"MORPHOLOGICAL ABNORMALITIES IN PLACENTA ASSOCIATED WITH INTRAUTERINE FETAL DEMISE- A HOSPITAL BASED OBSERVATIONAL STUDY"

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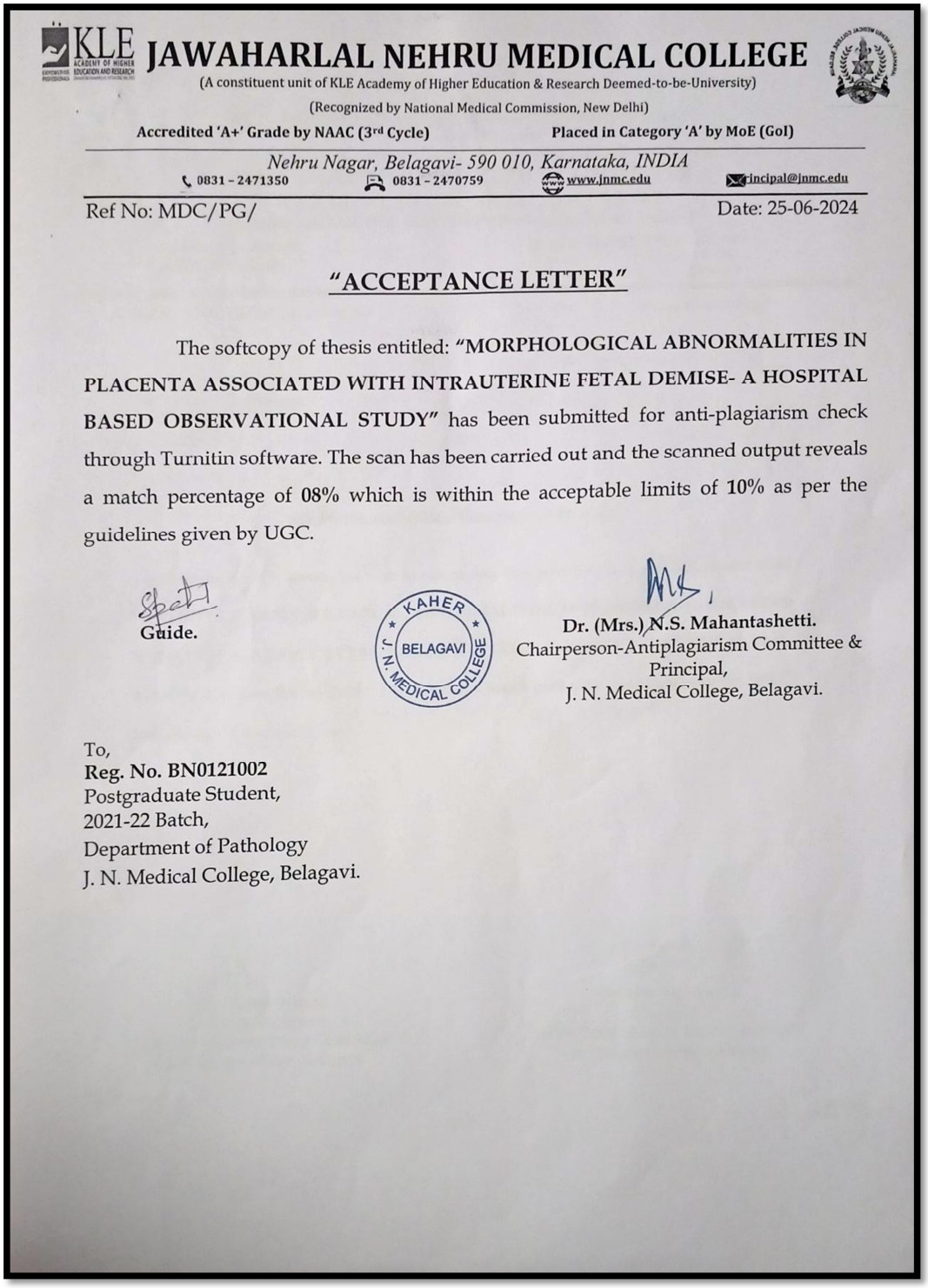

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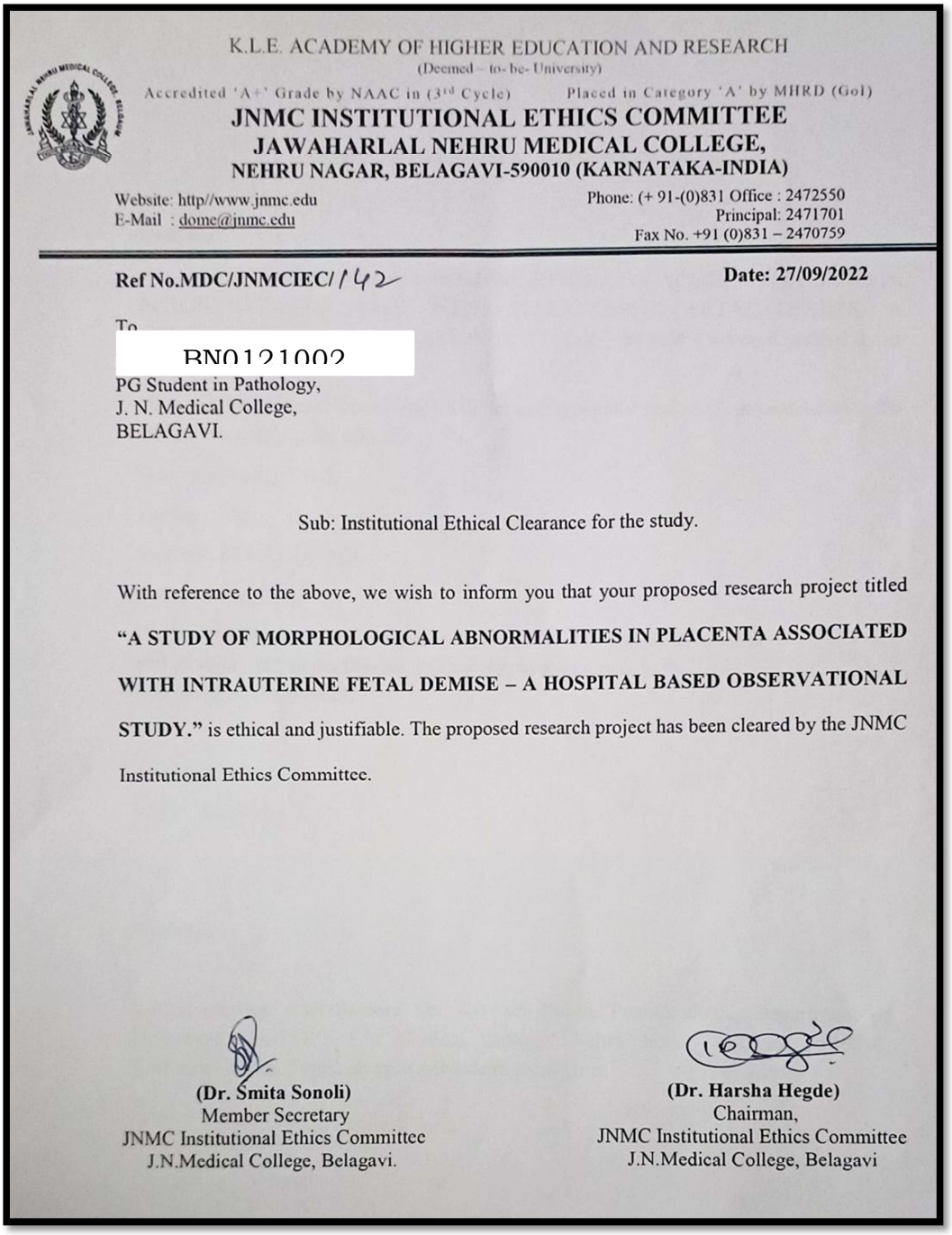

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LIST OF ABBREVIATIONS

APLA	Antiphospholipid Syndrome
AVM	Accelerated villous maturation
DVM	Delayed villous maturation
FVM	Fetal vascular malperfusion
GDM	Gestational Diabetes Mellitus
HCG	Human Chorionic Gonadotrophin
HELLP	Hemolysis Elevated liver Enzymes Low Platelet
IUFD	Intrauterine Fetal demise
MFI	Maternal floor infarction
MPVF	Massive perivillous fibrin deposition .
MVM	Maternal vascular malperfusion
PE	Pre- Eclampsia
VFN	Villous fibrinoid necrosis

ABSTRACT

Background: The primary obstetric challenge, IUFD, is largely contributed by placental factors. Our study aims at determining histopathological placental lesions in IUFD and its association with maternal clinical conditions.

Methods: The study included 100 cases of pregnant women suffered from IUFD. Placenta were collected for histopathological examination. Bits from representative area were given for processing and slides were stained with Hematoxyline and Eosin.

Results: Among the 100 cases included in this study the average maternal age group was 21-25 years and majority of the cases were primigravida with mean gestational age of 24 weeks. The average placental weight was 294 grams. Anemia was the most common maternal clinical condition observed. Majority of the lesions were in the category of maternal vascular malperfusion with accelerated villous maturation was the most common histopathological lesion observed. The most common placental lesion observed in cases of gestational diabetes mellitus was calcification and chorangiosis, with villitis and calcification were seen more in the cases of pre-eclampsia. Villous fibrinoid necrosis was seen in majority of the cases of hypothyroidism however in anemia and gestational hypertension infarction deciduitis and calcification were most common lesions. No significant association was observed between maternal clinical conditions and its effect on placental histopathology.

Conclusion: Our study concludes that placental histopathological lesions occur in the case of IUFD. Further studies are required to identify more causes of morphological placental lesions.

Keywords: IUFD, accelerated villous maturation, villous fibrinoid necrosis, anemia,gestational diabetes, hypothyroidism**,** gestational hypertension.

TABLE OF CONTENTS

SL NO.	TOPIC	PAGE NO.
01	INTRODUCTION	1
02	OBJECTIVES	2
03	REVIEW OF LITERATURE	3-23
04	MATERIALS AND METHODS	24-26
05	RESULTS	27-47
06	DISCUSSION	48-59
07	SUMMARY	60-61
08	CONCLUSION	62
09	LIMITATIONS	63
10	BIBLIOGRAPHY	64-75
11	ANNEXURES	76-80
	ANNEXURE-I – CONSENT FORMS	76-77
	ANNEXURE-II – PROFORMA	78
	ANNEXURE-III – H & E STAINING PROCEDURE	79
	ANNEXURE-IV – KEY TO MASTERCHART	80
	ANNEXURE-V - MASTERCHART	-

LIST OF FIGURES

FIG. NO.	TITLE	PAGE NO.
01	FORMATION OF CHORIONIC VILLI	**5**
02	FORMATION OF CYTOTROPHOBLASTIC SHELL	**6**
03	TYPES OF PLACENTA	**9**
04	TYPES OF PLACENTA BASED ON SHAPE	**9**
05	PLACENTA IN EARLY GESTATION	**10**
06	PLACENTA IN TERM GESTATION	**11**
07	AGE DISTRIBUTION	**27**
08	GRAVIDITY STATUS	**28**
09	CONSANGUINITY STATUS	**29**
10	HISTOPATHOLOGICAL LESIONS	**31**
11	TYPE OF LESION	**31**
12	ASSOCIATION BETWEEN STATUS OF GESTATIONAL DIABETES WITH HISTOPATHOLOGICAL PLACENTAL LESIONS.	**32**
13	ASSOCIATION BETWEEN STATUS OF PRE- ECLAMPSIA WITH HISTOPATHOLOGICAL PLACENTAL LESIONS	**33**
14	ASSOCIATION BETWEEN STATUS OF HYPOTHYROIDISM WITH HISTOPATHOLOGICAL PLACENTAL LESIONS	**34**
15	ASSOCIATION BETWEEN STATUS OF GESTATIONAL HYPERTENSION WITH HISTOPATHOLOGICAL PLACENTAL LESIONS	**35**
16	ASSOCIATION BETWEEN STATUS OF ANEMIA WITH HISTOPATHOLOGICAL PLACENTAL LESIONS	**36**
17	GROSS IMAGE OF PLACENTA SHOWING AREAS OF INFARCTION	**37**

18	GROSS IMAGE OF PLACENTA SHOWING AREAS OF HEMORRHAGE	**38**
19	GROSS IMAGE OF PLACENTA SHOWING AREAS OF HEMORRHAGE	**39**
20	PLACENTA SHOWING ACCELERATED VILLOUS MATURATION	**40**
21	PLACENTA SHOWING AVM WITH INCREASED SYNCYTIAL KNOTS	**40**
22	PLACENTA SHOWING GIANT SYNCYTIAL KNOTS	**41**
23	PLACENTA SHOWING AREAS OF CALCIFICATION	**41**
24	PLACENTA SHOWING AREAS OF CALCIFICATION	**42**
25	PLACENTA SHOWING AREAS OF INFARCTION	**42**
26	PLACENTA SHOWING AREAS OF INFARCTION AND CALCIFICATION	**43**
27	PLACENTA SHOWING CHORANGIOSIS	**43**
28	PLACENTA SHOWING CHORANGIOSIS	**44**
29	DECIDUITIS- PLACENTA SHOWING NEUTROPHILIC INFILTRATE IN DECIDUAL LAYER	**44**
30	FIBRINOID NECROSIS OF VESSEL WALL	**45**
31	VILLITIS-PLACENTA SHOWING NEUTROPHILIC INFILTRATE IN VILLI AND INTERVILLOUS SPACE.	**45**
32	VILLITIS-PLACENTA SHOWING NEUTROPHILIC INFILTRATE IN VILLI AND INTERVILLOUS SPACE	**46**
33	PLACENTA SHOWING VILLOUS FIBRINOID NECROSIS	**46**
34	PLACENTA SHOWING VILLOUS FIBRINOID NECROSIS	**47**

LIST OF TABLES

TABLE NO.	TITLE	PAGE NO.
01	GESTATIONAL AGE	**28**
02	PLACENTAL WEIGHT IN GRAMS AND PLACENTAL AREA	**29**
03	MATERNAL DISEASES	**30**
04	AGE DISTRIBUTION	**48**
05	CONSANGUINITY	**49**
06	PLACENTAL WEIGHT	**50**
07	MEDICAL DISEASES IN PREGNANCY	**50-51**
08	HISTOPATHOLOGICAL LESIONS	**53**
09	TYPE OF LESION	**54**
10	ASSOCIATION BETWEEN GESTATIONAL DIABETES AND PLACENTAL LESIONS	**55**
11	ASSOCIATION BETWEEN PRE-ECLAMPSIA AND PLACENTAL LESIONS.	**56**
12	ASSOCIATION BETWEEN HYPOTHYROIDISM AND PLACENTAL LESIONS.	**57**
13	ASSOCIATION BETWEEN GESTATIONAL HYPERTENSION AND PLACENTAL LESIONS.	**58**
14	ASSOCIATION BETWEEN ANEMIA AND PLACENTAL LESIONS.	**59**

INTRODUCTION

Intrauterine fetal demise (IUFD) is the most serious obstetric challenge. Fetal mortality that occurs after the 20th week of gestation is known as intrauterine fetal death, or IUFD[1]. The frequency of IUFD recorded from western countries ranges from 4.7 to 12 per 1000 live births, however the prevalence documented in India ranges from 24.4 to 41 per 1000 live births [2]. In India, there is an exceptionally high prevalence of maternal clinical risk factors during pregnancy, such as anemia, diabetes, hypothyroidism, and hypertension [2].

Approximately 60% of IUFD are thought to have placental causes. Even with enhanced prenatal screening, IUFD and obstetric complications are unavoidable [3]. Across all gestational ages, antepartum IUFD are multi factorial and are primarily caused by placental abnormalities [3]. The classification scheme used to report placental lesions varies, according to a thorough examination of the literature [4]. In view of this lack of specificity, placental factors causing intrauterine growth disorders have been reported at a higher rate, and despite studies from the same population group demonstrating the incidence and obstetric complications associated with IUFD, there is a dearth of literature on these factors [4,5].

Presently, the literature has inadequate data with findings of maternal conditions influencing placental morphology, and there are relatively few studies reporting placental lesions and their correlation with fetal deaths and unexplained stillbirths. This study therefore seeks to establish a correlation between clinical conditions of the mother affecting morphological changes in placenta, ultimately leading to unfavorable pregnancy outcomes.

OBJECTIVES

1. To study morphological abnormalities in placenta associated with intrauterine fetal demise.

2. To determine effect of maternal clinical diseases on placental morphology and its association with pregnancy outcome.

REVIEW OF LITERATURE

EMBRYOLOGICAL DEVELOPMENT OF PLACENTA

The Placenta functions as a temporary extracorporeal organ facilitating communication, nutritional exchange and protection between the growing fetus and mother [6]. It originates from the trophoblastic cells, which are precursor cells of the placenta in humans [6].

A unilaminar single fetal membrane is formed by the trophoblastic cells during the implantation process. After the blastocyst formation, they differentiate into bilaminar membrane, which are necessary for the development of chorionic villi [7].

The cell borders disappear from the trophoblastic cells closest to the decidua. These cells combine to form multiple layers which are devoid of distinct cell borders and form a single continuous sheet of cytoplasm with multiple nuclei [7]. This formed tissue is called as the syncytium. This trophoblastic layer is known as the syncytiotrophoblast or plasmodiotrophoblast layer [7].

The trophoblastic cells maintain their cell borders as they create the second layer, known as the cytotrophoblast or langhans layer, which is located on the extraembryonic mesoderm deep within the syncytium [7,8]. This distinct outlined single layer of cuboidal cells is in close proximity to the extraembryonic mesoderm. These three components- mesoderm, cytotrophoblast, and syncytiotrophoblast all contribute to the development of chorionic villi [7,8].

These three layers form the chorion along the developing embryo. Chorionic villi develop from the chorion and form a chorionic sac by the beginning of the 8th week of intrauterine life and are invaded by Allantoic vessels. The structure of the

chorionic villi varies at different developmental stages. The three types of villi are seen [7,8].

1. Primary villi: They are formed by a central core of cytotrophoblast covered by a layer of syncytiotrophoblast with adjacent villi separated by inter villous space [9].

2. Secondary villi: They are of three layers. The Outer layer of syncytiotrophoblast, intermediate layer of cytotrophoblast, and an inner layer of extraembryonic mesoderm [9].

3. Tertiary villi: They are similar to secondary villi with fetal blood capillaries present in the mesoderm [9].

The various processes in the formation of villi are :

1. Formation of Primary chorionic villi : The trabeculae and lacunae are filled with maternal blood and are arranged radially around the blastocyst which initially comprise the syncytiotrophoblastic cells. The cytotrophoblasts divide and grow into each trabeculus [7,9,10]. The trabeculus then develops a cytotrophoblastic core and an outer layer of syncytiotrophoblast. The formed trabeculus is known as the primary villus, and the lacunar space is known as the intervillous space [7,9,10].

1. Formation of Secondary chorionic villi: The center of primary villi is invaded by extraembryonic mesoderm. The villi now has a mesoderm core covered by syncytiotrophoblast and cytotrophoblast. This formed structure is called as secondary villi [7,9,10].

2. Formation of Tertiary chorionic villi: The Blood vessels invade the mesoderm and form the core of each villi. This type of villi is known as tertiary villi.

The blood vessels of the villi connect with the circulatory system of the embryo. The villi transport fetal blood, while the intervillous space transports maternal blood [7,9,10].

3. Formation of Cytotrophoblastic shell: The cytotrophoblast that forms the villi does not penetrate the entire thickness of the syncytium and thus does not make contact with the decidua. Each villus syncytium allows the cytotrophoblast to emerge from them[7,9,10]. The cytotrophoblasts spread out to form a layer that completely separates the syncytium from the decidua. This formation is termed as cytotrophoblastic shell layer. The cells in this shell proliferate to form the placenta which further grows in size [7,9,10].

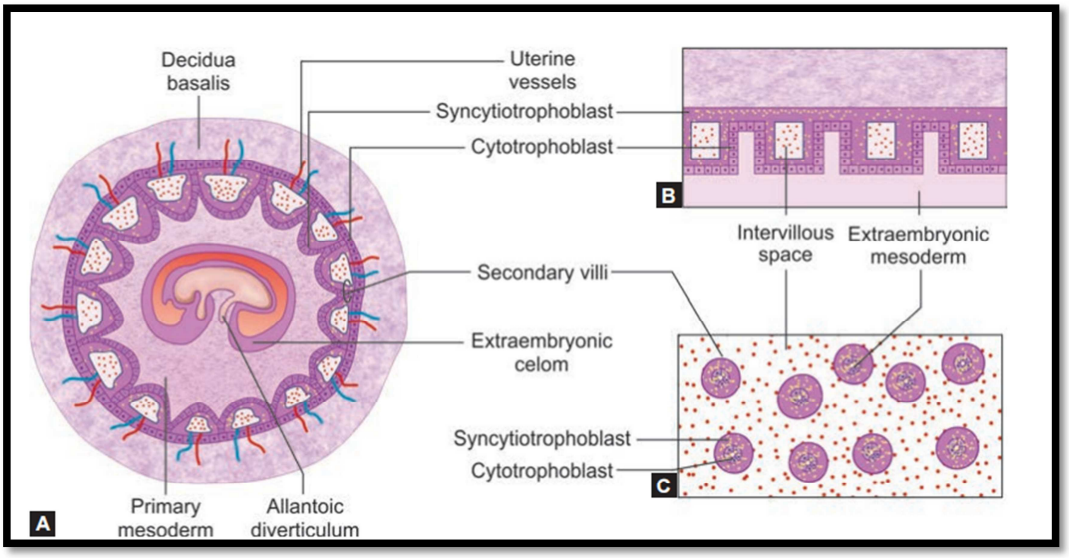


FIGURE 1: Formation of Chorionic Villi

(Image source: Singh I, Subhadra D. Inderbir Singh's Human embryology. Jaypee. 2018;73–97)[7]

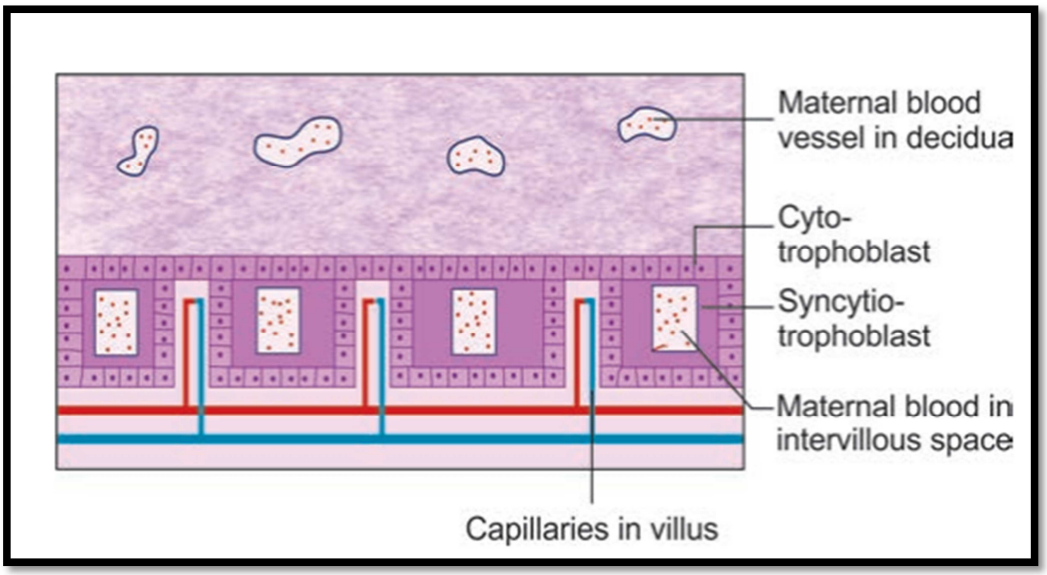


FIGURE 2: Formation of Cytotrophoblastic Shell

(Image source: Singh I, Subhadra D. Inderbir Singh's Human embryology. Jaypee. 2018;73–97)[7]

ANATOMY OF PLACENTA

The placenta is a discoid organ with fetal and maternal components . It is consists of two surfaces which are maternal and fetal , two types of cotyledons and a peripheral margin. At term the placenta weighs approximately 500gms, with diameter of 15-20cm and thickness of 3cm [7,11].

