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"Histogenesis of Human Fetal Spleen at Different Weeks of Gestational Age"

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KEYWORDS

Spleen, Lymphatic nodule, GA (Gestation age), White pulp, Red pulp

ABSTRACT:

Background: The spleen is the largest lymphoid organ with a rich blood supply. It appears approximately in the 6th week of gestation as a thickening of the coelomic epithelium of the dorsal mesogastrium near its cranial end. The underlying angiogenetic mesenchyme becomes vascularised and compacted due to the invasion of proliferating cells. The process takes place concurrently in multiple adjacent regions, which quickly unite to produce a lobulated spleen. During the third month of pregnancy, the spleen acquires its final morphological form, and its size progressively grows.

Aims: The study provides detailed knowledge about the cellular changes of the human fetal spleen. It also suggests the functional status of the spleen in the fetal period.

Materials and Methods: This study was conducted on 76 human fetuses (40 males and 36 females), 10% formalin-fixed fetuses with gestational ages ranging from 12 to 36 weeks in the Department of Anatomy, DVVPF's Medical College Campus, Ahilyanagar, and the Department of Pathology, Shree Narayan Medical Institute and Hospital, Saharsa.

Results: In the present study, immature types of lymphocytes were seen at 11th weeks of GA, Number and maturity of lymphocytes were growing with age advancement. Up to the 14th weeks lymphocytes were arranged irregular manner. At 15th weeks onwards, lymphocytes start appearing around some arterioles, and lymphatic nodules were ill-define. Till the 18th week of GA, there is undifferentiated white and red pulp. At the 19th week, lymphocytes were present around the central arterioles, and lymphatic nodules were well defined at the same time, white pulp and red pulps were ill defined.

Conclusion: we conclude from our study that the capsule, trabeculae, and cells of white and red pulp showed variations at different age groups. A thorough understanding of the histogenesis of the human fetal spleen is also provided by this study. Additionally, it implies the spleen's functional state during the fetal stage.

Introduction:

Numerous scholars are constantly interested in studying human growth. Every single organ in the human body performs a variety of vital tasks that are essential to the survival of the species. Embryologists are highly interested in learning how each human organ develops. The spleen is one of the most significant of them. From classical times, humans have been aware of the spleen.[**1]** The spleen is the largest lymphoid organ with a rich blood supply. It appears approximately in the 6th week of gestation as a thickening of the coelomic epithelium of the dorsal mesogastrium near its cranial end. The underlying angiogenetic mesenchyme becomes vascularised and compacted due to the invasion of proliferating cells. The process takes place concurrently in multiple adjacent regions, which quickly unite to produce a lobulated spleen. [**3, 4, 5]** During the third month of pregnancy, the spleen acquires its final morphological form, and its size progressively grows. **[6]** Mesenchymal cells in the body of the cellular mass differentiate into reticular cells that provide the splenic reticular stroma. **[7]** The vascular reticulum, which has many closely spaced thin-walled

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vascular loops and immature reticulocytes, fully forms at 8 to 9 weeks of gestational age. The spleen was sometimes referred to as the organ of sorrow. **[3,8]** Up to 14 weeks, the spleen is exclusively hematopoietic and begins its life as a hematopoietic organ. It then develops its apparent lymphoid appearance. **[9]** The germinal center appears only after birth. [**10]** It is concerned with phagocytosis, lymphopoiesis, and blood cell storage. It functions as a blood filter, displays immunity to antigens, and produces erythrocytes and granulocytes during fetal development as a hematopoietic organ. The parenchyma of the adult human spleen is divided into two main components under the microscope. Based on how the red and white pulp appear when the fresh spleen is transected. The lymphatic tissue found in the white pulp takes the form of lymphoid follicles, which contain T and B lymphocytes, and the periarteriolar lymphatic sheath. Most of the splenic volume (75%) is contributed by the red pulp. The fibrocellular network of the splenic cord divides the numerous venous sinusoids that make up this structure from one another. **[11,12,13,14]**

Further development consists of the development of the white and red pulp, which is divided into three stages, namely primary vascular reticulum stage (up to 14th week), transformation stage (15"h to 17th week), and stage of lymphoid colonization (18th week onwards). **[15,16]** The most frequent medical condition during pregnancy that might cause difficulties is hypertension, which affects 3% to 8% of pregnancies globally. **[17].** Preeclampsia, chronic hypertension, gestational hypertension, and pre-eclampsia superimposed on pre-existing hypertension are the classifications used by the National Heart, Lung, and Blood Institute to describe high blood pressure during pregnancy. Hypertension is known to cause intrauterine growth restriction **[18]**. An interesting outcome of a study done by Singh MV et al. revealed the fact that the spleen, a source of T lymphocytes, itself can cause hypertension, which is said to be immune-mediated **[19].**

Aims: The study provides detailed knowledge about the cellular changes of the human fetal spleen. It also suggests the functional status of the spleen in the fetal period.

