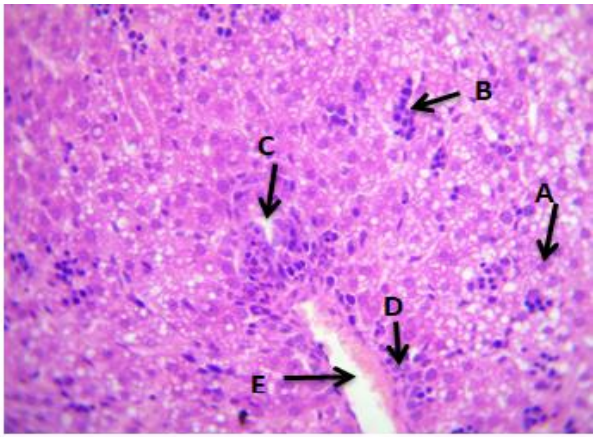

Figure 5: parenchyma of liver tissue at one day postnatally, crowded liver alls with multiple vacuoles(A), hematopoietic cells foci (B), bile ductule (C), WBCs (D) around portal vein (E). (H&E X40).

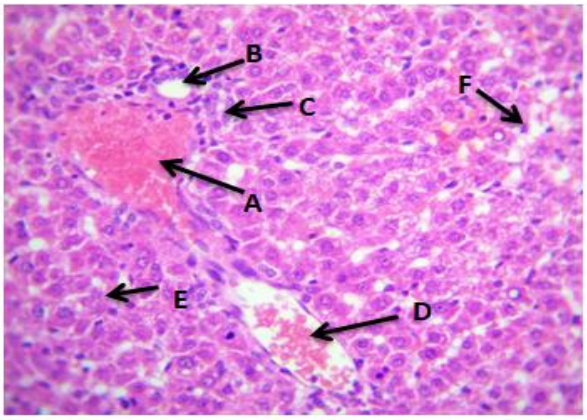

Figure 6: liver tissue at 7 day postnatally, Hyperaemic portal vein (A), bile ductule branch (B), WBCs (C), central vein with blood clot (D) columas of polygonal liver cells (E), blood sinusoid with kupffer cells (F). (H&E X40).

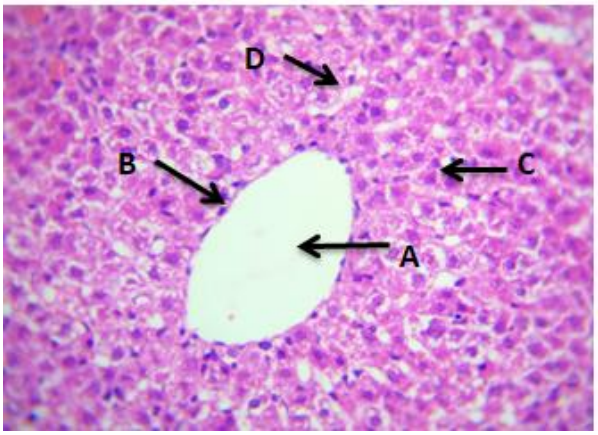

Figure 7: liver tissue at 7 day post natally Wide central vein at (A), Endothelium (B), liver cells with spherical nuclei (C), blood sinusoid with Kupffer cells (D). (H&E X40).

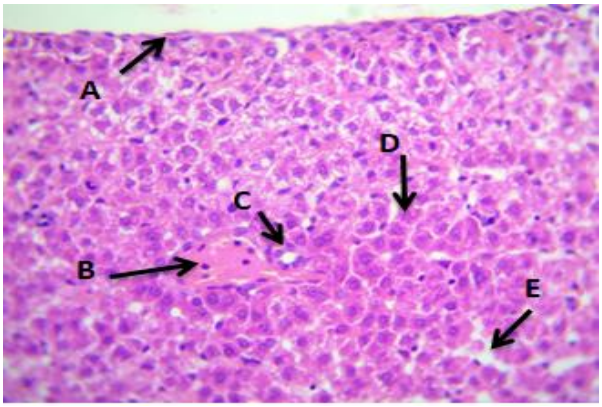

Figure 8: Liver tissue at 7 day postnatally, Delicate connective tissue of capsule (A), hemolyzed blood of portal vein (B), bile ducteles (C),groups of liver cells (D), narrow blood sinusoid(E). (H&E X40).

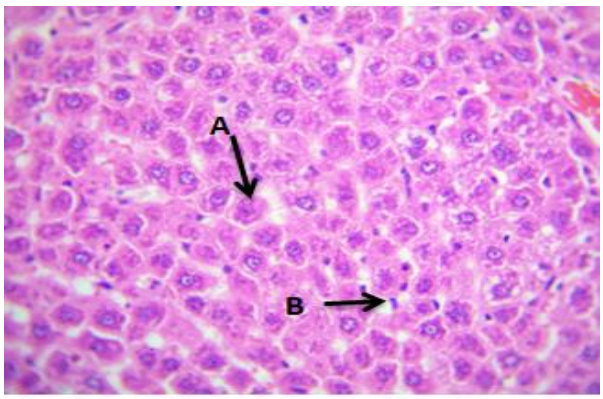

Figure 9: At adulthoud stage, liver parenchyma polygonal liver cells in the form of honey- comb like (A), blood sinusoids with few Kupffer cells (B). (H&E X40).