Maternal Components*:* The endometrial decidual plate is a contributing factor of maternal component of placenta. Maternal side of placenta has an uneven and rough surface. These are known as maternal cotyledons and are divided into several lobes [7,11] . The septae extend into the intervillous space through maternal surface. The base of the septa are visible as grooves and cotyledons appear as convex areas bounded by the grooves. The placenta has between 15-20 maternal cotyledons [7,11]. The anchoring villi and their branches are present in two to four per maternal cotyledon. Fetal

cotyledons consist of one anchoring villi and its offshoots, the ramus chorii, ramuli chorii, and floating villi [7,11].

Fetal components*:* Chorionic plate, also known as chorion frondosum, is responsible for the formation of fetal components. The fetal membrane amnion covers the surface, and the umbilical cord is attached close to its center. The fetal surface is smooth and has an amnion covering over it [7,11]. The umbilical cord is attached near its center. Fetal cotyledons which are 40–60 extensions, emerge from the chorionic plate and move in the direction of the decidua basalis [7,11,12]. Every fetal cotyledon has a stem villus chorii that ramifies into several branches called ramus chorii, each of which further subdivides into ramuli chorii in a manner akin to a tree's branches [7,11,12].

Their terminal ramifications are referred to as chorionic villi, and they resemble fingers. Anchoring villi are those that are affixed to decidua basalis. Some are referred to as floating villi because they float in the maternal blood that runs between the villi.

The periphery of placenta displays the fetal membrane, which is supplied from the inside out by the decidua capsularis, decidua parietalis, chorion and amnion. The decidua and placenta are expelled after birth[11,12].

TYPES OF PLACENTA

They are classified as follows

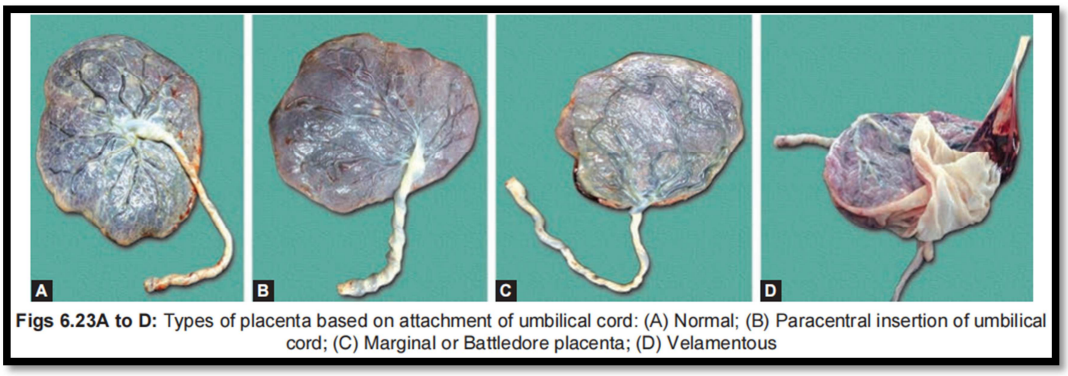
A) Depending on the shape of placenta they are classified as:[7]

1. Discoid : The placenta is round or disc shaped [7].
2. Bidiscoidal: It is made of two discs [7] .
3. Oval [7] .

4. Triangular [7] .
5. Irregular [7] .
6. Lobed : It is divided into lobes [7].
7. Diffuse placenta membranacea : The chorionic villi are present all-round the blastocyst [7].
8. Placenta succenturiata: One small part of the placenta is separated from the rest of the placenta [7].
9. Fenestrated : The placenta shows opening [7] .
10. Circumvallate : The peripheral edge of placenta is covered by a circular fold of decidua [7].

B) According to the Insertion of umbilical cord they are classified as [7].

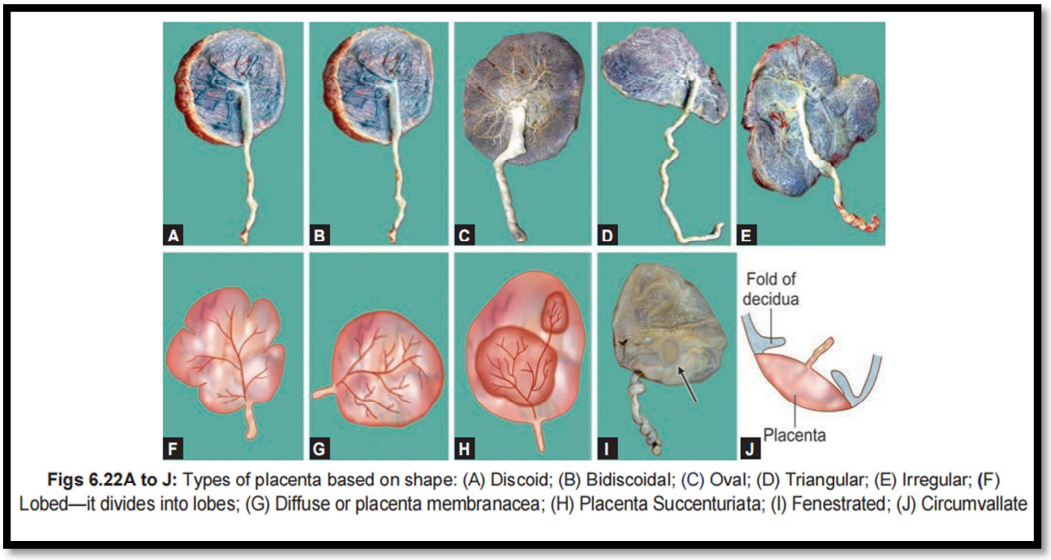
1. Normal :Central insertion[7] .
2. Paracentral[7].
3. Marginal or battledore placenta : The umbilical cord is attached to placental margin[7] .
4. Velamentous : The Umbilical cord is attached to the fetal membrane close to the peripheral margin of placenta[7].



Figs 6.23A to D: Types of placenta based on attachment of umbilical cord: (A) Normal; (B) Paracentral insertion of umbilical cord; (C) Marginal or Battledore placenta; (D) Velamentous

FIGURE 3: Types of placenta

(Image source: Singh I, Subhadra D. Inderbir Singh's Human embryology. Jaypee. 2018;73–97)[7]



Figs 6.22A to J: Types of placenta based on shape: (A) Discoid; (B) Bidiscoidal; (C) Oval; (D) Triangular; (E) Irregular; (F) Lobed—it divides into lobes; (G) Diffuse or placenta membranacea; (H) Placenta Succenturiata; (I) Fenestrated; (J) Circumvallate

FIGURE 4: Types of placenta based on shape

(Image source: Singh I, Subhadra D. Inderbir Singh's Human embryology. Jaypee. 2018;73–97**)**[7]

NORMAL HISTOLOGY OF PLACENTA

A) The placenta in early gestation shows presence of branching villi growing into lacunar system which is filled with maternal blood as gestation progresses. There is presence of cores of cytotrophoblasts and intermediate trophoblast involved in further branching of villi. The villi are lined by inner layer of cytotrophoblasts and outer layer of syncytiotrophoblast[13] .

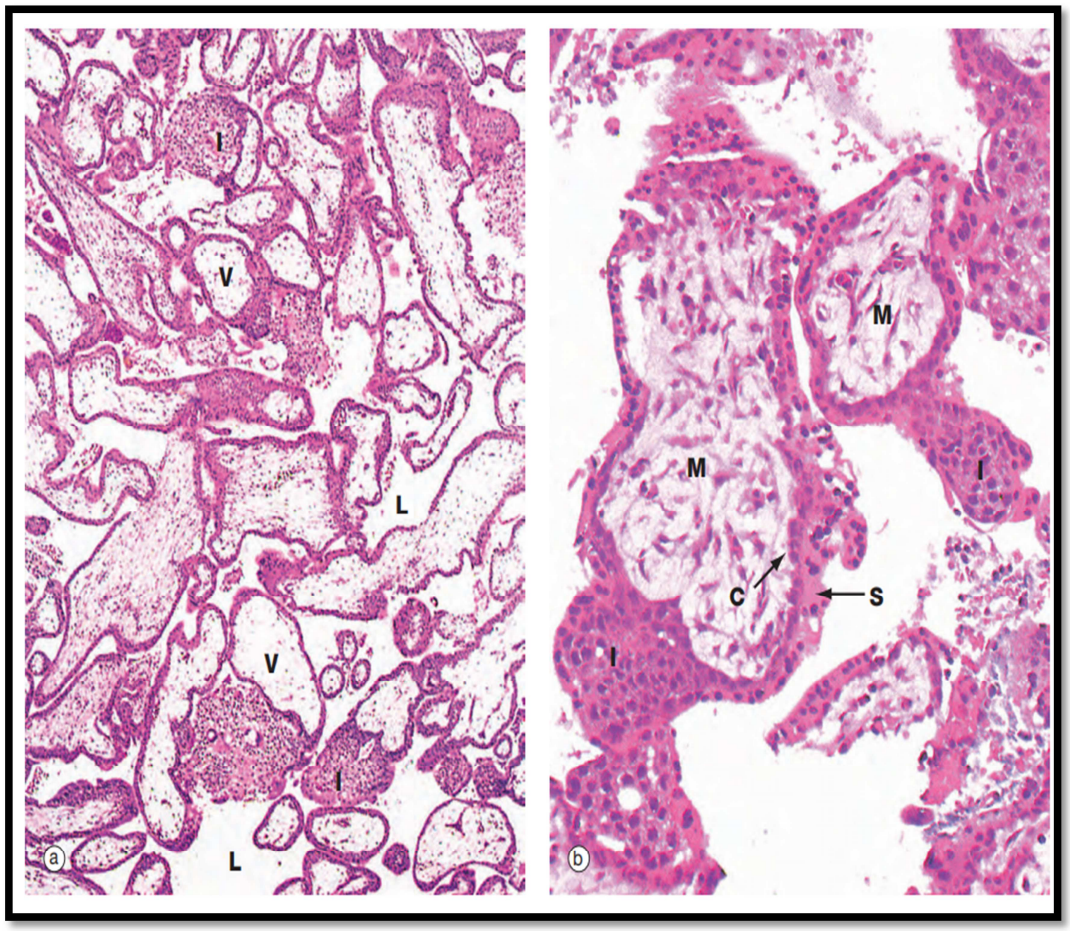


FIGURE 5 : Placenta in Early Gestation

(**Image source:** Young B, Woodford P, O'dowd G, Wheater PR. Wheater's functional histology : a text and colour atlas. 6th ed. Edinburgh: Churchill Livingstone; 2014.)[13]

B) Placenta in Term Gestation : The villi are smaller and show terminal branching. The villous cores are vascular compared to placenta in early gestation and the lacunae are seen to be filled with maternal blood. The feature of term placenta is syncytial knots. It is an aggregation of syncytiotrophoblastic nuclei with rim of cytoplasm without nucleus [13].

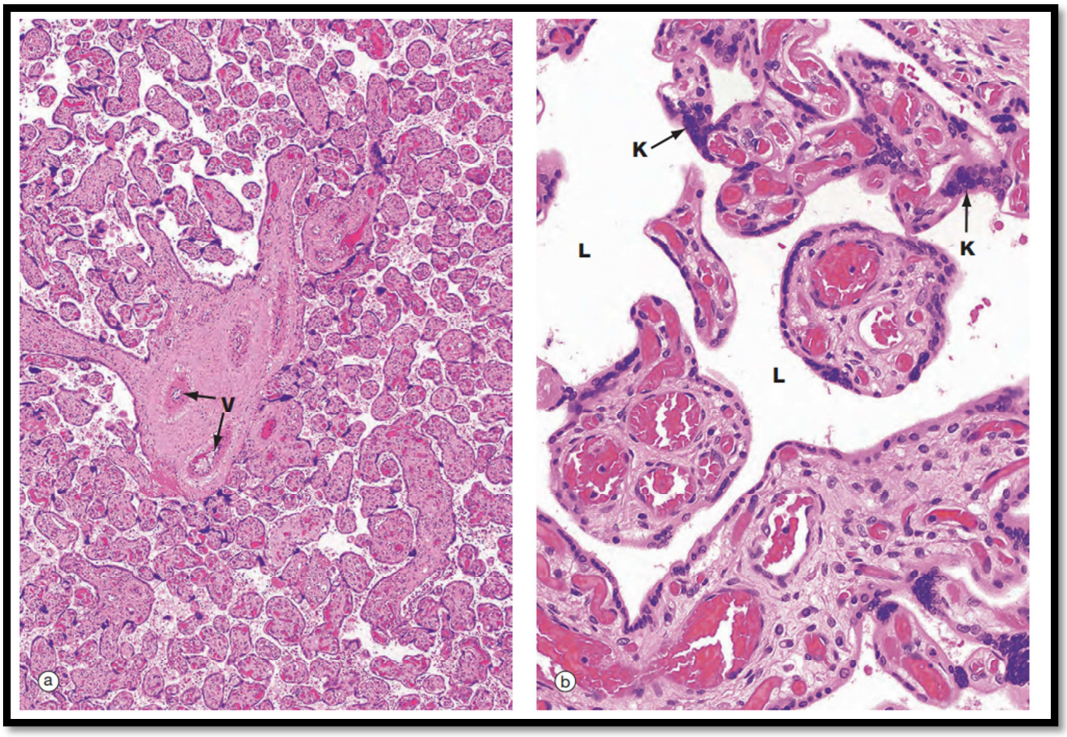


FIGURE 6 : Placenta in Term Gestation

(**Image source:**Young B, Woodford P, O'dowd G, Wheater PR. Wheater's functional histology : a text and colour atlas. 6th ed. Edinburgh: Churchill Livingstone; 2014. 375-76)[13]

PHYSIOLOGICAL FUNCTIONS OF PLACENTA

The placenta has the ability to shield the developing embryo from infections, certain xenobiotic molecules, and diseases that affect mothers. Furthermore, it secretes hormones into the circulations of both the mother and the fetus, which impact various physiological processes such as pregnancy, metabolism, fetal growth, and parturition [14] .

The physiological functions of placenta are as follows :

1. **Transport and metabolism :** The placenta transports carbohydrates, amino acids, lipids, water, vitamins, minerals, inorganic ions, oxygen to the growing fetus. Glucose from the maternal blood is transported to the fetus with the involvement of GLUT receptors as the fetus has less capacity for gluconeogenesis [6,14] .

During pregnancy, the syncytiotrophoblastic basal and microvillous membranes carry amino acids to the developing foetus. The placenta's maternal surface has lipoprotein lipase, which is able to liberate fats from the lipoprotein complexes in the mother's plasma circulation. Free fatty acids as well as glycerols can easily cross the placental syncytiotrophoblast membranes. Osmotic and hydrostatic pressures allow the water to move across the placenta [6,14].

2) Endocrine Function of Placenta : The placenta produces various endocrine, paracrine, and/or autocrine factors, such as Estrogens (produced in conjunction with the fetal adrenal gland and possibly fetal liver), Progesterone, Human chorionic gonadotropin (HCG), Human placental lactogen [14,15] .

Placental growth hormone is one of several growth factors (such as insulin like growth factors I and II, platelet-derived growth factors, and epidermal growth factor)

chemokines, eicosanoids, cytokines, and connected substances, vasoactive autacoids, Placental-derived Pregnancy-associated proteins, Corticotrophin-releasing hormone, Gonadotrophin-releasing hormone, and Thyrotrophin-releasing hormone [14,15].

The progesterone helps in maintenance of pregnancy and prevents uterine contractions. The trophoblasts produces the dimeric glycoprotein known as Human Chorionic Gonadotrophin (HCG), which is primarily secreted into the maternal circulation. It is mostly produced in the early stages of pregnancy, reaching its peak at around 8 weeks, then declining to low levels starting at about 12 weeks, before increasing once more in the later stages [6,14,15] .

The HCG level of more than 25mIU/ml is considered as significant for pregnancy and the value less than 5mIU/ml is considered as negative. It peaks at about 1000-2000mIU/ml as the gestation progresses [14,15] .

Human growth hormone and Prolactin share similarities with human placental lactogen. The syncytiotrophoblast produces it and release into the circulation of the mother and the fetus. Human placental lactogen functions to alter the course of embryonic development, control intermediary metabolism, and increase production of pulmonary surfactant, insulin, adrenocortical hormones, and insulin-like growth factors [14,15] .

2) **Protective function of Placenta :** The placenta protects fetus against circulating xenobiotic compounds in maternal blood along with exposure to various pathogens including bacteria, viruses, protozoa. It also acts as the physical protective barrier for the fetus [14,15].

PLACENTAL ABNORMALITIES

In Intra Uterine Fetal Demise (IUFD), placental abnormalities are frequently the cause of death. There are uterine artery Doppler ultrasounds available, but neither first nor second trimester placental function tests are routinely used in clinical settings to accurately predict stillbirths [16].

Promising results are shown by indices and maternal serum pregnancy associated plasmaprotein-A levels. As a result, diagnosis of placental abnormalities is frequently made based on placental histological examination only after fetal death [16].

The Amsterdam Criteria 2016 divides the placental lesions into the following [17]:

A. Maternal vascular malperfusion (MVM)[17]:

1. Retroplacental hematoma.
2. Decidual vasculopathy.
3. Delayed villous maturation.
4. Intraparenchymal hematoma.
5. Accelerated villous maturation
6. Infarction

B.Fetal vascular malperfusion(FVM)[17]:

1. Avascular villi.
2. Villous stromal vascular karyorrhexis.
3. Occlusive and non-occlusive thrombi in fetal vessels.
4. 4.Chorangioma.

Inflammatory lesions[17]:

1. Chorioamnionitis.
2. Fetal inflammatory response.
3. Villitis.
4. Intervillositis.
5. Deciduitis.

Idiopathic[17]:

1. Massive perivillous fibrin deposition (MPVF).
2. Maternal floor infarction (MFI).

MATERNAL ENVIRONMENT AFFECTING THE PLACENTA

Pregnancy related changes to the maternal environment, such as hypoxia, stress, obesity, diabetes Hypertension, Thyroid disorders, toxins, altered diet, inflammation, and decreased utero-placental blood flow, might influence the fetus growth and raise the chance of problems later in life [18,19]. Placenta being a tissue with a high metabolic activity, it reacts to these disruptions by controlling the fetus intake of oxygen and nutrients as well as the release of hormones into the circulation of the mother and fetus [18,19].

The relationship between the primary clinical features, both maternal and neonatal, and the histological examination of the placenta, which is categorized in accordance with the Amsterdam criteria, is done in order to determine the degree to which this histological examination represents placental function and the degree to which it can be utilized for the prognosis and prevention of subsequent pregnancies [17,18,19].

The maternal conditions which can affect the placenta and pregnancy outcomes are Maternal Anemia in pregnancy, Hypertension, Gestational Diabetes, Pre Eclampsia, Hypothyroidism, Gestational Thyrotoxicosis, Antiphospholipid Syndrome (APLA), Hemolysis Elevated liver Enzymes Low Platelet (HELLP) syndrome, Coagulopathies, Abnormal placental positions like Placenta Previa, Abruptio placenta [18,19].

LITERATURE SURVEY:

IUFD

Deep JP et al conducted a cross-sectional descriptive study in 2020 to investigate the prevalence of IUFD in tertiary care hospitals. 1441 births were recorded. In the third trimester between 37 and 42 weeks had the highest stillbirth rate (50.61%), with 85.18% of the population was unemployed, 36% of cases were primigravida, and 46.91% were from 20–24 age group who were affected. Hypertensive disorders accounted for 14.81% of all obstetric complications, followed by unexplained cases (13.58%) [20].

Reddy G Thapasya et al From September 2014 to September 2016 studied 344 cases of intrauterine fetal death at the Government Medical College, Haldwani. In this series, there are 41.78 IUFD's for every 1000 births. The three main causes of IUDs were abruptio placenta, eclampsia, and PE.The maximum age range for which it occurred was 21–30. IUFD prevalence peaked in multiparous. The majority of cases included unbooked emergency admissions. Male gender made up 52% of IUDF s, while female newborns made up 48%. Less than 2.5 kg was the average weight of the fetuses. Labor pains began spontaneously in 57.55% of patients. 42.44% of the patients had an induced labor. 84.88% of patients were delivered vaginally; 3.77% of

cases were delivered with outlet forceps; 12.55% of cases were delivered with an emergency LSCS. For uterine rupture, laparotomy was performed [21] .

Noor N et al conducted prospective observational analytical study A total of 3900 deliveries were reported during the course of this study; 160 of the women experienced stillbirths.For every 1000 live births, there were 41 instances of IUFD.

The mothers' most significant age range was between 20 and 25 years old. The majority of intrauterine fetal mortality cases were discovered between 32 and 36 weeks of gestation. The remaining 48 (30%) women were booked, and the remaining 112 (70%) women were unbooked and had not received any prenatal appointments. Sixty-seven (62%) of the stillbirths had weighed less than 2,500 mg. Of the causes that could be identified, 32 (20%) of the women had severe pre-eclampsia. This was established as the most frequent cause of IUFD, with anemia ranking in second with 26 (16%) of the women, fever with 10 (6.2%), gestational diabetes mellitus with 7 (5.3%), UTI with 5 (4.1%), abnormal coagulation with 7 (3.4%), and abnormal RFT with 1 (0.6%) [22] .

Budal EB et al carried out a study to assess placental pathology in both preterm and post term infants.When compared to early-term and term births, late-term and post-term babies showed noticeably greater rates of fetal inflammatory response, clinical chorioamnionitis (CCA), histological chorioamnionitis (HCA), and transfer to the newborn intensive care unit (NICU). An adjusted study revealed a correlation between HCA and maternal smoking during pregnancy and unfavorable outcomes [23].