Materials and Methods:

This study was conducted on 76 human fetuses (40 males and 36 females), 10% formalin-fixed fetuses with gestational ages ranging from 12 to 36 weeks in the Department of Anatomy, DVVPF's Medical College Campus, Ahilyanagar, and the Department of Pathology, Shree Narayan Medical Institute and Hospital, Saharsa. This study was conducted from July-2024 to October 2025. The ethical committee approval and consent of the relatives were obtained. Dissection of the fetus was done following the standard protocol as described by Romanes. A midline incision starting from the xiphisternum to the pubic symphysis was taken. The second incision was taken along the costal margin, starting from the Xiphisternum and extending up to the left midaxillary line. The third incision was taken starting from the pubic symphysis to the Anterior superior iliac spine. The anterior abdominal wall flap was reflected laterally. Finally, the spleen was removed. The specimen were categorized into 10 groups Group A(12 weeks), Group B(13-14 weeks), Group C(15-16 weeks), Group D(17-18 Weeks), Group E(19-20 weeks), Group F(21-22 weeks), Group G(23-24 weeks), Group H(25-26 weeks), Group I(27-28 weeks) and Group J(29-36 weeks). The entire spleen was dissected into two parts. From one-part bits of the entire spleen, starting from the hilum, were taken, processed, blocks prepared, and sections as thin as 5 mm were taken. Slides were prepared and stained with Hematoxylin and Eosin. The slides were studied using 4x, 10x, 40x, and 100x objectives and interpreted.

Results:

The following microscopic features at different gestational ages of the fetus were observed.

Group A(11-12 weeks):

A capsule was noted, and it contained a few collagen fibers, fibroblasts, and fibrocytes. Whereas trabecular was not seen. Sinusoid was seen with a large number of hemopoietic cells. Hemopoietic cells are an immature type. Immature types of lymphocytes were seen, and they lie in irregular arrangements. Lymphatic nodules and eccentric arteries were not seen. The central vein is observed, and the lumen of the central vein contains a large number of haemopoietic cells.

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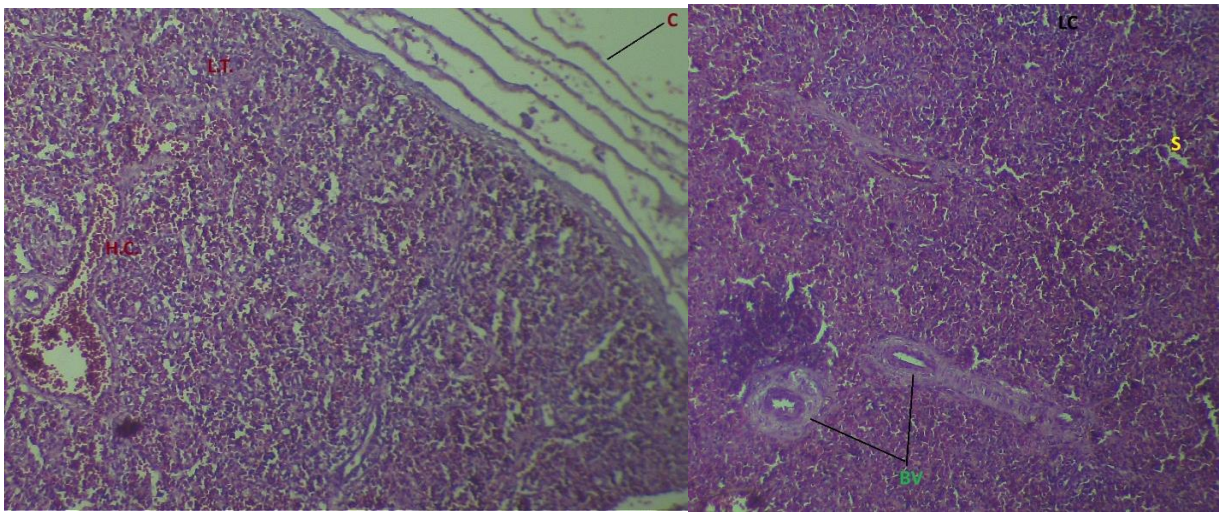

Fig No 01: Showing Histology of Fetal spleen at 12 weeks of GA. (LT- Lymphatic tissues, HC- Hemopoietic cell, C—Capsule, S- Sinusoid, and BV- Blood vessels)

Group B(13-14 weeks):

A thick capsule was observed, it contain more collagen fibers, fibroblasts, and fibrocytes. Whereas, ill-defined trabeculae were noted. A large number of sinusoids with large hemopoietic cells were observed. Central veins were noted with a large number of immature types of hemopoietic cells. Lymphocytes were arranged in an irregular pattern, and lymphatic nodules were not seen. A few of the central arterioles were seen.