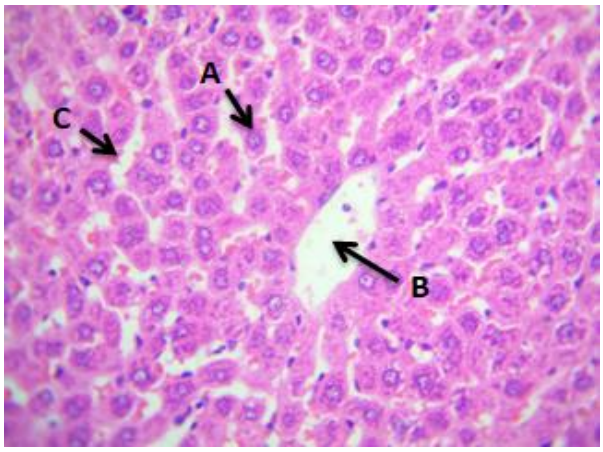

Figure 10: At adulthoud stage,columns of polygonal liver cells in the form of radial pattern (A), toward the central vein(B), network of blood sinusoids with Kupffer cells (C). (H&E X40).

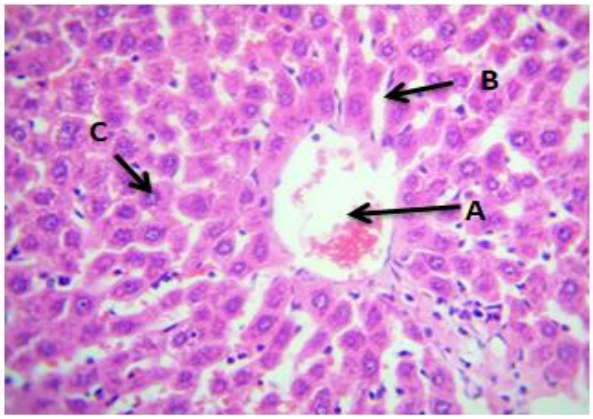

Figure 11: At adulthoud stage,wide lumen of central vein with few RBCs (A), network of blood sinusoids with kupffer cells (B), hepatocyte (C). (H&E X40).

Conclusion

This study demonstrates the structural development of the liver from the embryonic stage to adulthood. In the embryonic liver, hematopoietic activity predominates, with scattered primitive hepatocytes and a rudimentary vascular network. Postnatally, hepatocytes begin to organize into columns, with sinusoidal dilation, lipid droplet accumulation, and peripheral infiltration of white blood cells, reflecting preparation for metabolic and hematopoietic functions. By adulthood, the liver exhibits fully mature parenchyma, with polygonal hepatocytes arranged radially around the central vein and an integrated sinusoidal network containing Kupffer cells, indicating complete structural and functional maturation necessary for normal physiological performance.

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التطور النسيجي والتركيبي لكبد الجرذان من المرحلة الجنينية الى مرحلة البلوغ

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الملخص

تم اجراء هذه الدراسة في البيت الحيواني التابع لكلية الطب البيطري/ جامعة تكريت أذ شملت الدراسة (24) من الجرذان البيض و 4 من ذكور الجرذان استخدمت لغرض التزاوج فقط ، ونم توزيعها الى اربعة مجاميع متساوية كل مجموعة ضمت 6 عينات من كبد الجرذان البيض (المرحلة الجنينية، عمر يوم واحد بعد الولاة، عمر 7 ايام بعد الولادة ومرحلة البلوغ). أظهر الفحص النسجي لكبد الجرذان البيض تطورًا تدريجيًا من المرحلة الجنينية وصولًا إلى مرحلة البلوغ على مستوى الخلايا الكبدية، الجيوب الدموية، القنوات الصفراوية و الفصوص الكبدية. في الكبد الجنيني، كان الوريد المركزي مبطنًا ببطانة بسيطة حرشفية، مع وجود خلايا كبدية متناثرة ، وظهور جيوب دموية متوسعة، وتجمعات من الخلايا المكوّنة للدم، بما في ذلك الخلايا اللمفاوية وخلايا الدم الحمر وبعض الخلايا النواعية. بعد يوم واحد من الولادة، أظهر الكبد حديثي الولادة كثافة عالية في تراص الخلايا الكبدية مع سيتوبلازم حمضي ووجود قطرات دهنية، وتمدّد الجيوب الدموية التي تحتوي على خلايا مكوّنة للدم، إلى جانب ارتشاح خلايا الدم البيض في النسيج الضام المحيطي. في اليوم السابع بعد الولادة، لوحظ ترتيب الخلايا الكبدية على هيئة أعمدة ثنائية الخلية، مع وضوح فروع الوريد البابي والقنوات الصفراوية مع ارتشاح خلايا الدم البيضاء، وظهور بؤر معزولة من الخلايا المكوّنة للدم والقنيّات الصفراوية البدائية.

اما بالنسبة لكبد الجرذان البالغة، كانت الخلايا الكبدية متعددة الأضلاع مرتبة شعاعيًا حول الوريد المركزي، مع شبكة جيبية متكاملة تحتوي على خلايا كوبفر ، مما يعكس النضج البنيوي والوظيفي للكبد. توضح هذه النتائج التطور التدريجي للكبد من نشاطه الدموي الجنيني إلى التنظيم بعد الولادة ونضج الشبكة الوعائية، وصولًا إلى بنية فصيصية ناضجة بالكامل مما يساهم في الوظائف الفسيولوجية للكبد.

الكلمات المفتاحية: بنيان الكبد الجنيني، بنيان كبد حديثي الولادة ،بنيان كبد البالغ، التطور النسجي للكبد، التطور الهيكلي للكبد.