Sundari Amirthakatesan A et al conducted a study with objective of the research was to examine the histological and gross alterations in the placentas of fetuses with growth restriction. Sample size was 50. Infarcts, intervillous thrombus,

and anomalies of the umbilical cord were the most common gross lesions found. The two prevalent histological findings were fetal vascular malperfusion (FVM) and maternal vascular malperfusion (MVM) [24].

Arora D et al conducted a study to investigate pathological characteristics such as micro vascular lesions in the placenta of pregnant patients infected with SARS-CoV-2. There were 42 cases .In 19 cases (45%), the characteristics of maternal vascular malperfusion (MVM) were evident. Of the ten instances, 23.8% had characteristics of fetal vascular malperfusion (FVM) present. Twenty patients (47.6%) had at least one acute inflammatory pathology (AIP) trait, while eighteen cases (42.8%) had indications of chronic inflammatory pathology (CIP) [25].

Feenstra ME et al conducted a randomized control trial study with 191 cases in IUGR. The pregnant women group had a greater prevalence of chorioamnionitis and maternal vascular malperfusion ($p < 0.05$ and $p < 0.01$, respectively). There were no variations observed in the placental weight or placenta maturation between the expectant management group and the group that underwent induction of labor. The groups did not vary in terms of fetal vascular malperfusion, nucleated red blood cell count, or villitis of unknown cause [26].

MATERNAL ANEMIA

Iron deficiency anemia is a prevalent pregnancy condition that affects 20–40% of expectant mothers. According to the World Health Organization, anemia in pregnancy is present if Hemoglobin (Hb) is less than 11 mg/dl and Hematocrit is less than 31% [27,28]. The placenta actively contributes to fetal programming throughout the intrauterine phase. A fully formed villous tree and improved capillarization are both essential for the spontaneous labor and are signs of placental maturity [29,30].

Sinha A et al conducted a cross-sectional descriptive study for assessing the severity of anemia in pregnancy. 200 cases were examined. Ninety percent of pregnant women had anemia overall, according to results. In accordance to the World Health Organization's classification, the majority of anemic individuals (60.5%) fall into the intermediate severity category. The time of the first prenatal visit, gravidity, and socioeconomic level were the three characteristics that were considerably linked ($P < 0.05$) to the occurrence of anemia during pregnancy [31].

Shi H et al conducted retrospective cohort study. The 17.78% of the 18 948 443 pregnant women, who were between the ages of 15 and 49, had anemia during their pregnancy. Of them, 9.04% had mild anemia, 2.62% had moderate anemia, 0.21% had severe anemia, and 5.90% had anemia of undetermined severity. Severe anemia during pregnancy was linked to higher chances of preterm birth, severe postpartum hemorrhage, and placental abruption compared to not having anemia [32].

GESTATIONAL DIABETES MELLITUS

The World Health Organization (WHO) states that hyperglycemia, or elevated plasma glucose levels, is a complication of gestational diabetes mellitus (GDM)[33] . A plasma glucose reading that is higher than the usual 7 mmol/L (126 mg/dl) and that increases to 11.1 mmol/L after loading with 75 g of glucose two hours after an oral glucose test. (200 mg/dl) is defined as Gestational Diabetes Mellitus [33,34].

Rajput R et al conducted this study to ascertain the incidence of GDM and risk factors related to it among women utilizing the ANC clinic at the tertiary care hospital in Haryana. 43 (7.1%) of the 607 women who took part in the study were diagnosed with GDM. An additional 66 women (10.87%) had a single abnormal value. Age, educational attainment, socioeconomic position, pre-pregnancy weight and BMI,

weight gain, acanthosis nigricans, and a family history of diabetes or hypertension were identified to be risk factors for GDM on bi variate analysis [35].

Vinoth N et al carried out a cross-sectional study to examine the risk factors linked to GDM and its prevalence. In the 164 studied population, GDM prevalence was 23.78%. Increased body mass index (BMI) was substantially correlated with a higher prevalence of GDM patients. Strong correlation exists between BMI>25 kg/m2 (0.001%). There is a high correlation between a family history of diabetes, a prior history of GDM ($p<0.00001$), and macrosomia/large for gestational age (LGA) babies. While parity was not statistically associated with increased prevalence of GDM ($p=0.358$), maternal age beyond 25 years old (0.001) was. Pre-eclampsia and polyhydramnios were substantially more common in GDM patients [36].

PRE-ECLAPSIA

It has been known that the placenta is essential for the development of pre-eclampsia. It is believed that changes to the arteries feeding the intervillous space are a significant factor in the origin of pre-eclampsia [37,38].

Tandur AN et al conducted a prospective observational study was carried out in 2023 at Basaveshwara Medical College in Chitradurga. 583 cases were examined thoroughly. Pre-eclampsia was present in 91 cases (15.67%) and eclampsia in 54 cases (9.26%). Pre-eclampsia and eclampsia were found to be connected with risk factors such as age, primigravida, birth interval, pre-existing disease, placental anomalies, multiple pregnancy, prior history, and proteinuria, with a statistically varying significance level of $p=0.00001$ to 0.05. Complications included preterm birth, low platelets, hemolysis, increased liver enzymes, and newborn mortality, as well as foetal development limitation [39].

F Kahnamouei et al conducted a cross-sectional study (2015) in which eight participants (3%) had eclampsia and the remaining cases (55.2%) had pre-eclampsia (41.7% with severe PE and 55.2% with mild PE). Variables like age, family history, twin birth, abortion, thrombophilia, infertility, renal failure, and urinary symptoms did not significantly correlate with the risk of Pre-eclampsia or Eclampsia [40].

HYPOTHYROIDISM

Premature labor has been linked to low thyroid function, and pre-eclampsia and fetal growth restriction, two unfavorable pregnancy outcomes that may result from impaired placentation in the early stages of gestation, have been linked to high thyroid function [41,42,43].

Dhanwal DK et al carried out a multi center, cross-sectional study that enrolled 2599 pregnant women. 13% of pregnant women (n = 388) had hypothyroidism, according to the research population, using a threshold TSH level of 4.5 µIU/ml. By applying the American Thyroid Association guidelines, this prevalence was significantly greater. Of all pregnant women (n = 613), 20.74% had anti-TPO antibodies, while pregnant women with hypothyroidism had anti-TPO antibodies in 40% of cases (n = 155) [44].

Abadi KK et al carried out a cross-sectional study to examine the extent of hypothyroidism and its effects on pregnancy. There were 23.6% of cases with hypothyroidism. Preterm birth, hypertension during pregnancy, history of recurrent pregnancy loss, overt diabetes mellitus, and hyperthyroidism were all linked to hypothyroidism during pregnancy [45].

ANTIPHOSPHOLIPID ANTIBODY (APLA) SYNDROME

Antiphospholipid syndrome (APLA Syndrome) is an autoimmune disease characterized by the presence of Antiphospholipid antibodies and clinical manifestations, including anomalies related to pregnancy and venous, arterial, or small vessel thrombotic symptoms[46,47]. Pregnancy-related APLA Syndrome is known as obstetrical APS (OAPS), and it can manifest with or without systemic symptoms [48,49].

Ravindran A et al carried out a study in a tertiary care center on the prevalence of Antiphospholipid Syndrome in women who had a poor pregnancy outcome. 27 cases or 12.5% of the 216 cases of patients with unfavorable pregnancy outcomes were found to be APLA positive [50].

Sahoo G et at conducted an observational study from March 2020 to March 2021 among pregnant women at the OBG Department, IMS, and SUM Hospital in Bhubaneswar. 25 cases out of 1260 were found to have ALPA syndrome, representing a 1.98% prevalence rate. With a mean age of 28.83 ± 3.26 years, the most common age group (40%) was 26–30 years old [51].

HELLP SYNDROME

The symptoms of the HELLP syndrome include low platelet counts, elevated liver enzymes, and microangiopathic hemolysis. In 20% of cases, it makes severe Pre eclampsia more complicated [52,53].

Kundaikar SL et al - 400 cases were studied in order to determine the incidence of HELLP syndrome in pre-eclampsia. It was discovered that 9.25% of pre-eclampsia cases had HELLP syndrome. placental abruption (35.14%), acute renal

failure (16.22%), eclampsia (5.4%), papilledema (5.41%), DIC (5.41%), and maternal mortality (8.11%) in cases of HELLP syndrome were the main maternal complications [54].

Lakshmi NK et al carried out a retrospective analysis on 102 cases of eclampsia and pre-eclampsia.Out of 91 cases of pre-eclampsia, HELLP syndrome was developed in 12 cases. Three of the eleven eclampsia cases had HELLP syndrome development [55].

MATERIALS AND METHODS

STUDY DESIGN: One year hospital based observational study.

STUDY PERIOD: January 01, 2023 to December 31, 2023

STUDY POPULATION: Pregnant women admitted in maternity ward with Intrauterine fetal demise (IUFD) at KLE's Dr. Prabhakar Kore Hospital and MRC, Belagavi.

INCLUSION CRITERIA:

1. All pregnant women with Intrauterine fetal demise after 20 weeks of gestation(second trimester and above).
2. Age more than 18 years.

EXCLUSION CRITERIA:

1. All pregnant women with Intrauterine fetal demise in 1st Trimester.
2. All placentas that were from medical termination of pregnancy due to abnormalities in fetal scan.

METHODOLOGY:

A total of 100 cases of pregnant women who suffered with intrauterine fetal demise admitted in maternity ward at KLE's Dr. Prabhakar Kore hospital, Belagavi, Karnataka were selected for the study. An informed written consent was taken in all the cases.

The information about the maternal clinical parameters and maternal clinical history was obtained from the patient records from Medical Records Department, Department of Obstetrics and Gynecology and Department of Pathology, KLE's Dr. Prabhakar Kore hospital, Belagavi.

After obtaining the above information, the placentas of the dead fetuses were collected in neutral buffered formalin and were sent in department of pathology for histopathological examination. Gross examination findings were noted and sections from representative area were taken for processing and embedding. 3-4 micron thick sections were taken and were stained with routine Hematoxyline and Eosin. The slides were examined for microscopic placental lesions.

PLACENTAL LESIONS:

The microscopic placental lesions defined according to Amsterdam Placental Workshop Group Consensus Statement (2016) are [17] :

1. **Infarction**- It is categorized under Maternal vascular malperfusion (MVM). Ischemia is seen in the villi from the periphery to the center. Tan, white patches can also be used to morphologically identify these lesions. Villi are crowded in early infarcts, and the stromal nuclear staining is lost. Persistent infarcts exhibit nuclear pyknosis and karyorrhexis together with a lack of nuclear staining, known as "ghost villi" [17,56,57.]

2.Retroplacental Haemorrhage- It is described as a collection of blood on the placental surface combined with parenchymal congestion or compression.

Microscopically there is presence of hemorrhage under decidual layer and intervillous space, along with villous crowding [17,56,57].

3.Accelerated villous maturation- In this condition short and hypermature villi for the gestational age are observed. It is also classified under maternal vascular malperfusion. Increased syncytial knots is also a feature along with alternating areas

of villous crowding and paucity. Sometimes infarcts adjacent to it can also be seen. It is a feature of pre-eclampsia, utero placental insufficiency [17,56,57].

4.Distal Villous Hypoplasia- In this condition there is reduction in number of villi compared to stem villi. There are increased syncytial knots with thin and elongated villi. It is seen in placentas with small for gestational age [17,56,57].

5.Decidual Vasculopathy- In this condition there is damage to the maternal arterioles and spiral arteries. It shows presence of atherosis, fibrinoid necrosis either with presence or absence of foam cells and mural hypertrophy [17,56,57].

6.Delayed villous maturation- It consists of villi with centrally located capillaries with reduced vasculosyncytial membranes [17,56,57].

7.Avascular Villi- It consists of 3 or more foci of 2 to 4 terminal villi with loss of capillaries with hyaline fibrosis [17,56,57].

8. **Chorangiosis**- It consists of ten or more villi with ten or more capillaries [17,56,57].

9.Intramural fibrin deposition- Fibrinoid is accumulated subendothelial or intramuscularly in the fetal blood vessels with calcification [17,56,57].

10.Villous stromal vascular karyorrhexis- Three or more foci of terminal villi consisting of karyorrhexis of fetal cells [17,56,57].

11.Villous fibrinoid necrosis- There is deposition of fibrinoid under syncytiotrophoblast and outside of the trophoblastic basement membrane [17,56,57].

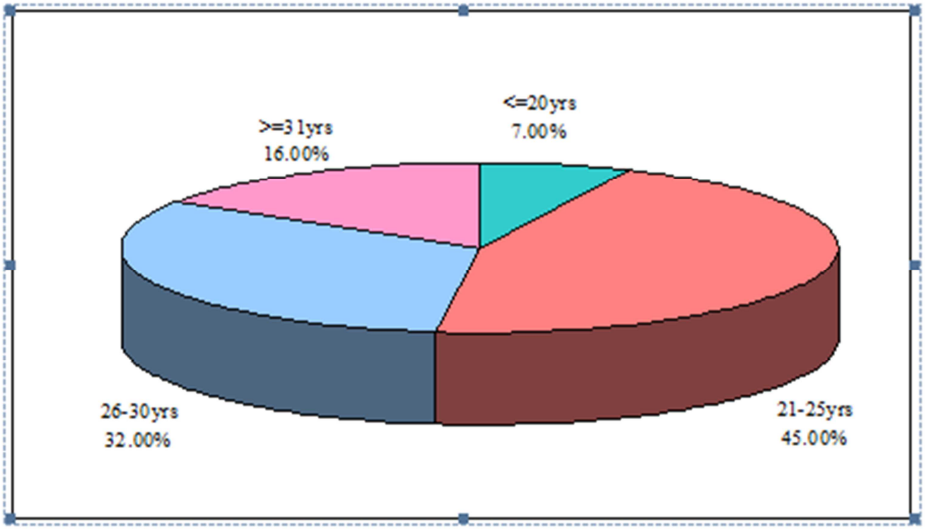
The statistical analysis was done using SPSS version 23 software and chi square test was applied for association. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

The study was conducted at KLE's Dr. Prabhakar Kore Hospital Belagavi.

100 cases of Pregnant women admitted in maternity ward with suspected fetal death and women experiencing still birth meeting the inclusion and exclusion criteria were included in the study. Histopathological examination of placentas was performed and results are as follows.

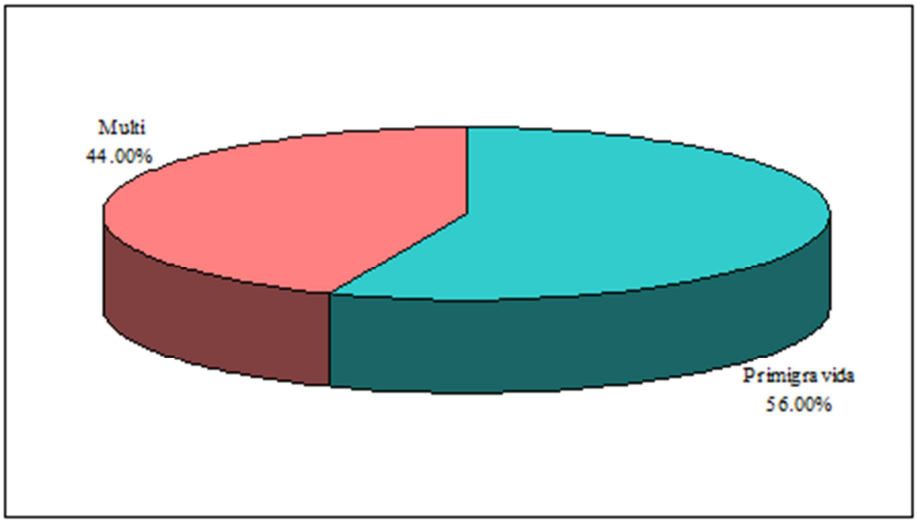
1.Age distribution



Mean Age	25.87

Patients within the age group of 21-25 years made up 45%, those with 26-30 years made up 32% while patients with above 31 years of age made upto 16%. Only 07%. were less than 20 years of age. The average age was 25.8 years. All cases were females.

2. Gravid Status



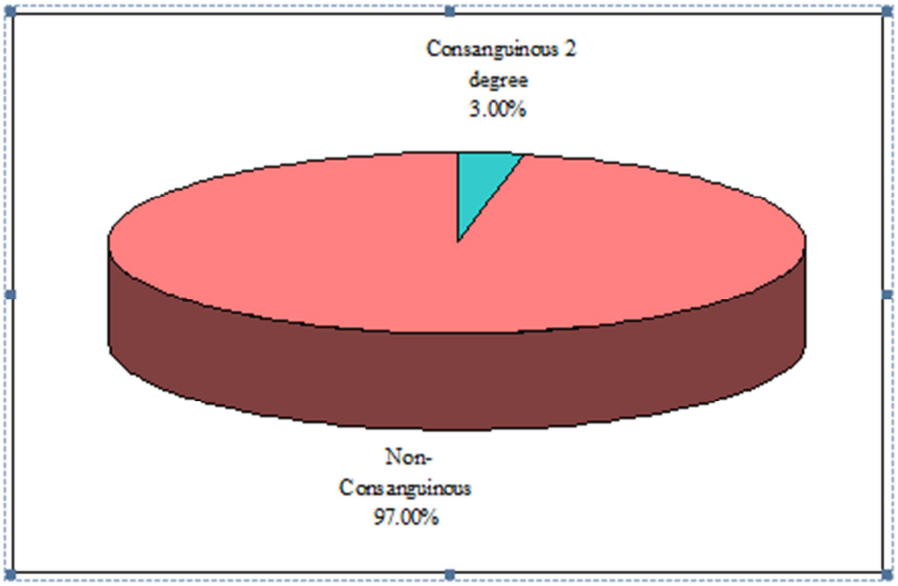
56% of the patients were Primigravida where as 44% were multigravida.

3. Gestational Age

Gestational Age	Summery
Mean	24.20
SD	4.73

The average gestational age was 24.20 weeks

4. Consanguinity Status



97% showed Non- consanguinity while 3% showed second degree consanguinity.

5. Placental weight in grams and Placental area

Summery		Placental WEIGHT in grams	Placental area
n		100.00	100.00
Minimum		35.00	45.50
Maximum		520.00	720.00
Mean		294.45	262.80
Median		300.00	247.50
Std.Dev.		89.76	109.56
95% CI for mean	Lower	276.64	241.06
	Upper	312.26	284.54

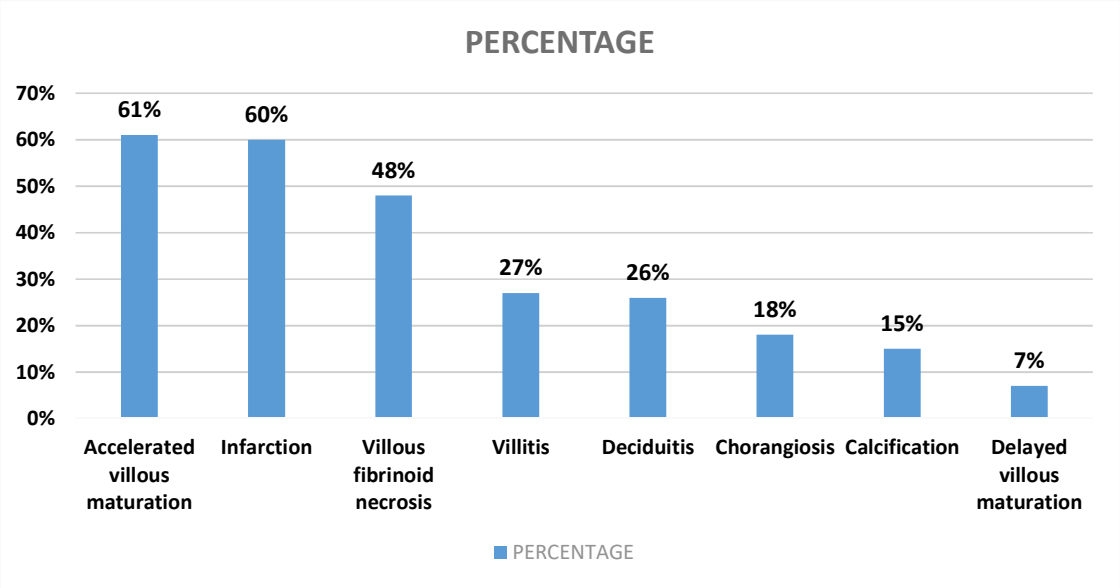
The average weight of placenta was 294.45 grams with average placental area of 262.80.

6. Maternal Diseases

Maternal disease conditions	Number	Percentage
Anemia	53	53.00
Gestational hypertension	29	29.00
Gestational diabetes	28	28.00
Pre-eclampsia	22	22.00
Hypothyroidism	12	12.00
Placenta Previa	3	3.00
Twin pregnancy	3	3.00
HELLP Syndrome	2	2.00
Abruptio placenta	1	1.00
Gestational Thyrotoxicosis	1	1.00

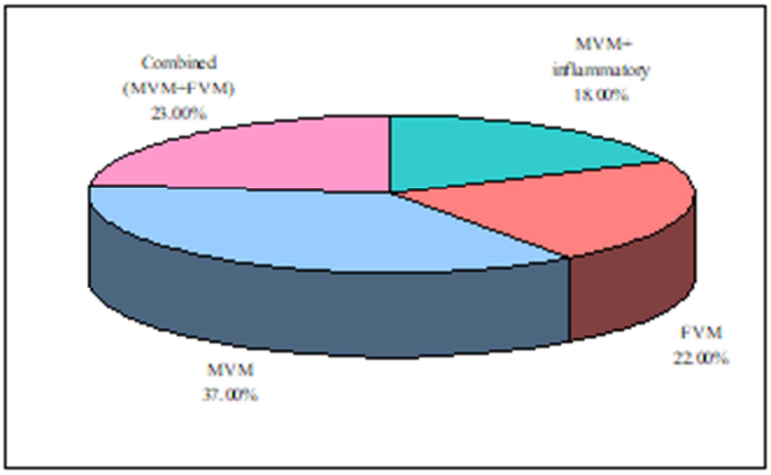
53 % of the patients were Anemic, 29% showed Gestational hypertension, 28% of the cases were of Gestational Diabetes, 22% of the cases were of Pre-Eclampsia, 12% showed Hypothyroidism, Twin Pregnancy was seen in 3%, 3% of the cases were of Placenta previa, 2 % were of HELLP Syndrome. Only 1 % of the cases were of Gestational Thyrotoxicosis, Abruptio placenta.