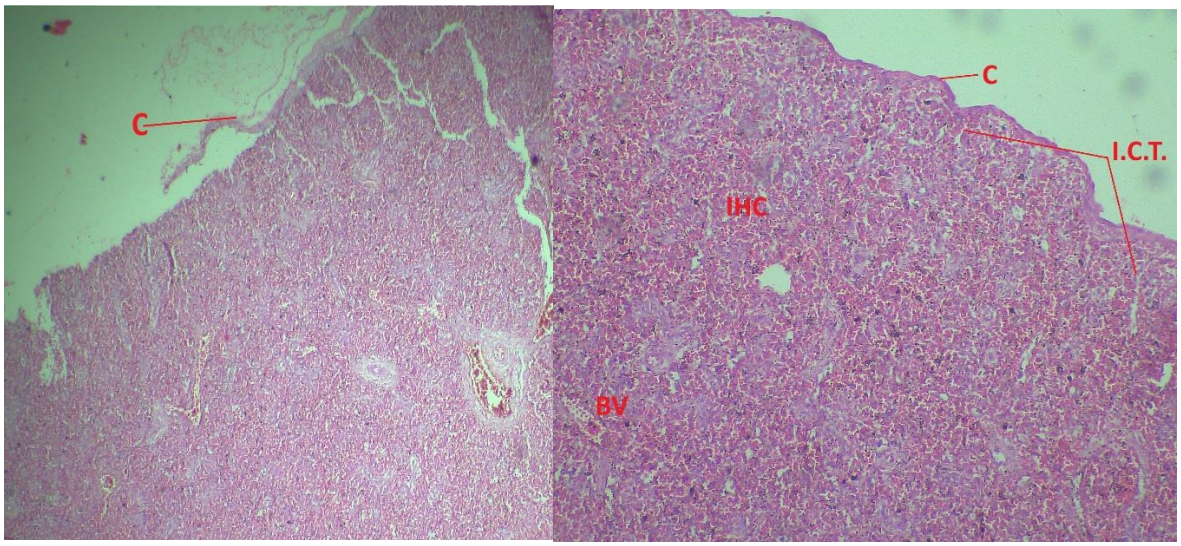

Fig No 02: Showing Histology of Fetal spleen at 14 weeks of GA. (C-capsule, ICT- Incomplete trabeculae, IHC-Immature haemopoietic cell and BV- Blood Vessels filled blood components).

Group C(15-16 weeks):

A thick and well-developed capsule was found, and moderately developed trabeculae were seen. Several arterioles were seen, and a few lymphocytes appeared around them. So, lymphatic nodules were ill-defined at this gestational age. The central vein is well developed, and the lumen is filled with blood products. A large number and size of sinusoids were seen, and a large number of blood components were found in them. Red and white pulp was not differentiated.

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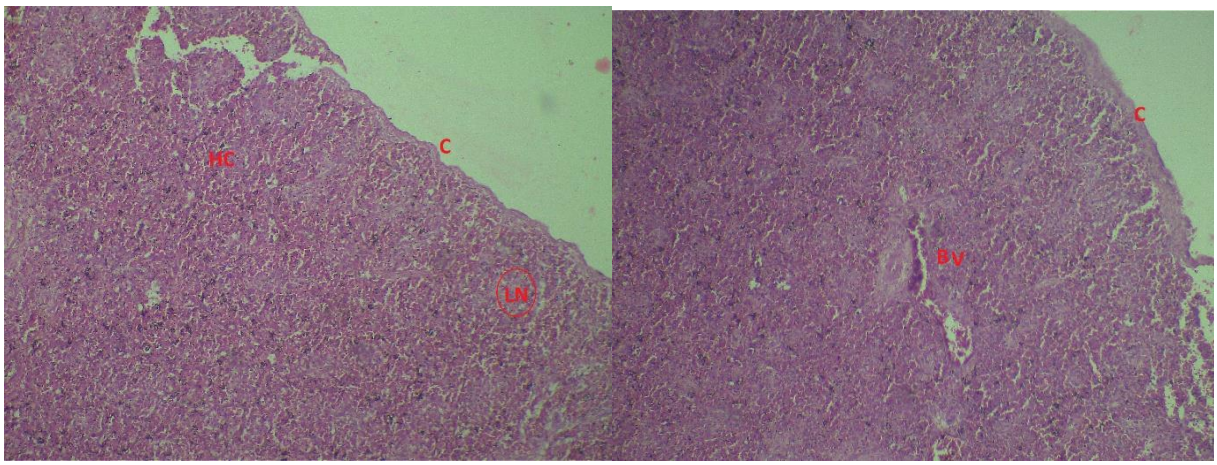

Fig No 03: Showing Histology of Fetal spleen at 16 weeks of GA. (C-capsule, HC-Haemopoietic cell and BV- Blood Vessels filled blood components).