7. Histopathological Lesions



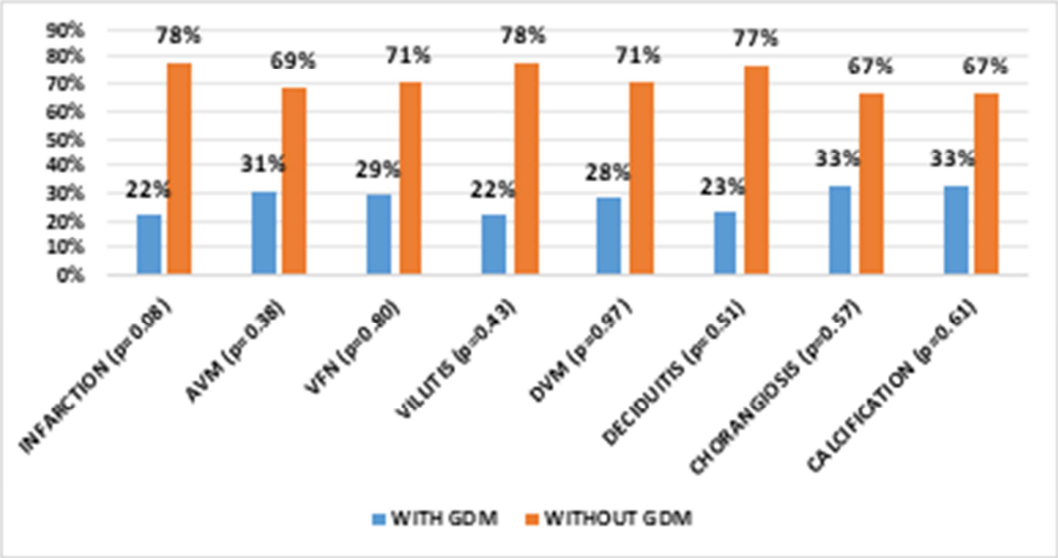
61 % of the cases were of Accelerated villous maturation, 60% showed Infarction, 48% of the cases were of Villous fibrinoid Necrosis, 27% of the cases were of Villitis, 26% showed Deciduitis, Chorangiosis was seen in 18%, 15% showed Calcification. 07% of the cases showed Delayed Villous Maturation.

8. Type of Lesion



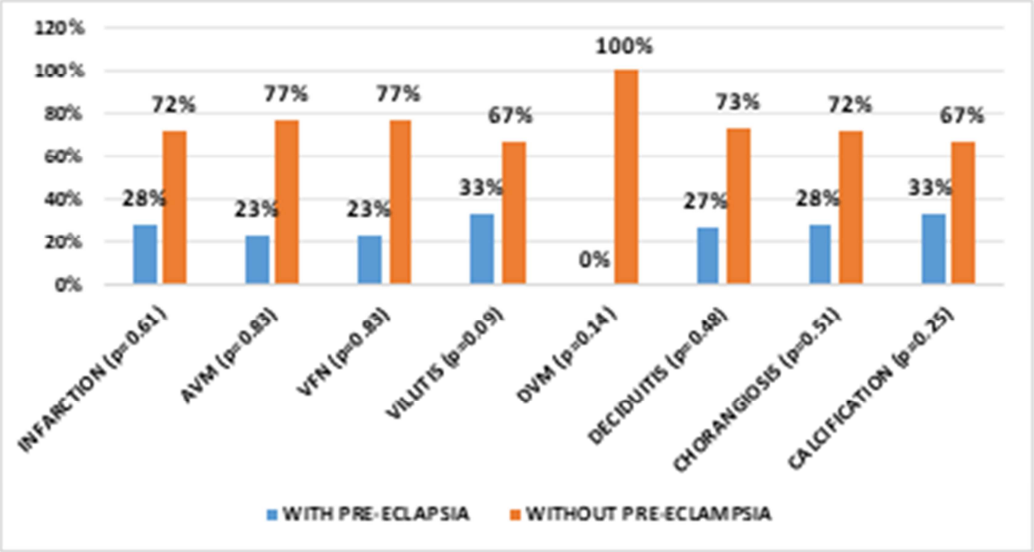
37% of the lesions were of Maternal Vascular Malformation(MVM), 22% were of Fetal Vascular Malformation (FVM), 23% were combined lesions (MVM+FVM), 18% showed maternal vascular malformation along with inflammatory lesions.

9. Association between status of Gestational diabetes with Histopathological placental lesions.



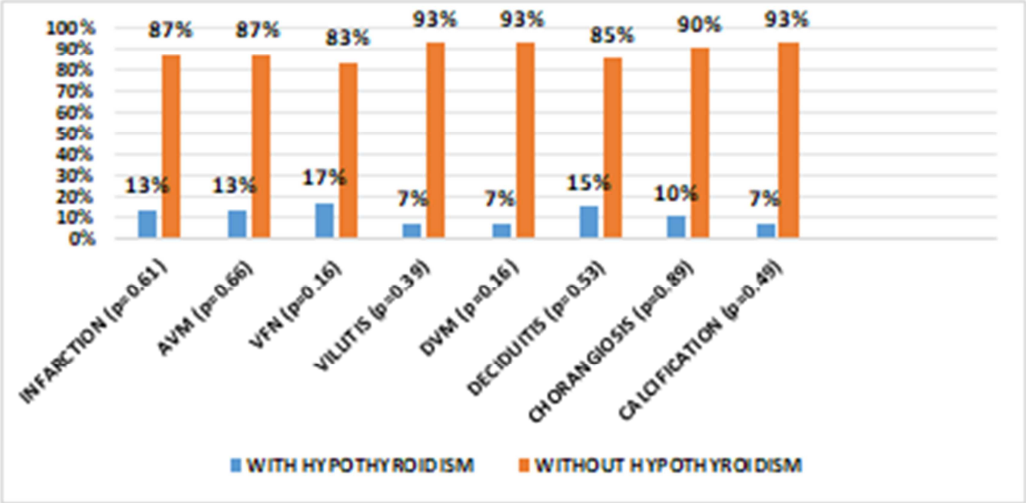
In the cases where along with placental histopathological lesions there was maternal history of gestational diabetes mellitus, p value was observed to be more than 0.05, there was no significant association between cases with history of gestational diabetes mellitus and its effect on placenta. In the cases where along with placental histopathological lesions there was no maternal history of gestational diabetes mellitus, p value was observed to be more than 0.05, there was no significant association between cases without history of gestational diabetes mellitus and its effect on placenta.

10. Association between status of Pre Eclampsia with Histopathological placental lesions



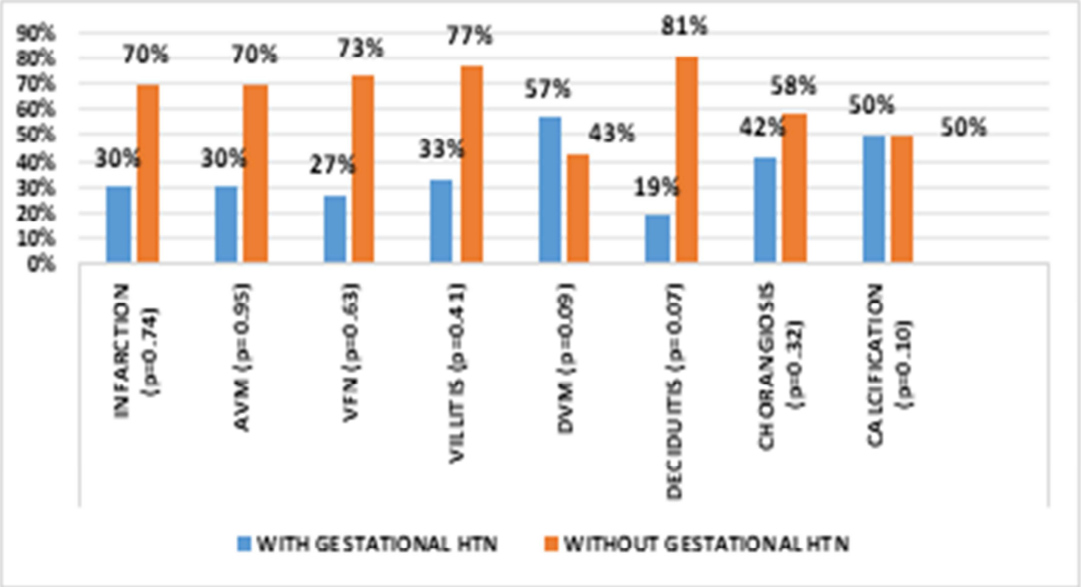
In the cases where along with placental histopathological lesions there was maternal history of pre-eclampsia, p value was observed to be more than 0.05, there was no significant association between cases with history of pre-eclampsia and its effect on placenta. In the cases where along with placental histopathological lesions there was no history of pre-eclampsia, p value was observed to be more than 0.05, there was no significant association between cases without history of pre-eclampsia and its effect on placenta.

11. Association between status of Hypothyroidism with Histopathological placental lesions



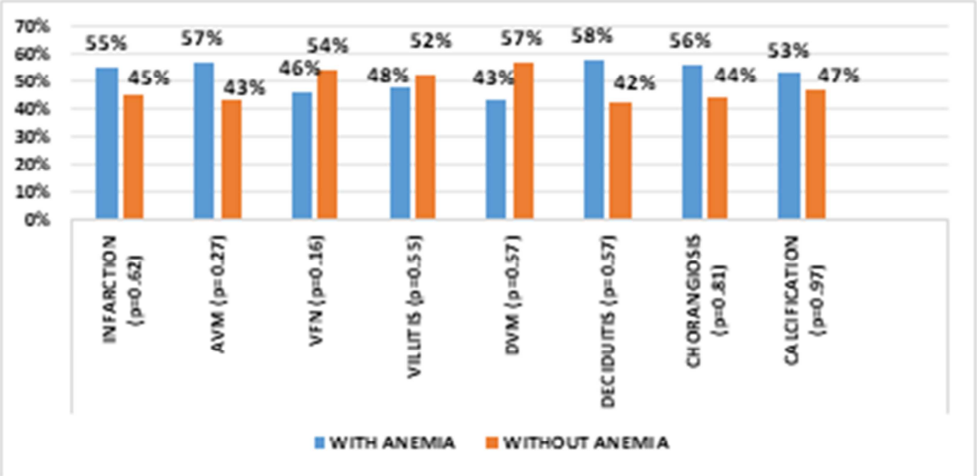
In the cases where along with placental histopathological lesions there was maternal history of hypothyroidism, p value was observed to be more than 0.05, there was no significant association between cases with history of hypothyroidism and its effect on placenta. In the cases where along with placental histopathological lesions there was no history of hypothyroidism, p value was observed to be more than 0.05, there was no significant association between cases without history of hypothyroidism and its effect on placenta.

12. Association between status of gestational hypertension with Histopathological placental lesions



In the cases where along with placental histopathological lesions there was maternal history of gestational hypertension, p value was observed to be more than 0.05, there was no significant association between cases with history of gestational hypertension and its effect on placenta. In the cases where along with placental histopathological lesions there was no history of gestational hypertension, p value was observed to be more than 0.05, there was no significant association between cases without history of gestational hypertension and its effect on placenta.

13. Association between status of Anemia with Histopathological placental lesions



In the cases where along with placental histopathological lesions there was maternal history of anemia, p value was observed to be more than 0.05, there was no significant association between cases with history of anemia and its effect on placenta. In the cases where along with placental histopathological lesions there was no history of anemia, p value was observed to be more than 0.05, there was no significant association between cases without history of anemia and its effect on placenta.

GROSS IMAGES

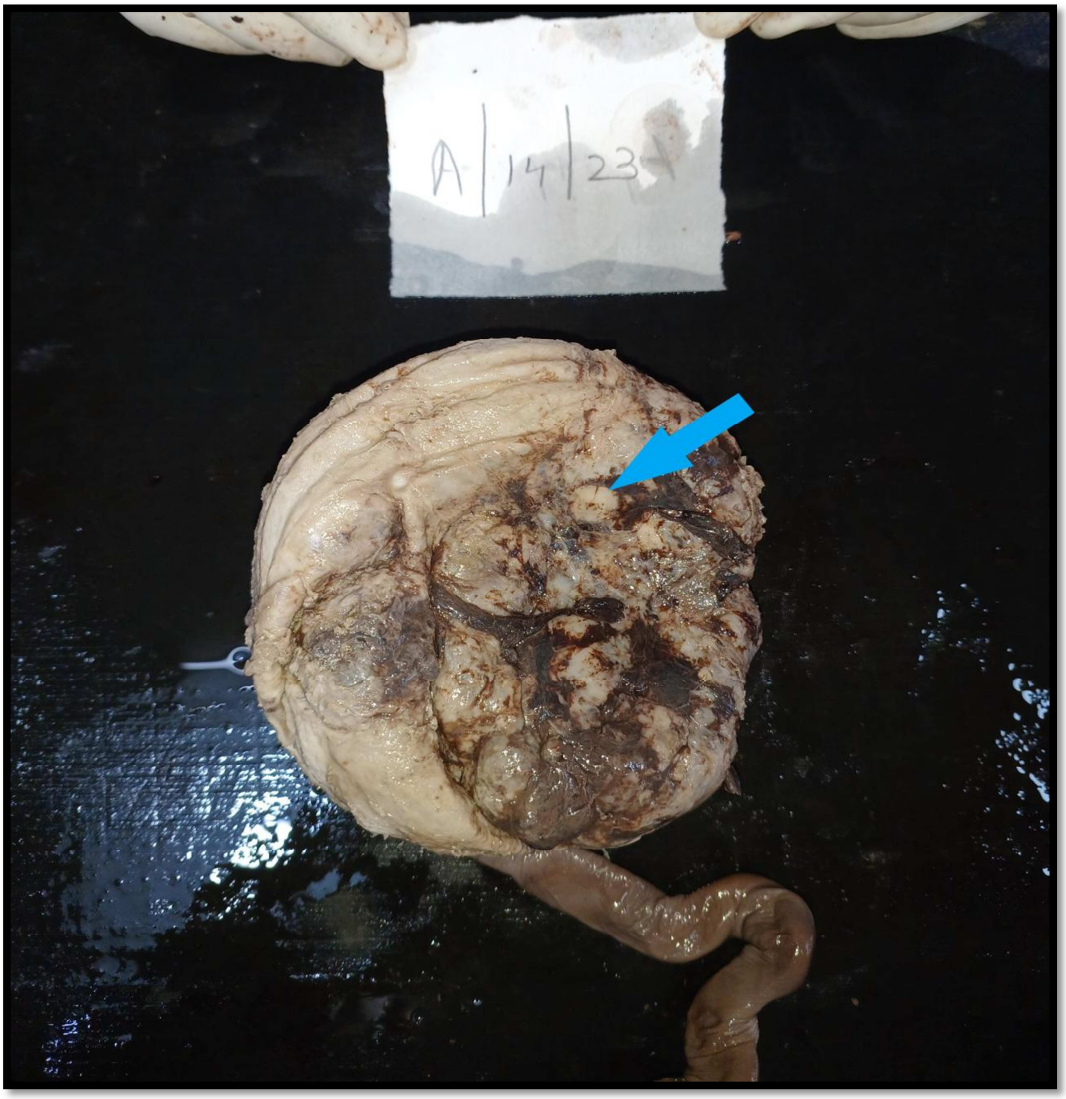


FIGURE 17 : GROSS IMAGE OF PLACENTA SHOWING AREAS OF INFARCTION

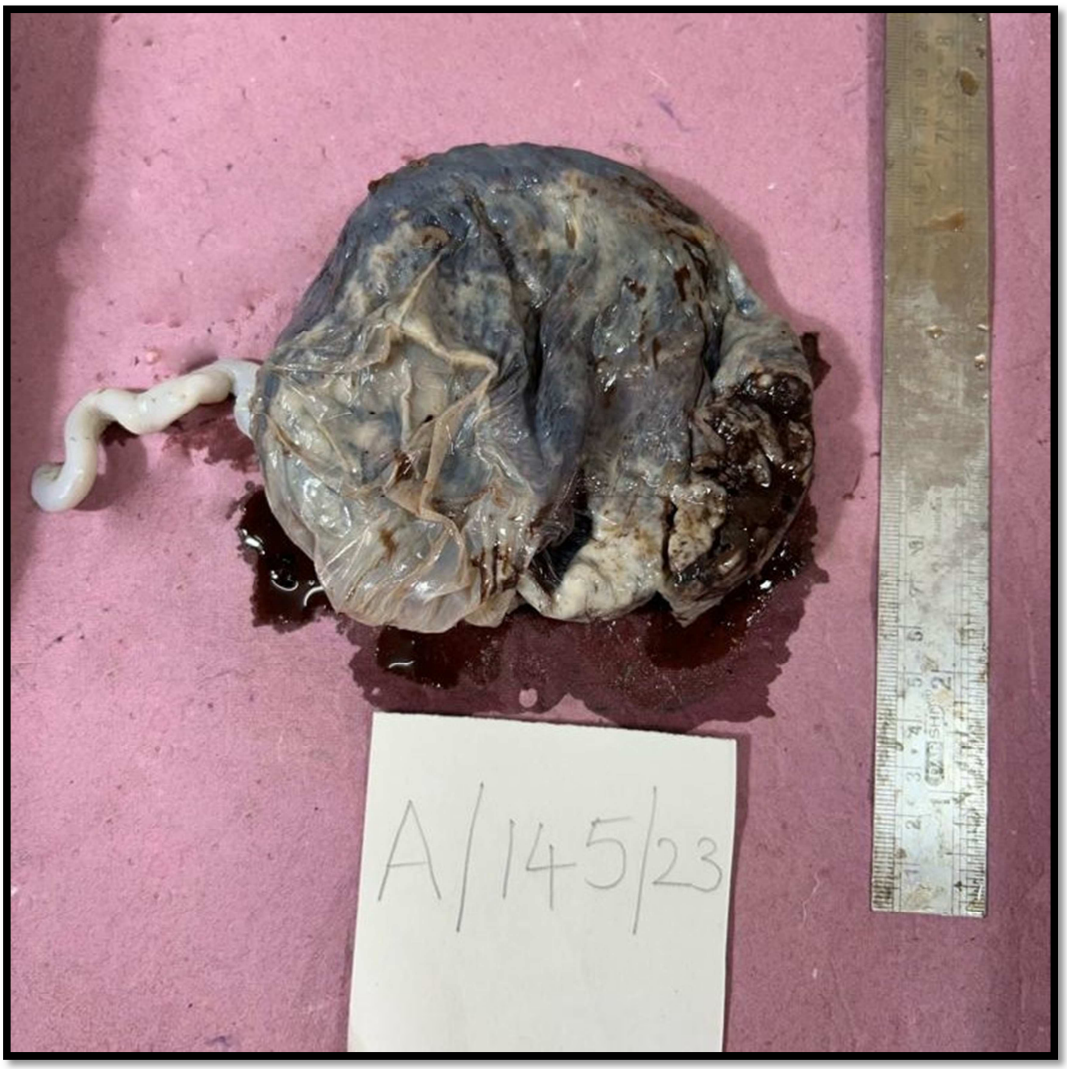


FIGURE 18 : GROSS IMAGE OF PLACENTA SHOWING AREAS OF HEMORRHAGE

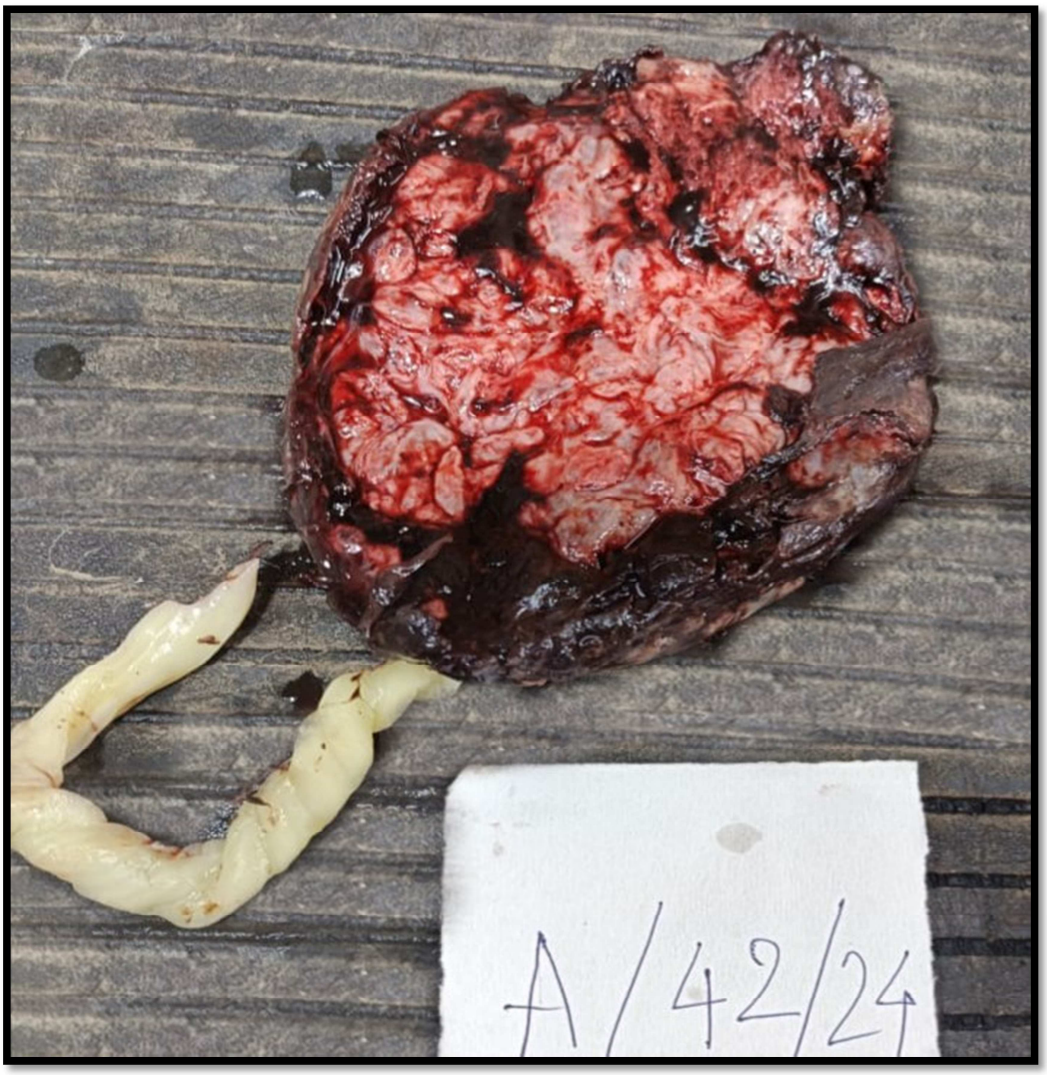


FIGURE 19 : GROSS IMAGE OF PLACENTA SHOWING AREAS OF HEMORRHAGE

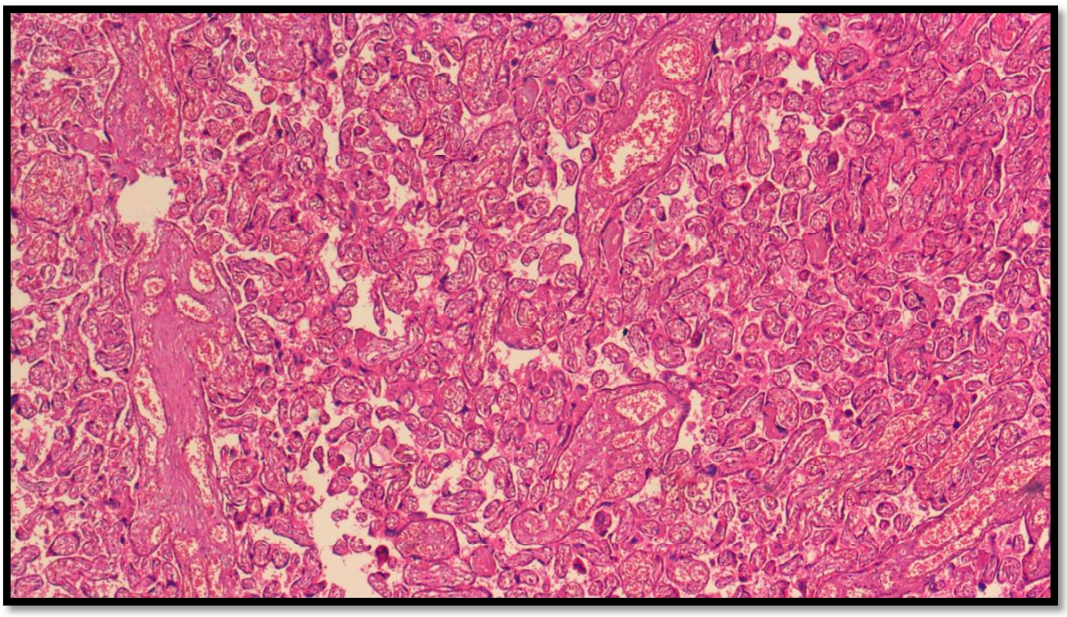


FIGURE 20 : Placenta showing Accelerated villous maturation (100X)

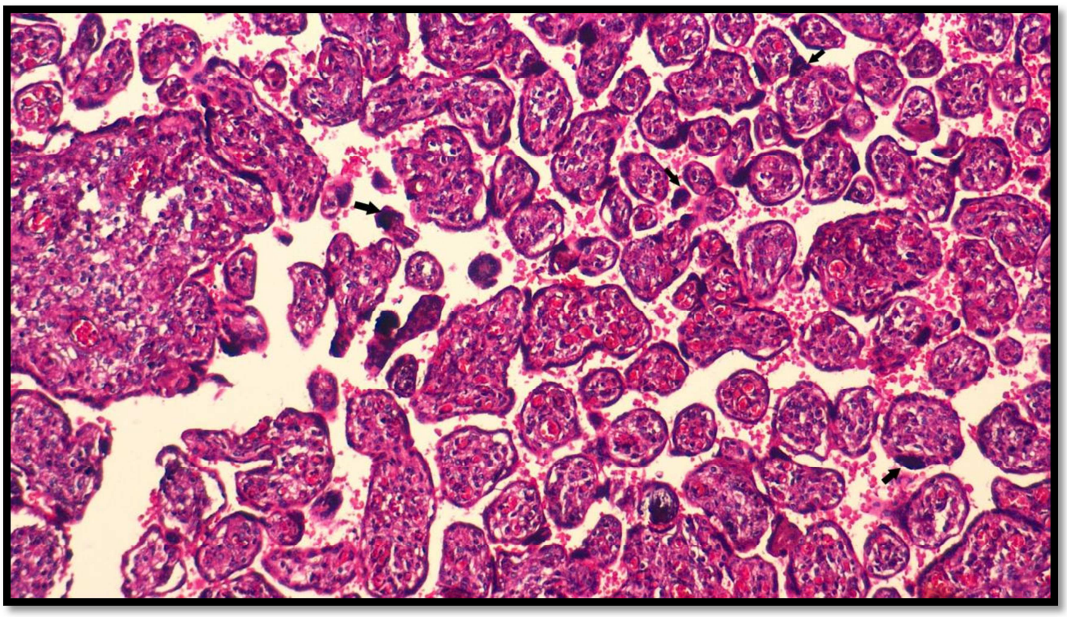


FIGURE 21 :Placenta showing AVM with increased syncytial knots(200X)

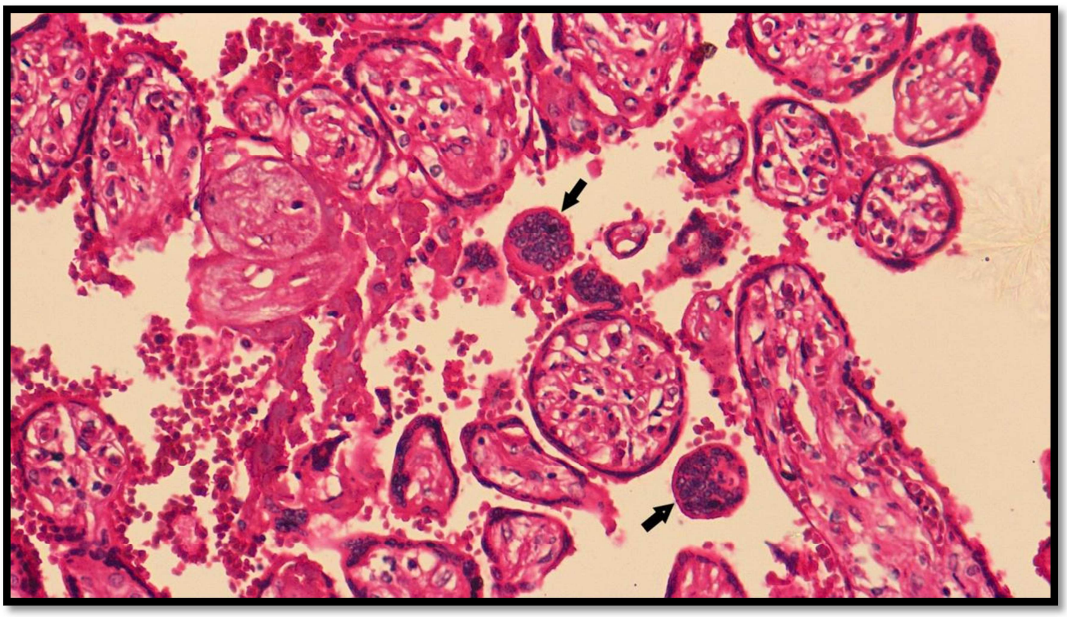


FIGURE 22 : Placenta showing Giant syncytial knots (400X)

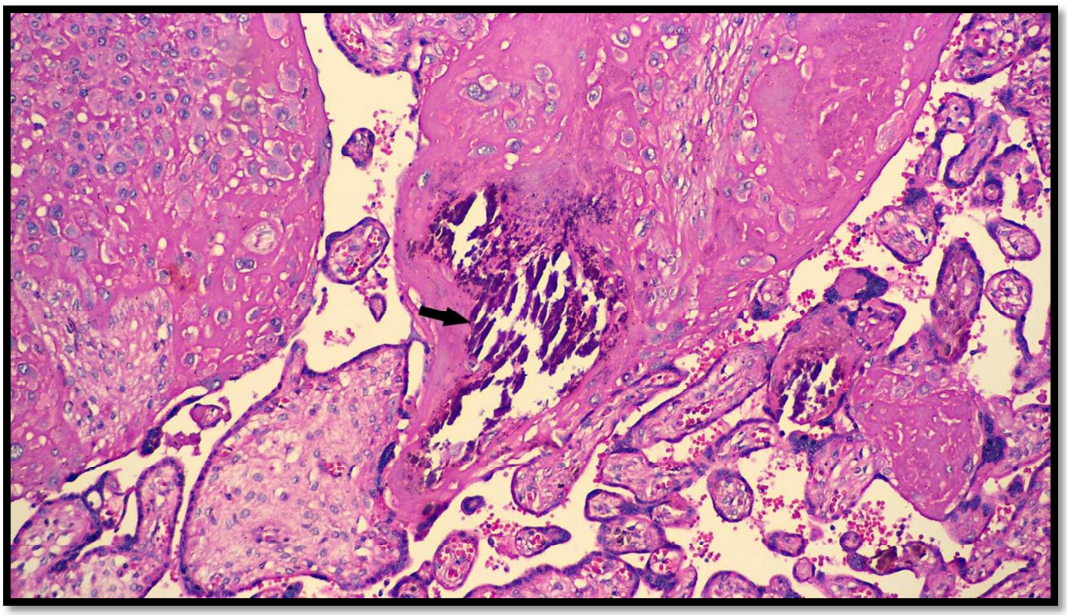


FIGURE 23 : Placenta showing Areas of Calcification (40X)

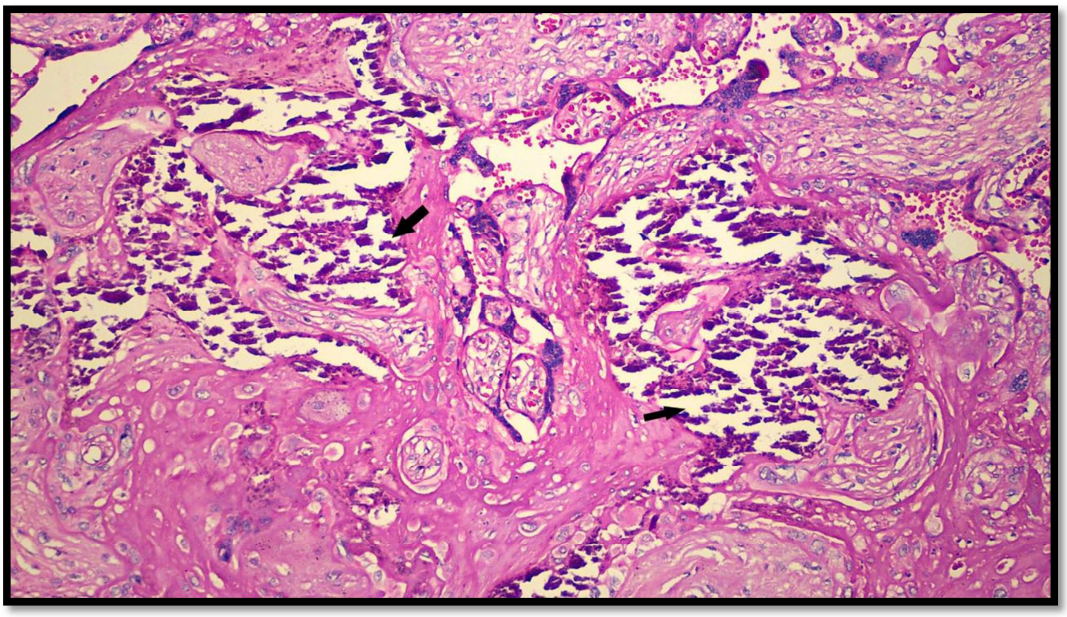


FIGURE 24: Placenta showing Areas of Calcification (200X)

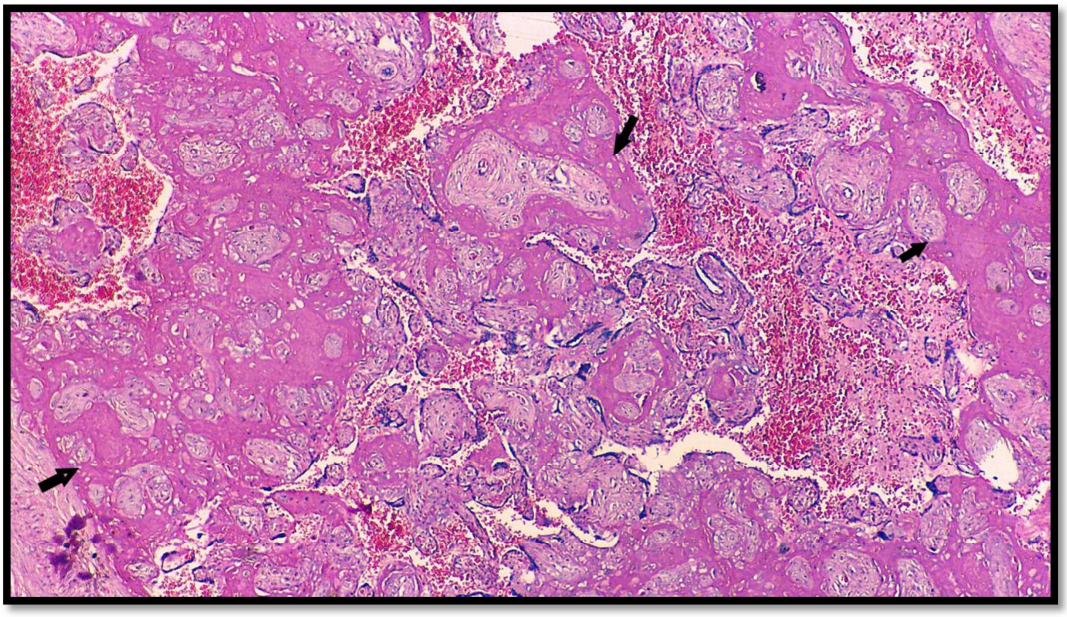


FIGURE 25: Placenta showing Areas of Infarction(200X)

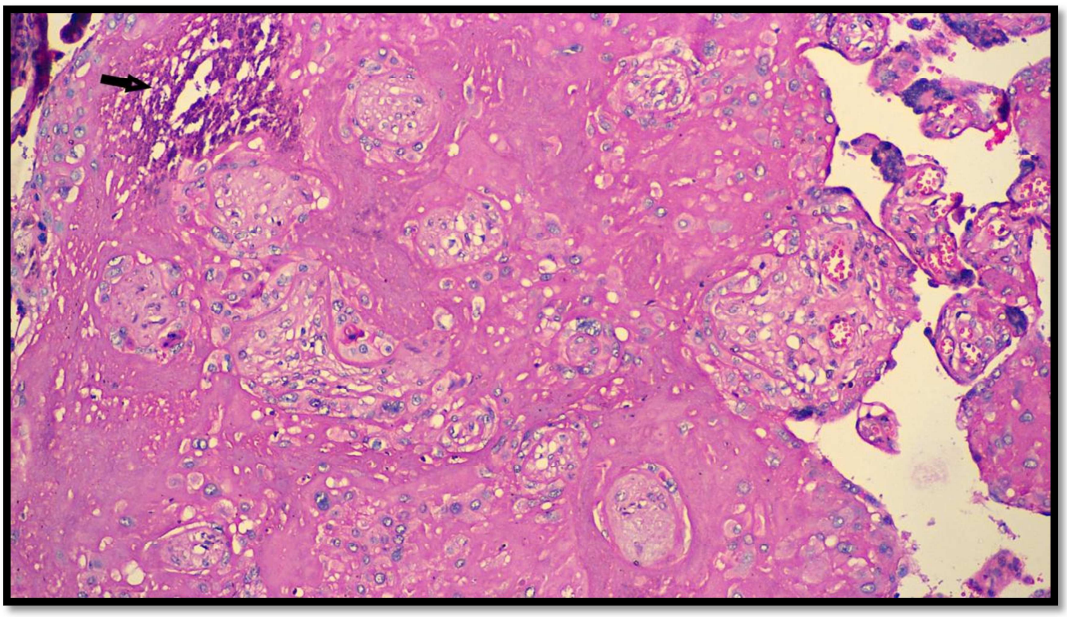


FIGURE 26: Placenta showing areas of infarction and calcification(400X)

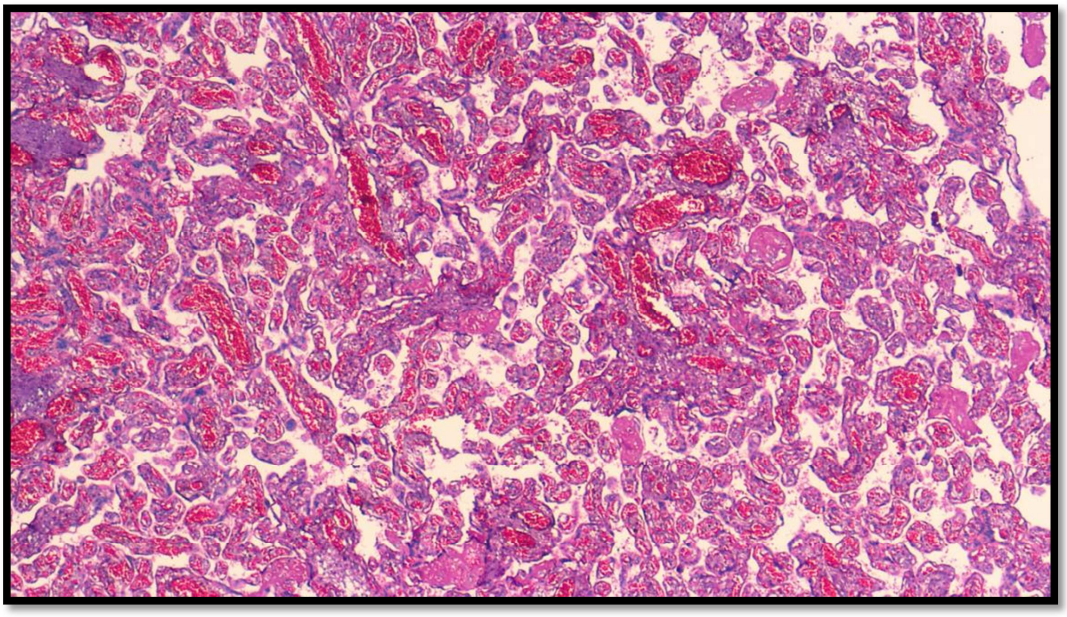


FIGURE 27: Placenta showing Chorangiosis(40X)

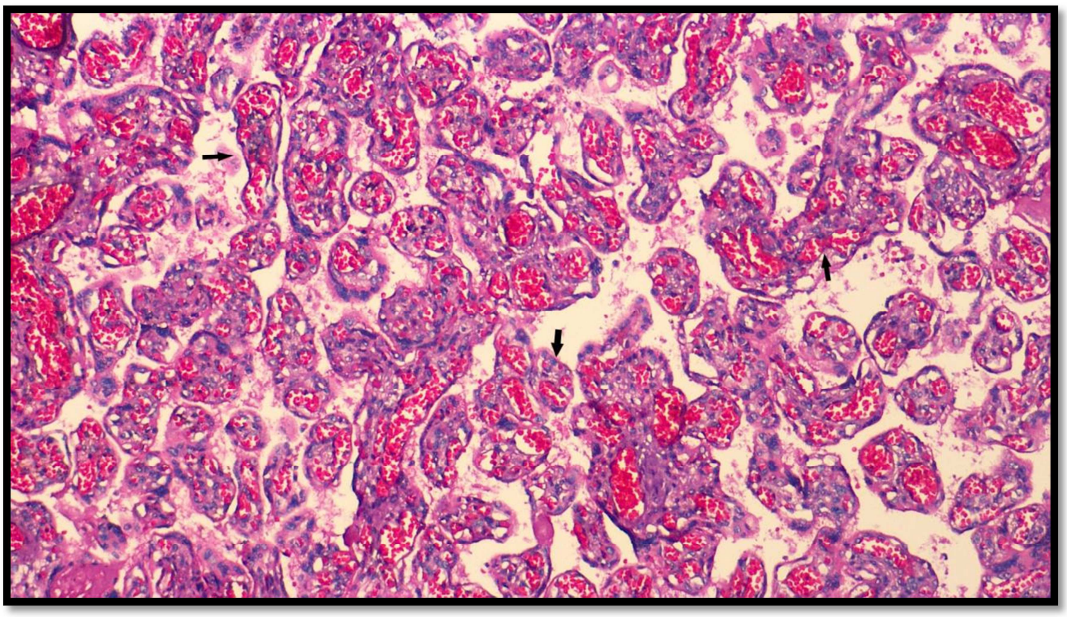


FIGURE 28 : Placenta showing Chorangiosis (400X)

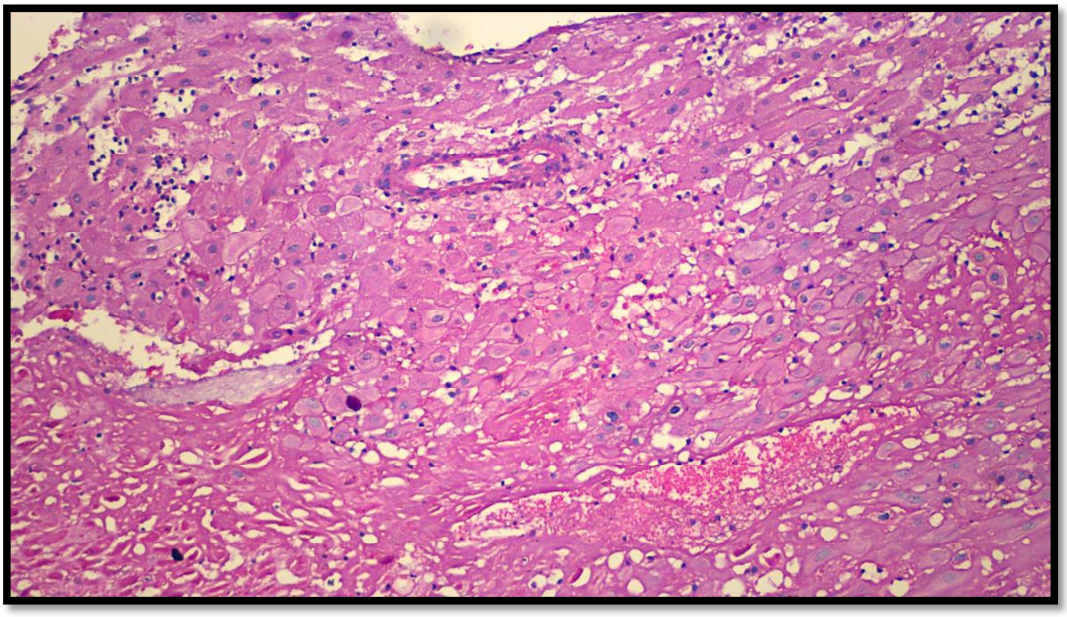


FIGURE 29: Deciduitis- Placenta showing neutrophilic infiltrate in decidual layer (200X).