Group D(17-18 weeks):

Thick, well-defined capsules and trabeculae were observed. A large number of arterioles were seen with aggregation of lymphocytes around them. So, lymphatic nodules begin to appear. Even the wall of the blood vessels was thick as compared with previous weeks. Still, red and white pulp are not separated. The central vein is fully occupied with reticular cells, and vessels are covered by a large amount of connective tissue.

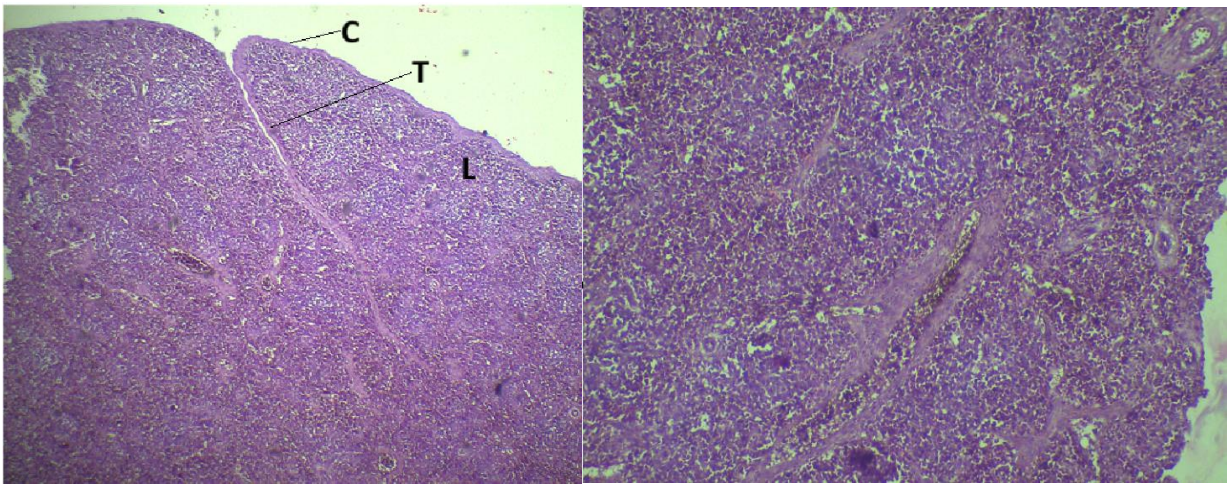

Fig No 04: Showing Histology of Fetal spleen at 18 weeks of GA. (C-capsule, T- Trabeculae and L- Lymphatic nodules).

Group E(19-20 weeks):

Thick and well-defined capsules were found with trabeculae. A large number of connective and reticular fibers were seen. Lymphatic nodules moderately appeared. The large number and size of sinusoids were filled with blood cells. Red and white pulp were ill-demarcated.

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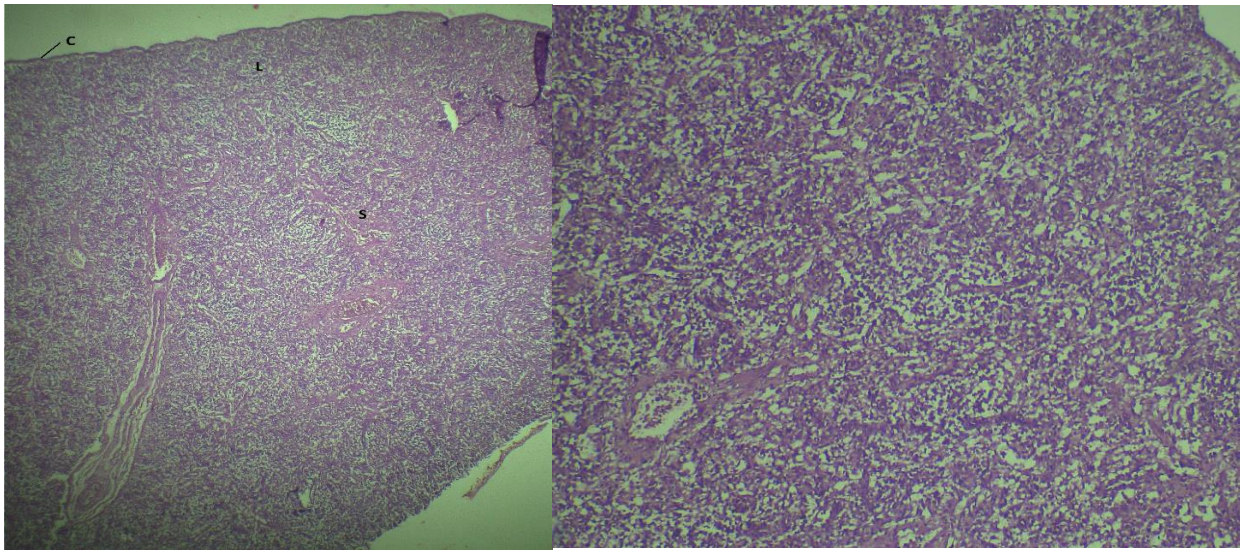

Fig No 05: Showing Histology of Fetal spleen at 19 weeks of GA. (C-capsule, S- sinusoids and L- Lymphatic nodules).

Group F(21-22 weeks):

Thick capsules with trabeculae were seen, and trabeculae had blood vessels in them. Lymphatic nodules were seen with eccentric arterioles. Red and white pulp are moderately differentiated. Red pulp has a large number and size of sinusoids, which contain all the cells of the circulating blood. A large number and mature types of RBCs were seen compared with previous weeks, it's less in number.

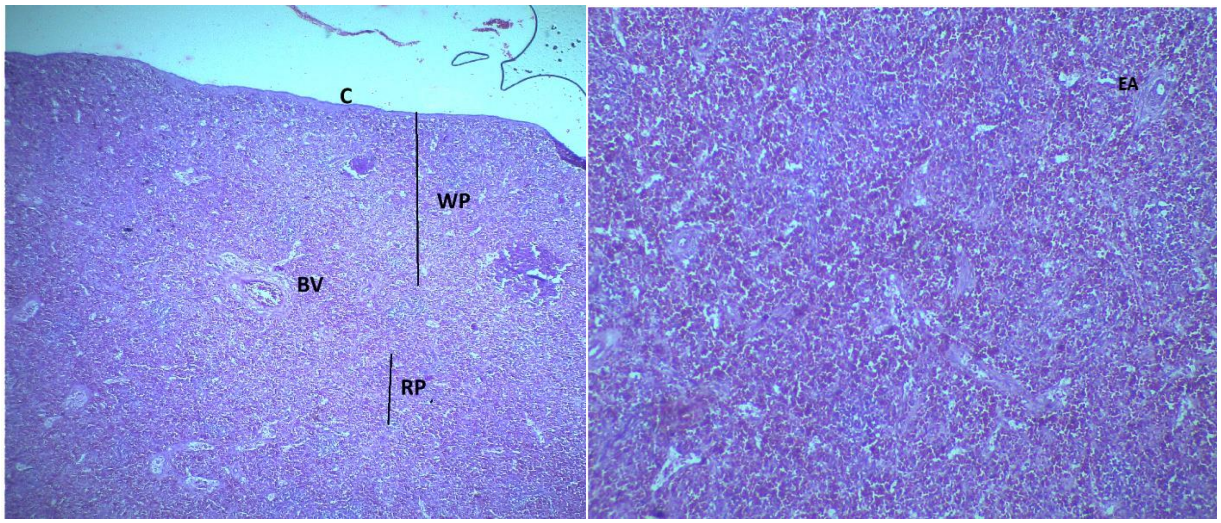

Fig No 06: Showing Histology of Fetal spleen at 22 weeks of GA. (C-capsule, WP- White Pulp, RP- Red pulp, BV- Blood Vessels and EA- eccentric arterioles).

Group E(23-24 weeks):

Thick capsules and well-developed trabeculae with blood vessels were seen. The large size of sinusoids was filled with blood components, and it had large vessels were observed. Some of the thick wall artery was seen with blood product in the lumen. Lymphatic nodules were well-developed. Red and white pulp were well differentiated.

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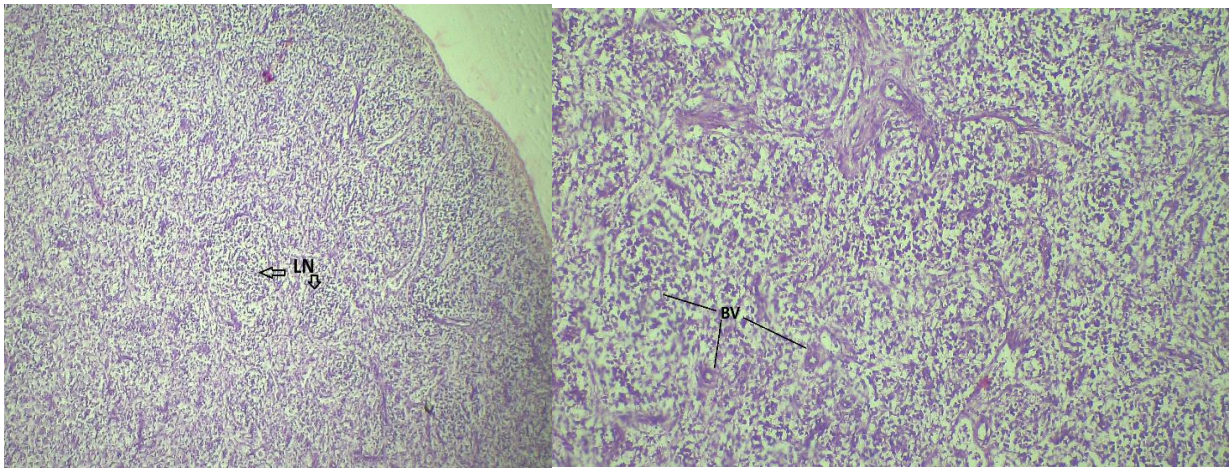