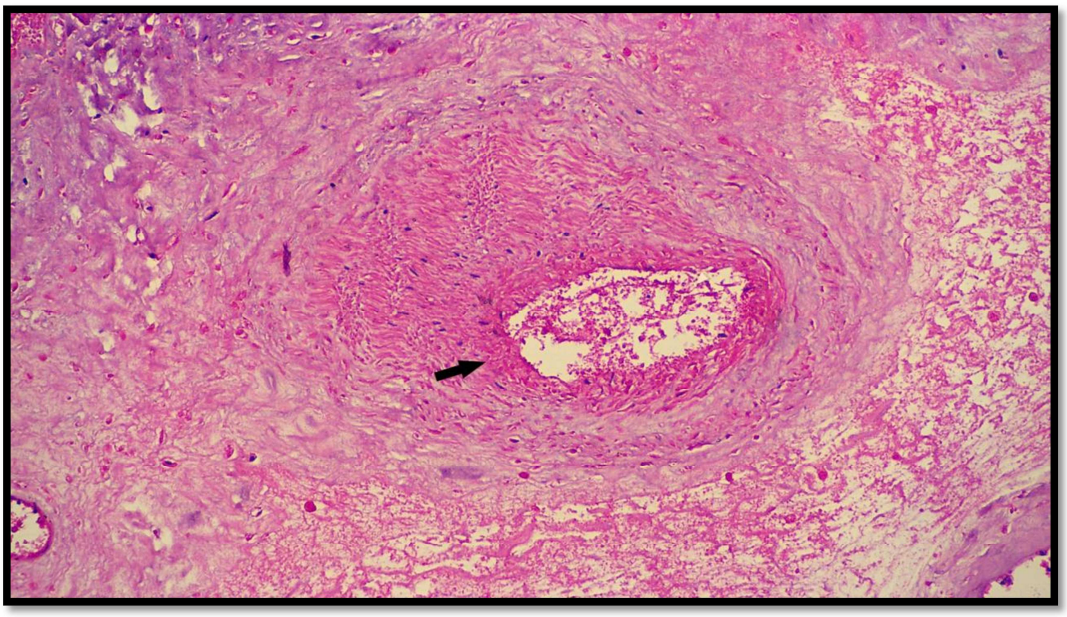


FIGURE 30 : Fibrinoid necrosis of vessel wall (400X).

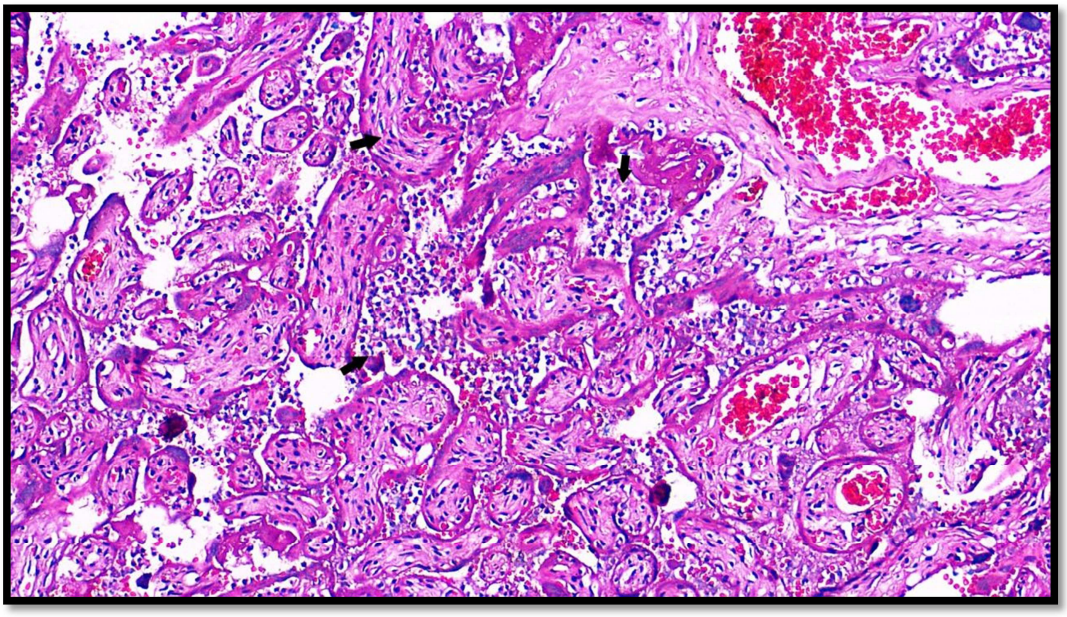


FIGURE 31 : Villitis-Placenta showing neutrophilic infiltrate in villi and intervillous space(200X).

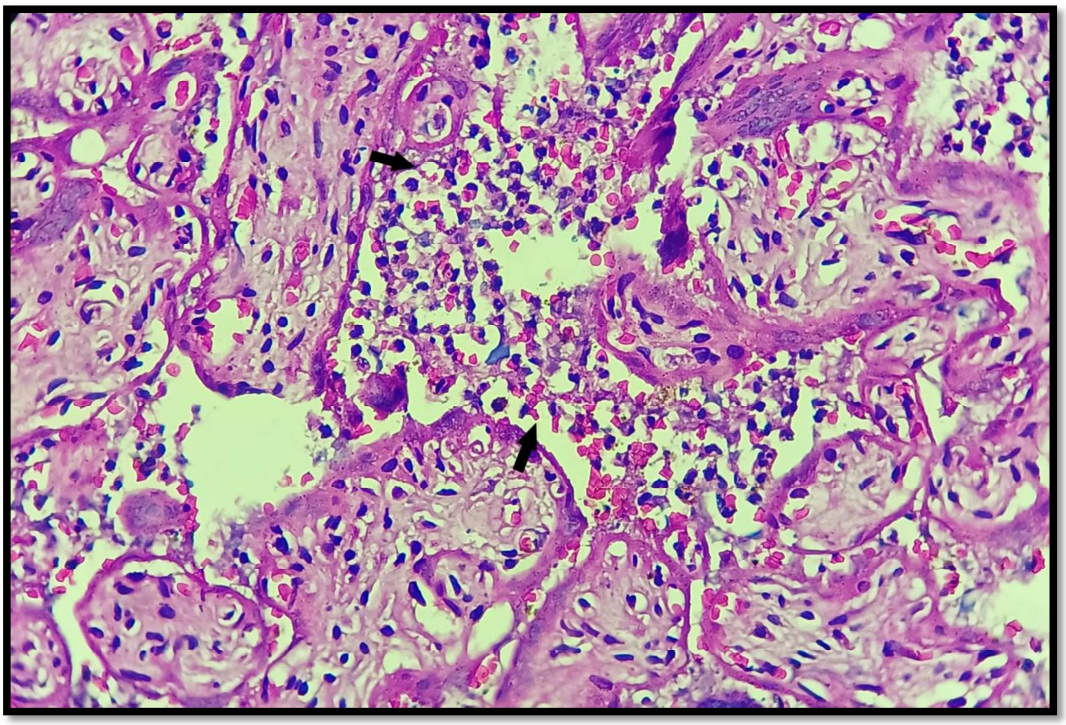


FIGURE 32- Villitis-Placenta showing neutrophilic infiltrate in villi and intervillous space(400X).

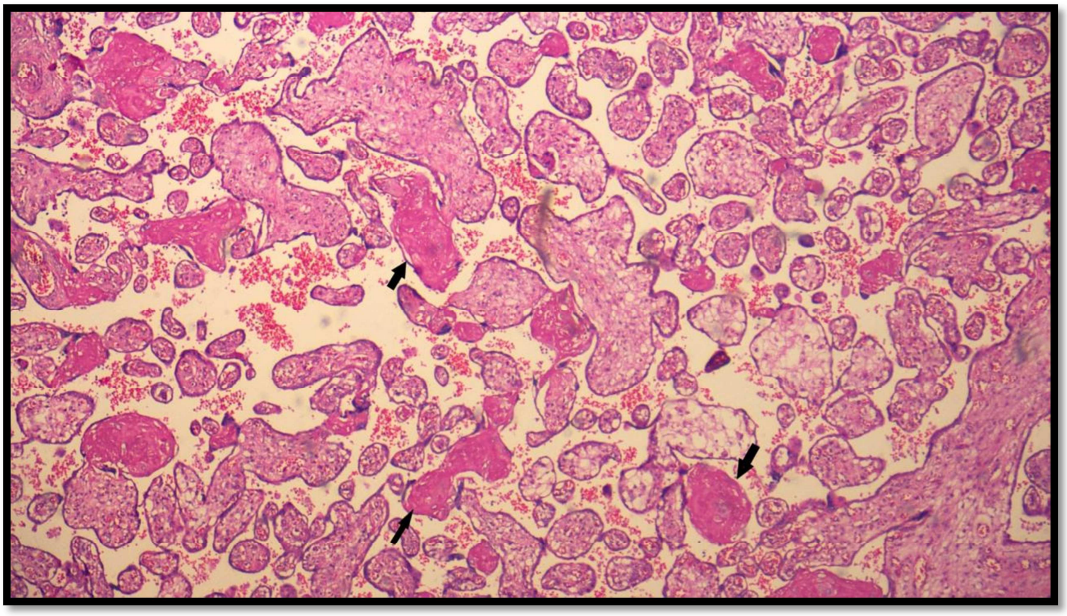


FIGURE 33- Placenta showing villous fibrinoid necrosis (200X).

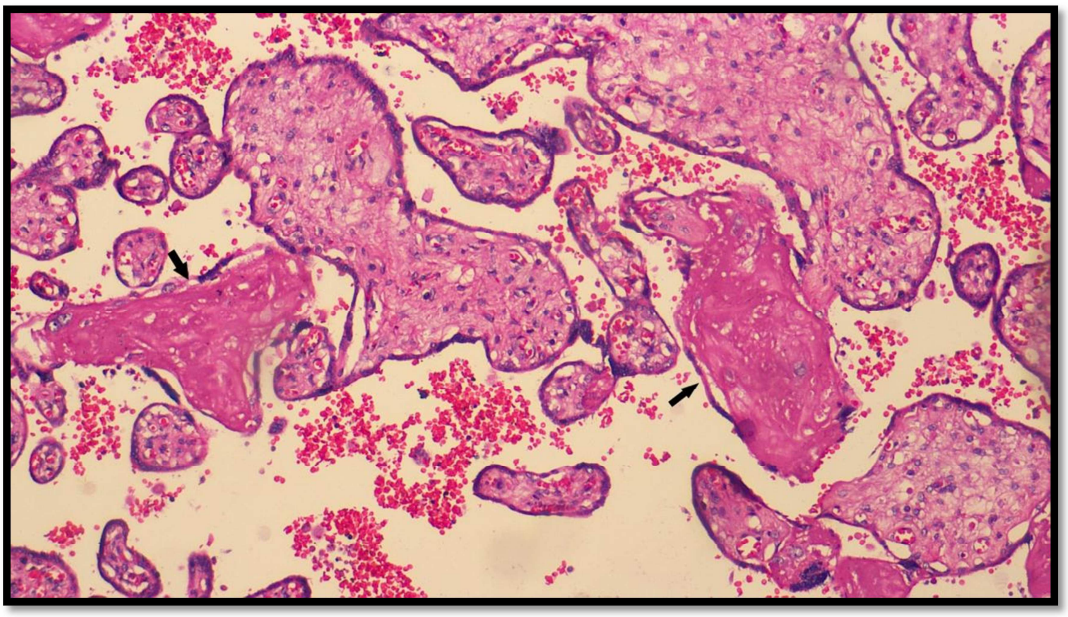


FIGURE 34 - Placenta showing villous fibrinoid necrosis (400X).

DISCUSSION

The placenta is a vital organ necessary for the fetal growth in-utero. In present study total 100 placentas were studied for histopathological examination and their association with maternal diseases was evaluated. This study included all pregnant women who suffered with intrauterine fetal demise in second trimester and above and of age more than 18 years.

1. Age Distribution

In the present study the most common age group observed was 21-25 years with mean age of 25.87 years. These results are consistent with the study done by Sharma S et al[58] ,Saha D et al [59],Shobharani MS et al [60] , Borade PD et al [61].

TABLE 4

Studies	Sharma S et al	Saha D et al	Shobharani MS et al	Borade PD et al	**Present Study**
Year	2021	2019	2020	-	**2024**
<=20 years	7.9%	11.7%	-	-	**7%**
21-25years	46.5%	40%	48% (18-25yrs)	49.49%	**45%**
26-30 years	32.5%	29%	36%	-	**32%**
>31 years	13.2%	12.38%	16%	-	**16%**

2. Gravidity

56% of the cases in the current study were primigravida, and 44% were multigravida which is comparable to the study by Patil NJ et al [62], where primigravida accounted for 53.8% of the cases.

3.Gestational Age

In this study the mean gestational age were 24.20 weeks. The study done by Meena L et al [63] also showed similar results (20-25 weeks).

4. Consanguinity

In the present study 3% showed second degree consanguinity and 97% showed Non-consanguinity. It is similar to the study done by Kanavi JV et al [2].

TABLE 5

Studies	Kanavi JV et al [2]	Present Study
Consanguinity	6.3%	3%
Non- Consanguinity	93.7%	97%

5. Placental weight

In the present study mean placental weight observed was 294.45 grams. It is similar to the study done by Manocha A et al [3] and Patil NJ [62].

TABLE 6

Studies	Manocha A et al	Patil NJ	Present Study
Placental weight	255 grams	200-500 grams	294grams

6. Maternal diseases in pregnancy

In the present study maternal anemia was found to be the most common maternal disease followed by gestational hypertension, gestational diabetes, pre-eclampsia, hypothyroidism. Conditions like placenta previa, gestational thyrotoxicosis, HELLP syndrome, abruptio placenta were seen in small percentages.

It is comparable with the study done by the following:

TABLE 7

Conditions	Studies	Cases	**Present study**
Maternal Anemia	Suryanarayana R et al	62%	**53%**
	Karale A et al	20.2%	
	Shravya MK et al	11.67%	
Gestational Hypertension	Loverro MT et al	23 (8.2%)	**29%**
	Singh N et al	5.3%	
	Sahoo G et al	1.35%	
Gestational diabetes	Loverro MT et al	44 (15.6%)	**28%**
	Noor N et al	10.81%	
	Singh N et al	24%	

Pre-eclampsia	Patel S et al Meena L et al Tandur AN et al	27 (33.7%) 23.68% 15.6%	**22%**
Hypothyroidism	Kumar R et al Mogan KA et al	32 % 43.7%	**12%**
Placenta Previa	Korde NV et al	7 (2.3%)	**3%**
Twin pregnancy	Chaudhary V et al	1.86%	**3%**
HELLP syndrome	Hudda S et al Lakshmi NK et al	1% 13.18%	**2%**
Abruptio placenta	Korde NV et al Kundaikar SL et al	21.9% 35.14%	**1%**
Gestational Thyrotoxicosis	Kumar R et al	2.3%	**1%**

Anemia was the most prevalent maternal disease in our study, which is comparable to the study done by Suryanarayana R et al[64], Karale A et al[65],Shravya MK et al[66] , which was found in 62% ,20.2%,11.67% of cases respectively. A study by Loverro MT et al[67] ,Singh N et al[68], Sahoo G et al[51] indicated that the rates of gestational hypertension were 8.2, 5.3%, 1.35% which were much less as compared to our study. Variations in sample size, inclusion and exclusion criteria compared to the current study can account for this discrepancy. In our study the cases of gestational diabetes were observed to be 28% which is comparable to the study done by Loverro MT et al[67], Noor N et al[22], Singh N et al[68] which were 15.6%,10.8% and 24% respectively. Our findings of 22% of pre-eclampsia cases was consistent with Patel S et al[69],Meena L et al[63], Tandur AN et al[39] which reported 33.7%,23.68%,15.6% of cases of pre-

eclampsia respectively. Our findings regarding cases of hypothyroidism was 12% which was lesser than the study conducted by Kumar R et al[70] and Mogan KA et al [71] which revealed to be 32% and 43.7% case rate of hypothyroidism respectively, however the case rate of gestational thyrotoxicosis was similar with our finding of 1%. Differences in prevalence of the disease compared to the current study can account for this discrepancy. Our findings regarding cases of placenta previa were similar with the study conducted by Korde NV et al[72] (2.3%), however their and study by Kundaikar SL et al[54] revealed a higher of cases of abruptio placenta 21.9% and 35.14% respectively. Dissimilarity in inclusion and exclusion criteria compared to the current study can account for this discrepancy. Our finding regarding HELLP syndrome cases was of 2% and were comparable to the study done by Hudda S et al [73], whereas study done by Lakshmi NK et al [55] revealed higher value of 13.18% than our finding of 2%. Difference in the prevalence of the disease compared to our study can account for this discrepancy. Our study and Chaudhary V et al [74] study had a comparable number of twin pregnancy cases 2% and 1.86% respectively.

7.Histopathological lesions

TABLE 8

Lesions	Studies Jaiman S et al	Spinillio A et al	Gunyeli I et al	**Present study**
AVM	20%	77.8%	-	**61%**
Infarction	35%	6.5%	57.7%	**60%**
VFN	-	-	53%	**48%**
Villitis	10.5%	3.7%	39%	**27%**
Deciduitis	39.2%	-	-	**26%**
Chorangiosis	-	-	-	**18%**
Calcification	-	-	-	**15%**
Delayed villous maturation	31%	-		**2%**

The most common placental histopathological lesion found in our study was AVM (61%),which was similar to the study done by Spinillio A et al [75] (77.8%). Our findings regarding AVM differed than the study done by Jaiman S et al[76] where it was found to be 20%. In our study infarction, villitis delayed villous maturation were 60%, 27% ,2% respectively, which differed than the study done by Jaiman S et al [76]. Greater sample size compared to the current study can account for this discrepancy, however our findings of deciduitis(26%) was similar with the study(39.2%). Our findings regarding VFN ,infarction and villitis was found to be 48%, 60%, 27% respectively, which were similar to the study done by Gunyeli I et al [77] 53%,57%,39% respectively.

TABLE 9 : Type of lesion

Type of lesion	Studies	**Present study**
MVM	30% Manocha A et al 58.4% Kulkarni VG et al 81.3% Tess EK et al 82% Guo X et al	**37%**
FVM	6% Manocha A et al 19% Kulkarni VG et al 85.2% Tess EK et al	**22%**
Combined (MVM+FVM)	10%Manocha A et al	**23%**
MVM + Inflammatory	18% Manocha A et al	**18%**

In accordance with our findings where maternal vascular malperfusion was observed in majority of the cases(37%), studies by Manocha A et al [3], Kulkarni VG et al [78], Tess EK et al[79] and Guo X et al [80] also found MVM was the most prevalent lesion at 30%, 58.4%,81.3%, 82% respectively. Our findings regarding MVM+ inflammatory lesion of 18% was similar to the study done by Manocha A et al [3] (18%). Similar to our findings, the study conducted by Kulkarni VG et al [78] observed that 19% of the lesions were FVM, however studies done by Tess EK et al [79](85.2%) and Manocha A et al [3] (6%) differed from our finding of 22%. More number of sample size in the study by Tess EK et al[79] can account for this discrepancy.

TABLE 10. Association between gestational diabetes and placental lesions

Studies	Huynh et al	Patil SS et al	Natarajan L et al	Daskalakis G et al	Lai YM et al	**Present study**
Calcification	-	-	-	-	-	**33%**
Chorangiosis	38.1%	-	1%	40%	18.5%	**33%**
AVM	-	-	3%	-	42.8%	**31%**
VFN	-	57.1%	-	82.5%	-	**29%**
DVM	-	-	-	-	-	**29%**
Deciduitis	-	-	-	-	1.9%	**23%**
Villitis	38.1%	-	-	-	14.8%	**22%**
Infarction	15.9%	-	2%	17.5%	1.9%	**22%**

In our study placentas showing histopathological lesions with history of gestational diabetes, infarction was seen to be 22%, study done by Huynh et al [81], Daskalakis G et al [82], Natarajan L et al [83], Lai YM et al [84] showed 15.9%,17.5%, 2%,1.9% respectively which was not consistent with our findings. This discordance can be explained by difference in sample size compared to the current study. Chorangiosis was observed to be 38.1%, 40%, 18.5% which is similar to our study. Our findings regarding VFN were 29%, study done by Patil SS et al [85] showed increased presence of VFN than in our finding which can be explained due to difference in study design than our study. AVM of 42.8% by Lai YM et al [84] was consistent with our study. Our study also observed cases where placental lesions of infarction (78%), AVM (69%), VFN (71%), villitis (78%), DVM(72%), deciduitis (77%), chorangiosis (67%) calcification(67%) were present but there was no history of maternal gestational diabetes, indicating no significant association between gestational diabetes and its effect on placenta.

TABLE 11. Association between Pre-eclampsia and placental lesions.

Studies	Gore CR et al	Genest DS et al	Vijayalakshmi B et al	Freedman A et al	**Present study**
Calcification	36.7%	-	35%	-	**33%**
Villitis	-	6%	-	-	**33%**
Infarction	66.7%	44%	48%	28.6%	**28%**
Chorangiosis	38.1%	6%	-	2.9%	**28%**
Deciduitis	-	-	-	-	**27%**
VFN	-	-	-	-	**23%**
AVM	-	32%	-	93.7%	**21%**
DVM	-	-	-	-	**0%**

In our study placentas with histopathological lesions and a history of pre-eclampsia indicated an infarction rate of 28%, studies by Gore CR et al [86] and Genet DS et al [87] and Vijayalakshmi B et al [88] reported higher rates of 66.7%, 44%, 48% respectively. However our findings were similar to the study done by Freedman A et al [89] (28%). Variations disease prevalence compared to the current study can account for this discrepancy. In accordance with our study, calcification and chorangiosis were found to be 36.7% and 38.1%, respectively in the study done by Gore CR et al [86]. As compared to our findings of AVM(21%) it was reported higher in the study by Freedman A et al(93.7%) [89]. Greater sample size of 728 in the study by Freedman A et al [89] compared to the current study can account for this discrepancy.

Our study also observed cases where placental lesions of infarction(72%), AVM (79%), VFN(77%), villitis(67%), DVM(100%), deciduitis(73%), chorangiosis (72%) calcification(67%) were present but there was no history of maternal pre-eclampsia, indicating no significant association between pre-eclampsia and its effect on placenta.

TABLE 12: Association between Hypothyroidism and placental lesions.

Studies	Garg P et al	Bargunam P et al	**Present study**
VFN	41.5%	-	**15%**
Deciduitis	-	-	**15%**
AVM	11.6%	14.8%	**13%**
Infarction	-	11.5%	**13%**
Chorangiosis	-	-	**11%**
DVM	-	1.6%	**7%**
Villitis	-	-	**7%**
Calcification	4.66%	6.67%	**7%**

Our placentas exhibiting histopathological abnormalities and a history of hypothyroidism showed AVM of 13% and calcification of 7% which was consistent with study done by Garg P et al [90] and Bargunam P et al [91]. Comparable to our findings of VFN(15%) the study done by Garg P et al [90] observed VFN was higher than our finding. More number of samples included in study done by Garg et al [90] compared to the current study can account for this discrepancy. Infarction in the study by Bargunam P et al [91] was consistent with our study. Our study also observed cases where placental lesions of infarction(87%), AVM(87%), VFN(83%), villitis(93%), DVM(72%), deciduitis (85%), chorangiosis(89%) calcification(93%) were present but there was no history of hypothyroidism, indicating no significant association between hypothyroidism and its effect on placenta.

TABLE 13 : Association between Gestational hypertension and placental lesions.