Fig No 07: Showing Histology of Fetal spleen at 24 weeks of GA. (LN- Lymphatic Nodule, BV- Newly forming blood vessels covering with lymphocytes).

Group F(25-26 weeks):

Thick capsules and well-developed trabeculae with blood vessels were seen. The large size of sinusoids was filled with blood components, and it had large vessels were observed. Lymphatic nodules were well-developed. Red and white pulp were well differentiated. More Mature cells were seen, and fewer immature cells were seen.

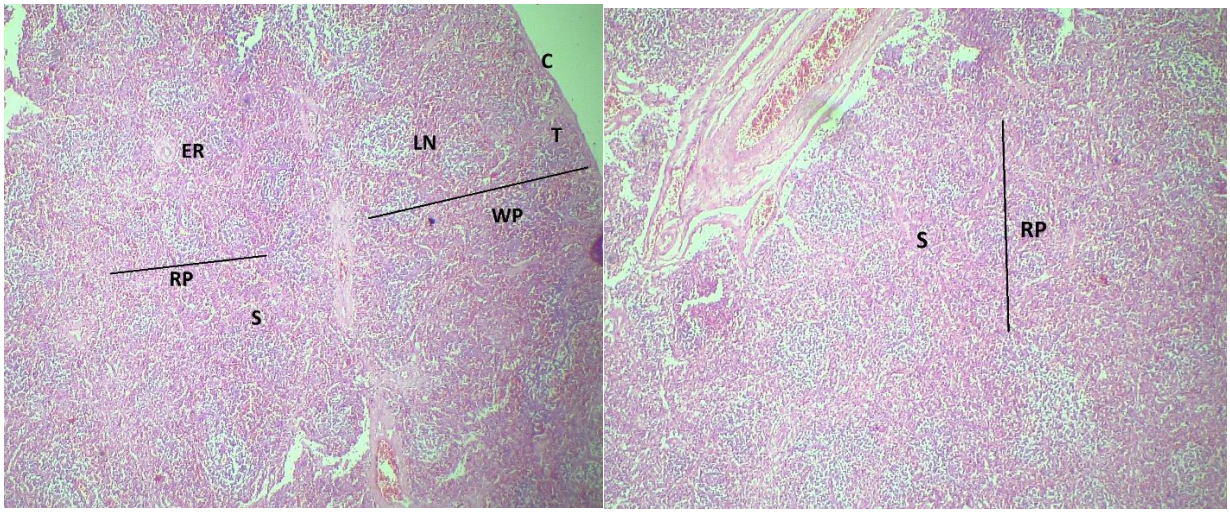

Fig No 08: Showing Histology of Fetal spleen at 24 weeks of GA. (C-capsule, T- Trabeculae, LN- Lymphatic Nodule, WP- White Pulp, RP- Red pulp and S- sinusoids).

Group G(27-28 weeks):

All findings were similar to Group F(25-26 weeks) findings, except that lymphatic nodules were darkly stained and eccentric arterioles were clearly seen. Red and white pulp was clearly observed. Certain large luminal vessels were observed to be fully occupied by Blood cells.

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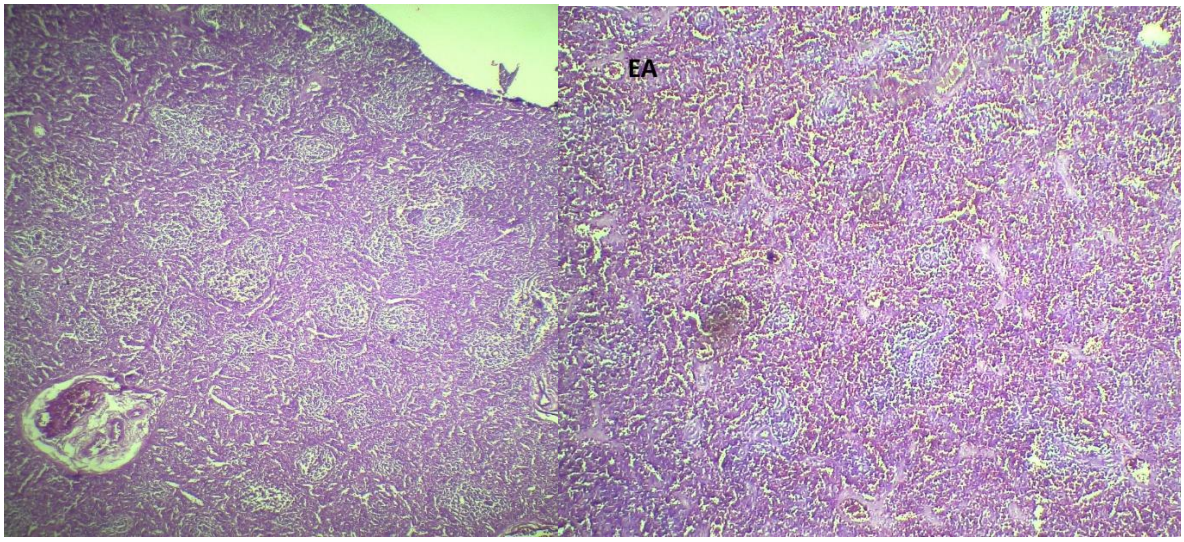

Fig No 09: Showing Histology of Fetal spleen at 27 weeks of GA.

Group H(29-36 weeks):

Well-defined capsule and trabeculae were seen in an adult spleen, it contains dense connective tissue, reticular cells, and reticular fibers which help to divide the parenchyma into different lobules. It has well-differentiated white and red pulp. White pulp contains a number of lymphatic nodules; the periphery of the lymphatic nodule is darker as compared to the center part, that's one is the germinal center. The Centre artery of the white pulp was clearly seen at the marginal part of the lymphatic nodules. The red pulp contains splenic sinusoids, which are filled with all types of blood components.

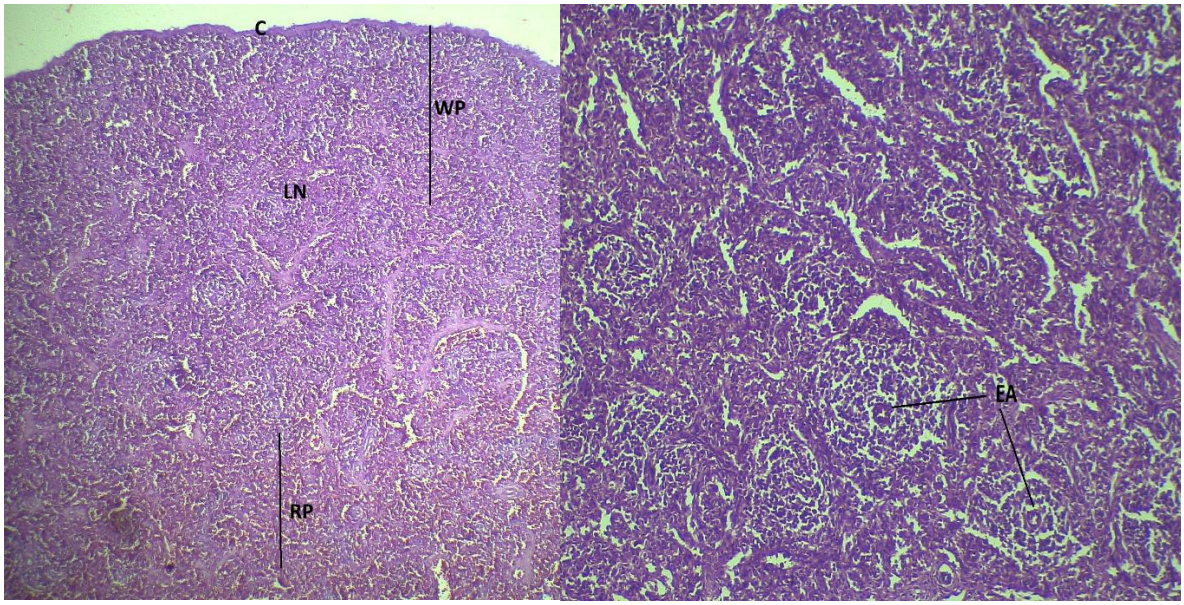

Fig No 10: Showing Histology of Fetal spleen at 27 weeks of GA. (C-capsule, T- Trabeculae, LN- Lymphatic Nodule, WP- White Pulp, RP- Red pulp and S- sinusoids).