Studies	Panday A et al	Samaddar A et al	Bar PK et al	Ahmed M et al	**Present study**
DVM	-	-	-	-	**57%**
Calcification	58.7%	44%	-	50%	**50%**
Chorangiosis	-	-	-	-	**42%**
Infarction	50%	46%	12.5%	59%	**31%**
AVM	80.9%	-	-	77.27%	**30%**
VFN	61.90%	-	100%	63.6%	**27%**
Villitis	52.3%	-	-	-	**23%**
Deciduitis	-	-	-	-	**19%**

The percentage of placentas in our study that had histopathological lesions and a history of gestational hypertension, infarction, AVM, VFN, or villitis was 31%, 30%, 27%, and 23%, respectively. This percentage was found to be lower than in the study conducted by Panday A et al [92], but the calcification rate of 58.7% was comparable with our finding. Lesser sample size in the study done by Panday et al [92] compared to the current study can account for this discrepancy. Similar to our finding, study by Ahmed M et al [93] And Samaddar A et al [94] showed infarction and calcification rates of 59%, 50%, 44%, 46% respectively. Compared to our findings study done by Bar PK et al [95] revealed infarction(12.5%) lesser than our study. Discordance in study design and sample size can account for this discrepancy. Our study also observed cases where placental lesions of infarction(70%), AVM(70%), VFN(73%), villitis(77%), DVM (43%), deciduitis(82%), chorangiosis (58%) calcification(50%) were present but there was no history of gestational hypertension, indicating no significant association between gestational hypertension and its effect on placenta.

TABLE 14 : Association between Anemia and placental lesions.

Studies	Ramteke R et al	Gebremeskel T et al	Sudele D et al	Malinowski AK et al	Mondal GC et al	**Present study**
Deciduitis	-	-	-	8%		**58%**
AVM	70%	81.8%	-	22%	83%	**57%**
Chorangiosis	60%	-	-	3%		**56%**
Infarction	-	-	-	18%		**55%**
Calcification	-	72.2%	60%	-	40%	**53%**
Villitis	-	-	-	-		**48%**
VFN	60%	-	13.3	-	27%	**46%**
DVM	-	-	-	6%		**7%**

AVM was found to be 57% in our analysis of placentas with histopathological abnormalities and a history of anemia, this was discovered to be lower than in studies conducted by Gebremeskel T et al [96] and Ramteke R et al [97] and Mondal GC et al [98]. Compared to our findings studies done by Gebremeskel T et al [96] , Sudele D et al [99], Mondal GC et al [98]. revealed calcification of 72.2%,60%, 40% respectively and VFN of 60%, which was observed to be higher than our study. The differences in study design and sample size can account for this discrepancy. Compared to our findings regarding DVM, it was similar in the study by Malinowski AK et al [100] (6%). Our study also observed cases where placental lesions of infarction(45%), AVM(43%), VFN(54%), villitis(52%), DVM(57%), deciduitis(42%), chorangiosis (44%) calcification(47%) were present but there was no history of maternal anemia, indicating no significant association between anemia and its effect on placenta.

SUMMARY

This was an observational study of 100 cases from January 01, 2023, to December 31, 2023 and was conducted in Department of Pathology of KAHER's Jawaharlal Nehru Medical College and Dr Prabhakar Kore Hospital Belagavi.

The aim of this research was to examine the morphological abnormalities in the placenta in cases of intrauterine fetal death and their correlation with maternal clinical conditions. The following are the significant results :

- Majority of the cases belonged to the age group 21-25 years.
- The mean gestational age observed was 24 weeks.
- Majority of the cases were primigravida.
- 3% of the cases showed second degree consanguinity.
- The mean placental weight observed was 294 grams.
- Anemia was the most common maternal clinical condition observed with 53% of the cases.
- The most common placental lesion observed was accelerated villous maturation in 61% of the cases.
- Majority of the cases belonged to category of maternal vascular malperfusion(37%).
- The most frequent placental lesions seen in instances of gestational diabetes mellitus were calcification (33%)and chorangiosis(33%).

- Villitis(67%) and calcification(67%) were seen to be more common in pre-eclampsia patients.
- The majority of hypothyroidism patients showed villous fibrinoid necrosis(17%).
- In cases gestational hypertension the two most common lesions were calcification(50%), DVM (57%).
- In cases of anemia the most common lesions seen were deciduitis(58%) and AVM(57%).
- There was no significant association between maternal clinical conditions and its effect on placental histopathological lesions ($p>0.05$).

CONCLUSION

The results of this research indicate that placental morphological lesions occur in IUFD cases. The majority of MVM lesions were identified, with Accelerated villous maturation being the most prevalent placental lesion and Delayed villous maturation being the least common. Anemia was the most prevalent clinical condition in mothers investigated, whereas abruptio placenta was the least common. The most frequent placental lesions seen in instances of gestational diabetes mellitus were calcification and chorangiosis; villitis and calcification were seen to be more common in pre-eclampsia patients. The majority of hypothyroidism patients showed villous fibrinoid necrosis, whereas in anemia and gestational hypertension the two most common lesions were deciduitis and infarction with calcification.

Maternal clinical diseases did not significantly correlate with placental histopathological abnormalities. In situations where the maternal clinical history is not relevant, more investigation is required to identify the etiology of morphological anomalies. Studies using immunohistochemistry and gene profiling may hold the key to the future.

LIMITATIONS

1. There was no significant association between maternal clinical conditions and its effect on placental morphology, this can occur due to smaller sample size in our study.
2. Further studies with immunohistochemistry markers of placental endothelial immaturity to determine placental pathology contributing to fetal death could be done in future.

BIBLIOGRAPHY

1. Jovanovic I, Ivanovic K, Kostic S, Tadic J, Dugalic S, Petronijevic M, et al. Intrauterine fetal death in term pregnancy-A single tertiary Clinic study. Life. 2023;13(12):2-11.
2. Kanavi JV, Shobha G, Kavita G. Incidence and risk factors for intrauterine foetal demise: a retrospective study in a tertiary care centre in India. Int J Pregn & Chi Birth. 2017;2(2):33–36.
3. Manocha A, Ravikumar G, Crasta J. Placenta in intrauterine fetal demise (IUFD): a comprehensive study from a tertiary care hospital. J Matern Fetal Neonatal Med. 2019 Dec;32(23):3939-47
4. Ptacek I, Sebire NJ, Man JA, Brownbill P, Heazell AE. Systematic review of placental pathology reported in association with stillbirth. Placenta. 2014 Aug;35(8):552-62.
5. Bonasoni MP, Muciaccia B, Pelligra CB, Goldoni M, Cecchi R. Third trimester intrauterine fetal death: proposal for the assessment of the chronology of umbilical cord and placental thrombosis. Int J Legal Med. 2022 May;136(3):705-11.
6. Burton GJ, Jauniaux E. What is the placenta? Am J Obstet Gynecol. 2015 Oct;213:1-8.
7. Singh I, Subhadra D. Inderbir Singh's Human embryology. Jaypee. 2018; 73–97.
8. Knöfler M, Haider S, Saleh L, Pollheimer J, Gamage TKJB, James J. Human placenta and trophoblast development: key molecular mechanisms and model systems. Cellular and Molecular Life Sciences. 2019 May 3;76(18):3479–96.

9. Huang C-C, Hsueh Y-W, Chang C-W, Hsu H-C, Yang T-C, Lin W-C, et al. Establishment of the fetal-maternal interface: developmental events in human implantation and placentation. Front Cell Dev Biol. 2023;11:1-23.
10. Kojima J, Ono M, Kuji N, Nishi H. Human Chorionic Villous Differentiation and Placental Development. Int J Mol Sci. 2022 Jul 20;23(14):2-18.
11. Gonzalez SN, Patel E, Riley CL. The placenta: Anatomy, physiology, uteroplacental blood flow, and drug transfer. In: Obstetric Anesthesia Practice. Oxford University Press.2021; 19–37.
12. Aplin JD, Lewis RM, Jones CJP. Development of the human placental villus. In: Reference Module in Biomedical Sciences. Elsevier; 2018.
13. Young B, Woodford P, O'dowd G, Wheater PR. Wheater's functional histology : a text and colour atlas. 6th ed. Edinburgh: Churchill Livingstone; 2014.
14. Gude NM, Roberts CT, Kalionis B, King RG. Growth and function of the normal human placenta. Thromb Res. 2004;114(5-6):397-407.
15. Macnab WR. Functions of the placenta. Anaesthesia & Intensive Care Medicine. 2022 Jun;23(6):344–6.
16. Man J, Hutchinson JC, Heazell AE, Ashworth M, Jeffrey I, Sebire NJ. Stillbirth and intrauterine fetal death: role of routine histopathological placental findings to determine cause of death. Ultrasound in Obstetrics & Gynecology. 2016 Oct 25;48(5):579–84.
17. Khong TY et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Arch Pathol Lab Med. 2016 Jul;140(7):698-713.
18. Dimasuay KG, Boeuf P, Powell TL, Jansson T. Placental Responses to Changes in the Maternal Environment Determine Fetal Growth. Front Physiol. 2016 Jan 29;7:1-9.

19. Núñez Estevez KJ, Rondón-Ortiz AN, Nguyen JQT, Kentner AC. Environmental influences on placental programming and offspring outcomes following maternal immune activation. Brain Behav Immun. 2020 Jan;83:44-55.
20. Deep JP, Sharma R, Ansari S, Shah RK, Raut RK, Shah P. Evaluation of Intrauterine Fetal Death at Tertiary Care Centre: A Descriptive Cross-Sectional Study. Medphoenix. 2023 Jan. 6;7(2):10-16.
21. Reddy G Thapasya , Jain Geeta, Singh CK. Clinical study of intrauterine fetal death in tertiary hospital. Indian Journal of applied research. 2017 May;7(5): 15-17.
22. Noor N, Parveen S, Madan I, Hoda A. Analytical Study of Intrauterine Fetal Death and Associated Maternal Conditions at a Tertiary Centre. East African Scholars Journal of Medical Sciences. 2020 Sep 30;3(9):346–50.
23. Budal EB et al. Placental histology predicted adverse outcomes in extremely premature neonates in Norway-population-based study. Acta Paediatr. 2022 Mar;111(3):546-53.
24. Sundari Amirthakatesan A, Devi Chandramohan S, Gurusamy UM. The Histomorphological Spectrum of Placenta in Growth Restricted Fetuses in A Tertiary Care Centre in South India. Iran J Pathol. 2023;18(1):12-23.
25. Arora D, Rajmohan KS, Singh S, Nair V, Barui S, Dey M, et al. Correlation between placental histopathology and perinatal outcome in COVID-19. Tzu Chi Med J.2022;34(3):329-36.
26. Feenstra ME et al. More Maternal Vascular Malperfusion and Chorioamnionitis in Placentas After Expectant Management vs. Immediate Delivery in Fetal Growth Restriction at Near Term: A Further Analysis of the DIGITAT Trial. Front Endocrinol. 2019 Apr 24;10:1-7.

27. Achebe MM, Gafter-Gvili A. How I treat anemia in pregnancy: iron, cobalamin, and folate. Blood. 2016 Dec 29;129(8):940–9.
28. Kanwar G, Prasad SR, Ratnani R. Incidence of anemia in pregnancy and its maternal-fetal outcome in admitted ANC patients in tertiary care center, Bhilai, Chhattisgarh, India. Int J Reprod Contracept Obstet Gynecol 2021;10:1411-4.
29. Singh M, Puri M, Choudhary V, Kapur A, GS Triveni, None Gunjan, et al. Impact of COVID-19 Pandemic on Maternofetal Outcome in Pregnant Women with Severe Anemia. Indian Journal of Community Medicine. 2023 Jan 1;48(4):556–61.
30. Ortega MA et al. The Pivotal Role of the Placenta in Normal and Pathological Pregnancies: A Focus on Preeclampsia, Fetal Growth Restriction, and Maternal Chronic Venous Disease. Cells. 2022 Feb 6;11(3):1-32.
31. Sinha A, Adhikary M, Phukan JP, Kedia S, Sinha T. A study on anemia and its risk factors among pregnant women attending antenatal clinic of a rural medical college of West Bengal. J Family Med Prim Care. 2021 Mar;10(3):1327-31.
32. Shi H, Chen L, Wang Y, et al. Severity of Anemia During Pregnancy and Adverse Maternal and Fetal Outcomes. *JAMA Netw Open.* 2022;5(2):1-13.
33. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011 Jan;34:S62-9.
34. Istrate-Ofiţeru AM, Berceanu C, Berceanu S, Busuioc CJ, Roşu GC, Diţescu D, et al. The influence of gestational diabetes mellitus (GDM) and gestational hypertension (GH) on placental morphological changes. Romanian Journal of Morphology and Embryology. 2020;61(2):371–84.
35. Rajput R, Yadav Y, Nanda S, Rajput M. Prevalence of gestational diabetes mellitus & associated risk factors at a tertiary care hospital in Haryana. Indian J Med Res. 2013 Apr;137(4):728-33.

36. Vinoth N, Jaget N, Sekar SG, Priyanka R.A study on prevalence of gestational diabetes mellitus and its associated risk indicators in pregnant women attending antenatal clinic in a tertiary health centre. Int J Reprod Contracept Obstet Gynecol 2023;12:1374-8.
37. Roberts JM, Escudero C. The placenta in preeclampsia. Pregnancy Hypertens. 2012 Apr 1;2(2):72-83.
38. Egbor M, Ansari T, Morris N, Green CJ, Sibbons PD. Morphometric placental villous and vascular abnormalities in early- and late-onset pre-eclampsia with and without fetal growth restriction. BJOG. 2006 May;113(5):580-89.
39. Tandur AN, KuriakoseA, Laldinpuia SK, Nataraj GR, Lokeshwari K.Assessment of prevalence and risk factors of pre-eclampsia and eclampsia in tertiary care hospital.Int J Reprod Contracept Obstet Gynecol 2024;13:324-31.
40. Kahnamouei, F Amani, S Hamidimoghaddam.Prevalence of pre-eclampsia and eclampsia risk factors among pregnant women, 2011-2013. Int J Adv Med 2015;2:128-32.
41. Alemu A, Terefe B, Abebe M, Biadgo B. Thyroid hormone dysfunction during pregnancy: A review. Int J Reprod Biomed. 2016 Nov;14(11):677-86.
42. Silva JF, Vidigal PN, Galvão DD, Boeloni JN, Nunes PP, Ocarino NM et al. Fetal growth restriction in hypothyroidism is associated with changes in proliferative activity, apoptosis and vascularisation of the placenta. Reprod Fertil Dev. 2012;24(7):923-31.
43. Srinivasan AP, Omprakash BO, Lavanya K, Subbulakshmi Murugesan P, Kandaswamy S. A prospective study of villous capillary lesions in complicated pregnancies. J Pregnancy. Nov 2014;193(9):25-39.

44. Dhanwal DK et al. Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. Indian J Endocrinol Metab. 2016 May-Jun;20(3):387-90.
45. Abadi KK, Jama AH, Legesse AY, Gebremichael AK. Prevalence of Hypothyroidism in Pregnancy and Its Associations with Adverse Pregnancy Outcomes Among Pregnant Women in A General Hospital: A Cross Sectional Study. Int J Womens Health. 2023 Oct 3;15:1481-90.
46. Antovic A, Sennström M, Bremme K, Svenungsson E. Obstetric antiphospholipid syndrome. Lupus Sci Med. 2018 Sep 25;5(1):1-9.
47. Ernst LM. Maternal vascular malperfusion of the placental bed. APMIS. 2018 Jul;126(7):551-60.
48. Abrahams VM, Chamley LW, Salmon JE. Emerging Treatment Models in Rheumatology: Antiphospholipid Syndrome and Pregnancy: Pathogenesis to Translation. Arthritis Rheumatol. 2017 Sep;69(9):1710-21.
49. Tong M, Viall CA, Chamley LW. Antiphospholipid antibodies and the placenta: a systematic review of their in vitro effects and modulation by treatment. Hum Reprod Update. 2015;21(1):97–118.
50. Ajitha Ravindran R K, Jayshree V Vaman, Nirmala C, Sujatha T L, Geetha M I. Study to assess the prevalence of antiphospholipid syndrome (APS) among women with adverse pregnancy outcome in a tertiary care centre. Obs Rev: J obstet Gynecol 2016;2(2):3-7.
51. Sahoo G, Sahu M. Prevalence and pregnancy outcome in antiphospholipid syndrome: an observational study. Multidiscip. Sci. J. 2023 Sep. 5;6(3):2024-33.
52. Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: clinical issues and management. A Review. BMC Pregnancy Childbirth. 2009 ;9(8):1-15.

53. Shelat PM, Vyas RC, Shah SR, Nathwani ND. Fetomaternal outcome in pregnancy with HELLP syndrome. Int J Reprod Contracept Obstet Gynecol 2020;9:2860-5.
54. Kundaikar SL, Thakur RN.Study of maternal and perinatal outcome in cases of a HELLP syndrome. Int J Reprod Contracept Obstet Gynecol 2023;12:2133-8.
55. Lakshmi NK, Kavitha G, Prabha Devi K, Gayathri KB. Study on HELLP syndrome -maternal and perinatal outcome.Int J Reprod Contracept Obstet Gynecol2017;6:714-9.
56. T. Yee. Khong, Mooney EE, Nikkels PGJ, Morgan TK, Gordijn SJ. Pathology of the Placenta: A Practical Guide; 2019.
57. Dureau ZJ, Rogers BB. Placental pathology. Diagn Histopathol.2019;25(9):341-9.
58. Sharma S, Singh S. Histopathological Study of Placenta in Intrauterine Fetal Death: A Comprehensive Study from A Tertiary Institution. JK Science 2023 Oct. 10;25(4):242-7.
59. Saha D, Kurude VN, Mundhe S.A study of intrauterine fetal death in a tertiary care hospital.Int J Reprod Contracept Obstet Gynecol2019;8:2647-51.
60. Shobharani MS. Incidence of Maternal Anemia and its Effects on Placenta and Neonates. Ann. Int. Med. Den. Res. 2020; 6(3):1-5.
61. Borade PD, Kanetkar SR, Kale PP, Hulwan AB, Shukla DB, Vohra NV. Study of placental pathology in cases of intrauterine fetal deaths. Ann Pathol Lab Med. 2018;5(10):A810-17.
62. Patil NJ, Shukla DB, Dhawan S . Placental pathology in intra: uterine foetal deaths. Int J Reprod Contracept Obstet Gynecol 2016; 5:2250-3.
63. Meena L, Gupta R. Study of intrauterine fetal death cases in a tertiary care center. Int J Reprod Contracept Obstet Gynecol 2020;9:1255-8.

64. Suryanarayana R, Chandrappa M, Santhuram A, Prathima S, Sheela SR. Prospective study on prevalence of anemia of pregnant women and its outcome: A community based study. J Family Med Prim Care. 2017;6(4):739-43.
65. Karale A, Shinde KK, Damle H. Intrauterine fetal demise: a retrospective study in tertiary care center in India. Int J Reprod Contracept Obstet Gynecol 2018;7:3069-73.
66. Shravya MK, Rathnamma P. A retrospective study of intrauterine fetal demise in a tertiary care centre. Int J Reprod Contracept Obstet Gynecol 2023;12:590-4.
67. Loverro MT, Naro D, Nicolardi E, Resta V, Mastrolia L, Schettini SA. Pregnancy Complications, Correlation With Placental Pathology and Neonatal Outcomes. Frontiers in Clinical Diabetes and Healthcare. 2002. Mar 8;2:8071-92.
68. Singh N, Pandey K, Gupta N, Arya AK, Pratap C, Naik R. A retrospective study of 296 cases of intra uterine fetal deaths at a tertiary care centre.Int J Reprod Contracept Obstet Gynecol 2013;2:141-6.
69. Patel S, Thaker R, Shah P, Majumder S. Study of causes and complications of intra uterine fetal death (IUFD). Int J Reprod Contracept Obstet Gynecol 2014;3:931-5.
70. Kumar R, Bansal R, Shergill HK, Garg P. Prevalence of thyroid dysfunction in pregnancy and its association with feto-maternal outcomes: A prospective observational study from a tertiary care institute in Northern India. Clin Epidemiol Glob Health. 2023;19(11):1-6.
71. KA Mogan, Venkatesh U, Kapoor R. Clinico-epidemiological profile of women with high risk pregnancy utilizing antenatal services in a rural primary health center in India. J Rural Med. 2023 Jan;18(1):15-20.
72. Korde NV, Gaikwad P. Causes of stillbirth. J Obstet Gynecol India. 2008;58(4):314-7.

73. Hudda S, Choudhary A. Histopathological Study of Placenta in Association with deranged Thyroid Profile, in Known Cases of pre- Eclampsia/ Eclampsia. Trop J Pathol Microbiol. 2022;8(2):36–40.
74. Chaudhary V, Thiyagarajan K, Patil Y, Gawali V.Maternal and neonatal outcome of twin pregnancy at a tertiary care center. Int J Reprod Contracept Obstet Gynecol 2021;10:4545-48.
75. Spinillo, A., Bellingeri, C., Cavagnoli, C et al. (2021). Maternal and foetal placental vascular malperfusion in pregnancies with anti-phospholipid antibodies. Rheumatology (Oxford, England); 60(3):1148–57.
76. Jaiman S, Romero R, Pacora P, Jung E, Bhatti G, Yeo L, Kim Y, Kim B, Kim C, Kim J, Qureshi F, Jacques S, Erez O, Gomez-Lopez N, Hsu C. Disorders of placental villous maturation in fetal death. Journal of Perinatal Medicine. 2020;48(4): 345-68.
77. Gunyeli I, Erdemoglu E, Ceylaner S, Zergeroglu S, Mungan T. Histopathological analysis of the placental lesions in pregnancies complicated with IUGR and stillbirths in comparison with non complicated pregnancies. J Turk Ger Gynecol Assoc. 2011;12(2):75–9.
78. Kulkarni VG, Sunilkumar KB, Nagaraj TS, Uddin Z, Ahmed I, Hwang K, et al. Maternal and fetal vascular lesions of malperfusion in the placentas associated with fetal and neonatal death: results of a prospective observational study. Am J Obstet Gynecol . 2021;225(6):660.e1-660.e12.
79. Tess E.K. Cersonsky, Silver RM, Saade GR, Dudley DJ, Reddy UM, Pinar H. Macroscopic lesions of maternal and fetal vascular malperfusion in stillborn placentas: Diagnosis in the absence of microscopic histopathological examination. Placenta. 2023 Sep 1;140:60–5.