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Discussions:

In the present study, we observed that capsules with few collagen fibers, fibroblasts, and fibrocytes were present from the 12th week of GA. Rajeev et.al [4] and Sandhya et.al [20] observed similar findings in their study, which we observed. But, Mrinmoy P et.al [1], Ajit H et.al [2] observed a capsule at 14th weeks of GA. Whereas our finding is earlier than the previous study, which was done by Mrinmoy P et.al [1], Ajit H et.al [2], Sonali et.al [16], and D Srivani [5]. In the present study, ill-defined trabeculae were noted at the 13th week of GA. Moderately developed trabeculae were seen at the 15th week of GA. whereas thick, well-defined capsules and trabeculae were observed in the 17th week of GA by some researchers. According to Mrinmoy P et.al [1], Rajeev M et.al [4], Sonali et.al [16], D Srivani [5], Ajit H et.al [2], and Sandhya V et.al [20] noted trabeculae at 14th, 15th, 16th, 18th, and 20th weeks of GA. So, our findings were analogous with previous studies done by Mrinmoy P et.al [1], Rajeev M et.al [4], Sonali T [16], D Srivani [5], and earlier as compared to Sandhya V et.al [20].

In the present study, sinusoids were seen with a large number of hemopoietic cells at 11th weeks of GA. Mrinmoy P et.al [1] noted the presence of sinusoids at the 14th week of GA, while Ajit H et.al [2] and D Srivani [5] observed sinusoids at the 16th week of GA. Splenic sinusoids were seen at the 17th week of GA by Rajeev M et.al [4] and Sandhya V et.al [20]. Our finding is earlier than the previous researchers' findings.

In the present study, the central vein was seen, and the lumen was filled with a large number of haemopoietic cells at 11th weeks of GA. Mrinmoy P et.al [1] observed a few blood arteries filled with blood cells in the interstitial tissue at the 10th week of GA. Ajit H et.al [2] observed a large number of blood vessels at 14th weeks of GA, and an eccentric artery was seen at 22nd weeks of GA, while Rajeev M et.al [4] noted a large number of blood vessels at 14th weeks of GA, and a central artery was seen at 21st week of GA. The central artery was seen at the 25th week of GA in a study done by D Srivani [5]. In the present study, large numbers of blood vessels were seen at 13th weeks of GA, and the central artery starts appearing at 14th week of GA. An eccentric artery was seen at the 21st week of GA. So, our finding is quite similar with previous finding.

In the present study, immature types of lymphocytes were seen at 11th weeks of GA, Number and maturity of lymphocytes were growing with age advancement. Up to the 14th weeks lymphocytes were arranged irregular manner. At 15th weeks onwards, lymphocytes start appearing around some arterioles, and lymphatic nodules were ill-define. Till the 18th week of GA, there is undifferentiated white and red pulp. At the 19th week, lymphocytes were present around the central arterioles, and lymphatic nodules were well defined at the same time, white pulp and red pulps were ill defined. At 21st week, red pulp and white pulp moderately differentiated. Whereas 23rd week onwards white pulp and red pulp were clearly visible. Mrinmoy P et.al [1] in their study observed that lymphocytes with cellular components could be detected at 13th weeks of GA. Aggregation of lymphocytes could be detected in the periphery of arterioles at 17th weeks of GA. White pulp and red pulp were seen at the 26th week of GA. In Ajit H et.al [2] study, white pulp and red pulp were seen at the 18th week of GA. whereas Rajeev M et al. [4] noted well differentiated at the 20th week of GA. In Rajeev M et al. [4] study, aggregation of lymphocytes is prominent at the 17th week of GA and appears around eccentric arterioles at the 20th week of GA. whereas white and red pulp were observed at the 21st week of GA. So, our finding is quite similar with previous study.

In the present study, we studied the histogenesis of the human spleen at different gestational age and tried to explain it. A precise knowledge of the development of parenchyma and vascular components is essential to understand the normal development of the spleen.

Conclusion:

The Present study was carried out on 76 human fetuses (40 males and 36 females), 10% formalin-fixed fetuses to find out the histogenesis of the spleen during its development. We observe that during the initial weeks of development spleen was composed of collagen fibers, fibroblast, fibrocytes, sinusoids, and haemopoietic cells. The capsule's thickness increases with age advancement. Earlier stage immature lymphocytes were seen and arranged in an irregular manner. At the 14th weeks lymphocytes were arranged as clustered, and at the 18th week onwards, lymphatic nodules were seen. At the 19th week, lymphocytes were present around the central arterioles, and lymphatic

nodules were well defined at the same time, while white pulp and red pulp were ill-defined. At 21st week, red pulp and white pulp moderately differentiated. Whereas from the 23rd week onwards, white pulp and red pulp were clearly visible. Therefore, we conclude from our study that the capsule, trabeculae, and cells of white and red pulp showed variations at different age groups. A thorough understanding of the histogenesis of the human fetal spleen is also provided by this study. Additionally, it implies the spleen's functional state during the fetal stage.

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