80. Guo X., Wang Y, & Yu, H. (2023). Relationship between placental pathology and neonatal outcomes. Frontiers in Pediatrics, 11.
81. Huynh J, Yamada J, Beauharnais C, Wenger JB, Thadhani RI, Wexler D, Roberts DJ, Bentley-Lewis R. Type 1, type 2 and gestational diabetes mellitus deferentially impact placental pathologic characteristics of uteroplacental malperfusion. Placenta. 2015 Oct;36(10):1161-6.
82. Daskalakis G, Marinopoulos S, Krielesi V, Papapanagiotou A, Papantoniou N, Mesogitis S, Antsaklis A. Placental pathology in women with gestational diabetes. Acta Obstet Gynecol Scand. 2008;87(4):403-7.
83. Natarajan L, Maheswari GU.Gestational hyperglycemia on diet and medication: impact on placental pathology and pregnancy outcomes.Int J Reprod Contracept Obstet Gynecol2019;8:3350-6.
84. Lai YM, Tan GC, Shah SA, Abd Rahman R, Mohd Saleh MF, Mansor S, et al. Non-hypertensive gestational diabetes mellitus: Placental histomorphology and its association with perinatal outcomes. Placenta. 2024;147:21–7.
85. Patil SS, Siddheshware R, Sambarey P. Clinical correlation with pathology of placenta in medical disorders of pregnancy and its comparison in normal pregnancy. International Journal of Reproduction, Contraception, Obstetrics and Gynecology.2016;6(1):127-32.
86. Gore CR, Pandey A, Shetty A, Rao R, Paranjape S. A study on histopathological changes in placenta in pre-eclampsia/eclampsia: A case control study in tertiary care centre, western India. Ind J Pathol Oncol, 2018;5(3):385-90.
87. Genest DS, Dal Soglio D, Girard S, Rey E. Association between proteinuria and placental pathology in preeclampsia: A retrospective study. SAGE Open Med. 2021;9:1-9.

88. Vijayalakshmi B, Kittali S. Morphological changes of placenta in cases of pre-eclampsia and perinatal outcome. Int J Sci Stud 2015;3(5):137-42.
89. Freedman AA, Suresh S, Ernst LM. Patterns of placental pathology associated with preeclampsia. Placenta. 2023;139:85–91.
90. Garg P, Saxena D. Maternal Hypothyroidism and Its Effect on Placenta and Newborn: A Morphometric and Histopathological Study. International Journal of Health and Clinical Research. 2021;4(13):130–4.
91. Bargunam P, Kanakaraya J, Jigalur P, Reddy P. Abnormal shape of placenta as a consequence of maternal thyroid disorders-does it leave any microscopic changes? National Journal of Laboratory Medicine.2023;12(2): 1-4.
92. Panday, A., S. Budania, and T. Bano. The histopathological changes of placenta in hypertensive disorders of pregnancy and their correlation with fetal outcome: a cross-sectional study. Asian Journal of Pharmaceutical and Clinical Research.2023; 16(7): 117-20.
93. Ahmed M, Daver RG. Study of placental changes in pregnancy induced hypertension. Int J Reprod Contracept Obstet Gynecol 2013;2:524-7.
94. Samaddar A, Roy UG, Saha I, Mangal S. Histopathological changes in placenta in pregnancy-induced hypertensive patients and correlation with fetal outcome – A tertiary care hospital study. Biomed Biotechnol Res J 2021;5:440-5.
95. Bar PK, Ghosh S, Gayen P, Mandal S. Morphological study of placenta in hypertensive disorders in pregnancy. Trop J Pathol Microbiol. 2019;5(6):366–73.
96. Gebremeskel T, Mulu A, Kumbi S, Ergete W. Histopathological changes of placenta associated with maternal anaemia in northeast Ethiopia: A comparative study. Ethiop J Health Sci . 2020;30(5):777-84.

97. Ramteke R, Madane R, Bharati T. Study of histopathological changes in placenta in anemia during pregnancy. International journal of current research. 2018;10(05):468–72.

98. Mondal GC, Baske A, Biswas S. Morphological changes of placenta associated with maternal anaemia. Int J Life-sci Sci Res. 2017;3(5):1400–7.

99. Sudele D, Department of Anatomy, Zydus Medical College, Dahod, Gujarat, India. Histological study of human placenta in normal and anemic cases. J Med Sci Clin Res. 2019;7(8):479-83.

100. Malinowski AK, Dziegielewski C, Keating S, Parks T, Kingdom J, et al. placental histopathology in sickle cell disease: A descriptive and hypothesis-generating study.Placenta.2020; 95:9-17.

ANNEXURE-I INFORMED CONSENT

KAHER's JNMC, BELAGAVI

"MORPHOLOGICAL ABNORMALITIES IN PLACENTA ASSOCIATED WITH INTRAUTERINE FETAL DEMISE - A HOSPITAL BASED OBSERVATIONAL STUDY"

Name of Student/Principal Investigator: Dr

Name of Guide/Co Investigators: Dr.

Objective: You are being asked to enroll as per the eligibility criteria for participation in this study. The purpose of this study is to detect placental abnormalities in cases of fetal death.

Explanation of procedure: During this study, placenta would be collected for Histopathological examination to detect abnormalities. The principal investigator of the study is **(PG)** under the guidance of .

If you agree to enroll yourself in this study, your pathological and biochemical reports will be used for research purpose.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: Dr. _____ Postgraduate , Department of Pathology, J.N. Medical College, Belagavi. Dr. _____Professor, Department of Pathology, J.N. Medical College, Belagavi. Ph No : _____ EMAIL: _____

If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052. **Legal rights:** By signing this consent form, we are not waving any of your legal rights.

ANNEXURE II - PROFORMA

MORPHOLOGICAL ABNORMALITIES IN PLACENTA ASSOCIATED WITH INTRAUTERINE FETAL DEMISE - A HOSPITAL BASED OBSERVATIONAL STUDY

Pregnant women admitted in labor ward with fetal death and still birth at KLE's Dr. Prabhakar Kore Hospital Belagavi are included in this study.

This study will include 92 women with fetal death and still birth.

This study is prospective cross sectional study. Data collected would be comprised of name, age, sex, Clinical History.

The placentas of the dead fetuses and still birth would be collected for the

Histopathological examination. The information about the clinical parameters would be obtained from Department of Pathology, KLE's Dr.Prabhakar Kore Hospital.

PATIENT DETAILS

Name : Sex:

Age :

IP no :

Brief Clinical history: Gravida Parity Live Birth Abortion

HYPOTHYROIDISM GESTATIONAL HYPERTENSION

GESTATIONAL DIABETES IUGR

TORCH INFECTION MULTIFETAL GESTATION

PRE ECLAMPSIA OLIGO/POLY HYDRAMNIOS

ABRUPTION PLACENTA

ANNEXURE III

HEMATOXYLIN AND EOSIN STAIN REAGENTS

1. Erhlich's Haematoxylin solution
2. Eosin Y solution 1%
3. 1% acid alcohol solution

HEMATOXYLIN AND EOSIN STAIN – PROCEDURE

1. Deparaffinise the tissue sections in xylene (Xylene 1 for 5 minutes + Xylene 2 for 5 minutes.)
2. Subject the tissue section to water through reducing grades of alcohol (90% alcohol for 5 mins + 70% alcohol for 5 mins)
3. Keep it in Hematoxyline for 8 to 10 minutes.
4. Rinse it in tap water for 2 mins.
5. Differentiate with 1% acid alcohol for 10 sec.
6. For bluing - place in tap water for about 10 minutes.
7. Counter stain by Eosin 1-2 minutes.
8. Rinse in water.
9. Dehydration increasing grades of alcohol (70% alcohol for 30 sec + 90% alcohol for 30 sec)
10. Clearing is done by Xylene (Xylene 1 for 5 mins + Xylene 2 for 5 mins
11. Mount it with Dibutylphalate Polystyrene Xylene (DPX).

ANNEXURE IV -KEY TO MASTER CHART

AVM	Accelerated villous maturation
DV	Decidual vasculopathy
DVH	Distal villous hypoplasia
DVM	Delayed villous maturation
FVM	Fetal vascular malperfusion
IFD	Intramural Fibrin deposition
MVM	Maternal vascular malperfusion
VFN	Villous fibrinoid necrosis
VSK	Villous stromal vascular karyorrhexis

ANNEXURE 5- MASTER CHART

Sr. No	Autopsy	Age/ sex	Obstetric Score	Consanguinity	Current Gestational Age	Type of Termination	Gestational diabetes	Pre Eclampsia	Hypothyroidism	Gestational Hypertension	Twin Pregnancy	APLA	Placenta Previa	Abruptio Placenta	HELLP Syndrome	Anemia	Gestational Thyrotoxicosis
1	11	20/F	Primigravida	Consanguinous 2 degree	35weeks 1 day	Spontaneous	Yes (HbA1c 6.5%)	Yes	No	Yes (146/100 mmhg)	No	No	No	No	No	No	No
2	12	22/F	Primigravida	Non-Consanguinous	22 weeks 3 days	Spontaneous	No	No	Yes (TSH 5.15 Iu/ml)	No (110/80 mmhg)	No	No	No	No	No	Yes (Hb 9 mg/dl)	No
3	14	23/F	G3 P1 L1	Non-Consanguinous	26 weeks	Spontaneous	No (HbA1c 4.7%)	Yes	No	Yes (160/100 mmhg)	No	No	No	No	Yes	Yes (Hb 10.6 mg/dl)	No
4	16	22/F	Primigravida	Non-Consanguinous	13 weeks 4 day	Spontaneous	No	No	No	No	No	No	Yes	No	No	No	No
5	17	19/F	Primigravida	Non-Consanguinous	36 weeks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10 mg/dl)	No
6	21	28/F	Primigravida	Non-Consanguinous	24 weeks 4 days	Spontaneous	No	No	No	No	Yes (DCDA)	No	No	No	No	Yes (Hb 8.8 mg/dl)	No
7	22	22/F	G2P1L1	Non-Consanguinous	19 weeks 1 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 8.9 mg/dl)	No
8	23	27/F	Primigravida	Non-Consanguinous	37 weeks 6 days	Spontaneous	No	No	No	No	No	No	Yes	No	No	No	No
9	27	26/F	G2P1L1	Non-Consanguinous	19 weeks 2 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10.7 mg/dl)	No
10	31	23/F	G3P1A2	Non-Consanguinous	25 weeks 3 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
11	33	22/F	Primigravida	Non-Consanguinous	22 weeks 1 days	Spontaneous	No	No	Yes	No	No	No	No	No	No	No	No
12	34	33/F	G5P4L4	Non-Consanguinous	22 weeks 6 days	Spontaneous	No	No	No	No	No	No	No	Yes	No	Yes (Hb 10.4 mg/dl)	No
13	42	27/F	Primigravida	Non-Consanguinous	18 weeks 6 days	Spontaneous	No	No	No	No	Yes	No	No	No	No	No	No
14	43	27/F	Primigravida	Non-Consanguinous	27 weeks 3 days	Spontaneous	No	No	No	No	Yes (DCDA)	No	No	No	No	No	No
15	44	26/F	G2P1L1	Non-Consanguinous	27 weeks 4 days	Spontaneous	No	Yes	No	Yes (146/100 mmhg)	No	No	No	No	No	No	No
16	46	27/F	Primigravida	Non-Consanguinous	19 weeks 6 day	Spontaneous	No	No	No	No	Yes (MCDA)	No	No	No	No	Yes (Hb 10.6 mg/dl)	Yes (TSH 0.01)
17	47	22/F	G2P1L1	Non-Consanguinous	28 weeks 1 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 8.5 mg/dl)	No
18	49	36/F	Primigravida	Non-Consanguinous	16 weeks 5 days	Spontaneous	No (HbA1c 5.5%)	No	No	No (112/76 mmhg)	No	No	No	No	No	Yes (Hb 9.7 mg/dl)	No
19	50	22/F	Primigravida	Non-Consanguinous	32 weeks 1 day	Spontaneous	No	Yes (160/110 mmhg)	No	Yes (160/110 mmhg)	No	No	No	No	Yes	No	No
20	55	19/F	G2A1	Non-Consanguinous	18 weeks 1 days	Spontaneous	No (HbA1c 5.6%)	No	No	No (124/74 mmhg)	No	No	No	No	No	No	No
21	57	38/F	Primigravida	Non-Consanguinous	21 weeks 6 days	Spontaneous	No	No	No	No (116/72 mmhg)	No	No	No	No	No	Yes (Hb 9.9 mg/dl)	No

22	58	28/F	G4P1L1A1	Non-Consanguinous	19 weeks 5day	Spontaneous	No	No	No	No (118/72 mmhg)	No	No	No	No	No	No	No
23	60	21/F	G2P1L1	Non-Consanguinous	21 weeks 4 days	Spontaneous	No (PPBS 70)	No	No	No (110/80 mmhg)	No	No	No	No	No	Yes (Hb 10.2 mg/dl)	No
24	63	19/F	Primigravida	Non-Consanguinous	26 weeks 4days	Spontaneous	No (FBS 70)	Yes (160/106 mmhg)	No	Yes (160/106 mmhg)	No	No	No	No	No	Yes (Hb 10.1mg/dl)	No
25	66	24/F	Primigravida	Non-Consanguinous	22 weeks	Spontaneous	No (HbA1c 5.7%)	No	No	No (110/76 mmhg)	No	No	No	No	No	Yes (Hb 9.9 mg/dl)	No
26	67	36/F	Primigravida	Non-Consanguinous	22 weeks 5 days	Spontaneous	No (DIPSI 84 mg/dl)	No	Yes (TSH 1.15 Iu/ml) K/C on Rx	No (128/74 mmhg)	No	No	No	No	No	Yes (Hb 10.4 mg/dl)	No
27	68	29/F	G3A1	Non-Consanguinous	29 weeks	Spontaneous	No (HbA1c 5.1%)	No	Yes (TSH 2.79 Iu/ml) K/C/ On Rx	No (116/74 mmhg)	No	No	No	No	No	No	No
28	69	25/F	Primigravida	Non-Consanguinous	18 weeks	Spontaneous	No (HbA1c 5.4%)	No	No	No (110/70 mmhg)	No	No	No	No	No	Yes (Hb 8.5 mg/dl)	No
29	71	22/F	G3 P1 L1	Non-Consanguinous	33 weeks	Spontaneous	No (DIPSI 68 mg/dl)	No	No	No (118/74 mmhg)	No	No	No	No	No	Yes (Hb 10.6 mg/dl)	No
30	73	23/F	G2A1	Non-Consanguinous	24 weeks 4 days	Spontaneous	No	No	Yes (TSH 6.12 Iu/ml)	No (114/74 mmhg)	No	No	No	No	No	Yes (Hb 10.6 mg/dl)	No
31	77	34/F	G2P2L2	Non-Consanguinous	22 weeks 2 days	Spontaneous	No (DIPSI 117 mg/dl)	No	No	No (110/78 mmhg)	No	No	No	No	No	Yes (Hb 9.6 mg/dl)	No
32	80	29/F	G3 P1 L1 A1	Non-Consanguinous	23 weeks 5 days	Spontaneous	No (HbA1c 5.7%)	No	No	No (128/80 mmhg)	No	No	No	No	No	Yes (Hb 9.6 mg/dl)	No
33	81	30/F	G2P1L1	Non-Consanguinous	21 weeks 3 days	Spontaneous	No	No	No	No (112/78 mmhg)	No	No	No	No	No	Yes (Hb 7.7 mg/dl)	No
34	86	27/F	G2P1L1	Non-Consanguinous	16 weeks 3 days	Spontaneous	No (HbA1c 4.7%)	No	No	No (112/72 mmhg)	No	No	No	No	No	Yes (Hb 10.7 mg/dl)	No
35	87	24/F	Primigravida	Non-Consanguinous	28 weeks 5 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 7.6 mg/dl)	No
36	90	24/F	G3 P1 L1 A1	Non-Consanguinous	22 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10.1mg/dl)	No
37	91	24/F	G2P1	Consanguinous 2 degree	23 weeks 2 days	Spontaneous	No (DIPSI 103 mg/dl)	No	No	No	No	No	Yes	No	No	Yes (Hb 10.6 mg/dl)	No
38	92	26/F	G2P2	Non-Consanguinous	22 weeks	Spontaneous	No	No	No	No (112/80 mmhg)	No	No	No	No	No	No	No
39	93	25/F	Primigravida	Non-Consanguinous	23 weeks 6 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
40	94	20/F	Primigravida	Consanguinous 2 degree	20 weeks 3 days	Spontaneous	No (DIPSI 87 mg/dl)	No	No	No	No	No	No	No	No	Yes (Hb 9.9 mg/dl)	No
41	98	21/F	Primigravida	Non-Consanguinous	22 weeks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
42	101	32/F	Primigravida	Non-Consanguinous	21 weeks 3 days	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10.6 mg/dl)	No
43	102	25/F	G2P1	Non-Consanguinous	19 weeks 6 day	Spontaneous	No	No	Yes (TSH 6.12 Iu/ml)	No	No	No	No	No	No	Yes (Hb 7.6 mg/dl)	No

44	103	30/F	G2P2L2	Non-Consanguinous	18 weeks	Spontaneous	No (DIPSI 80 mg/dl)	Yes (160/100 mmhg)	No	No	No	No	No	No	No	Yes (Hb 10 mg/dl)	No
45	104	19/F	Primigravida	Non-Consanguinous	32 weeks 1 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 9.9 mg/dl)	No
46	105	27/F	Primigravida	Non-Consanguinous	16 weeks 3 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
47	109	33/F	Primigravida	Non-Consanguinous	14 weeks	Spontaneous	No (DIPSI 66 mg/dl)	No	No	No	No	No	No	No	No	No	No
48	110	38/F	G2P1	Non-Consanguinous	18 weeks 6 days	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 9 mg/dl)	No
49	113	31/F	G2P1	Non-Consanguinous	25 weeks 3 days	Spontaneous	No	No	Yes (TSH 1.15 Iu/ml) K/C on Rx	No	No	No	No	No	No	Yes (Hb 10 mg/dl)	No
50	115	21/F	Primigravida	Non-Consanguinous	17 weeks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10.7 mg/dl)	No
51	116	25/F	G2 P1 L1	Non-Consanguinous	19 weeks 1 day	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
52	117	26/F	Primigravida	Non-Consanguinous	22 weeks	Spontaneous	Yes	No	No	No	No	No	No	No	No	No	No
53	123	24/F	G2P1	Non-Consanguinous	23 weeks 5 days	Spontaneous	No (FBS 75)	No	No	No	No	No	No	No	No	No	No
54	124	26/F	G2P1L1	Non-Consanguinous	26 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
55	125	22/F	Primigravida	Non-Consanguinous	28 weeks 1 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10 mg/dl)	No
56	126	31/F	G2A1	Non-Consanguinous	30 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
57	129	33/F	Primigravida	Non-Consanguinous	25 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
58	130	24/F	G2P2	Non-Consanguinous	22 weeks 3 days	Spontaneous	yes (HbA1c 6.5%)	No	No	No	No	No	No	No	No	Yes (Hb 10.4 mg/dl)	No
59	131	25/F	Primigravida	Non-Consanguinous	19 weeks 2 day	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10.6 mg/dl)	No
60	132	22/F	Primigravida	Non-Consanguinous	24 weeks 4 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
61	145	26/F	Primigravida	Non-Consanguinous	22 weeks	Spontaneous	No	Yes	No	No	No	No	No	No	No	No	No
62	148	22/F	G2P1	Non-Consanguinous	32 weeks 1 day	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
63	151	24/F	G2A1	Non-Consanguinous	25 weeks 3 days	Spontaneous	Yes	No	No	No	No	No	No	No	No	Yes (Hb 10.1mg/dl)	No
64	156	27/F	Primigravida	Non-Consanguinous	26 weeks	Spontaneous	No	Yes	No	Yes	No	No	No	No	No	Yes (Hb 10.7 mg/dl)	No
65	157	33/F	Primigravida	Non-Consanguinous	25 weeks	Spontaneous	No	No	Yes	No	No	No	No	No	No	Yes (Hb 10.6 mg/dl)	No
66	158	30/F	G2P2	Non-Consanguinous	21 weeks 3 days	Spontaneous	Yes	No	No	No	No	No	No	No	No	No	No

67	161	22/F	Primigravida	Non-Consanguinous	26 weeks	Spontaneous	No	Yes	No	Yes	No	No	No	No	No	No	No
68	162	33/F	Primigravida	Non-Consanguinous	20 weeks	Spontaneous	Yes	No	No	No	No	No	No	No	No	No	No
69	164	21/F	Primigravida	Non-Consanguinous	26 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10 mg/dl)	No
70	165	28/F	G3A1	Non-Consanguinous	27 weeks 2 days	Spontaneous	No	Yes	No	No	No	No	No	No	No	Yes (Hb 10.7 mg/dl)	No
71	166	29/F	G2A1	Non-Consanguinous	23 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
72	169	22/F	Primigravida	Non-Consanguinous	24 weeks 4 days	Spontaneous	No	No	Yes	No	No	No	No	No	No	No	No
73	173	21/F	Primigravida	Non-Consanguinous	25 weeks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
74	174	25/F	Primigravida	Non-Consanguinous	25 weeks	Spontaneous	No	No	Yes	No	No	No	No	No	No	Yes (Hb 10.2 mg/dl)	No
75	179	24/F	Primigravida	Non-Consanguinous	27 weeks 4 days	Spontaneous	No	No	No	No	No	No	No	No	No	Yes (Hb 10.4 mg/dl)	No
76	181	26/F	G2P1	Non-Consanguinous	26 weeks	Spontaneous	No	Yes	No	Yes	No	No	No	No	No	No	No
77	1	28/F	G2A1	Non-Consanguinous	25 weeks 1 days	Spontaneous	Yes	Yes	No	No	No	No	No	No	No	No	No
78	2	30/F	G2P1L1	Non-Consanguinous	23 weeks	Spontaneous	No	Yes	No	No	No	No	No	No	No	yes	No
79	6	20/F	Primigravida	Non-Consanguinous	28 weeks 2 days	Spontaneous	No	Yes	No	No	No	No	No	No	No	yes	No
80	10	21/F	Primigravida	Non-Consanguinous	26 weeks	Spontaneous	Yes	No	No	No	No	No	No	No	No	No	No
81	11	30/F	Primigravida	Non-Consanguinous	28 weeks 1 day	Spontaneous	No	Yes	No	No	No	No	No	No	No	No	No
82	12	30/F	G2A1	Non-Consanguinous	25 weeks 1 days	Spontaneous	No	Yes	No	No	No	No	No	No	No	yes	No
83	19	24/F	Primigravida	Non-Consanguinous	20 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
84	22	33/F	Primigravida	Non-Consanguinous	25 weeks 1 days	Spontaneous	No	No	Yes	No	No	No	No	No	No	No	No
85	24	22/F	Primigravida	Non-Consanguinous	23 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
86	25	21/F	Primigravida	Non-Consanguinous	17 weeks 1 days	Spontaneous	No	No	No	No	No	No	No	No	No	yes	No
87	27	22/F	Primigravida	Non-Consanguinous	25 weeks 1 days	Spontaneous	Yes	NO	NO	No	No	NO	NO	NO	No	No	No
88	28	26/F	G2P1	Non-Consanguinous	20 weeks	Spontaneous	No	Yes	No	No	No	No	No	No	No	yes	No
89	29	33/F	G2A1	Non-Consanguinous	28 weeks 1 day	Spontaneous	No	Yes	No	No	No	No	No	No	No	yes	No
90	30	28/F	G2P2	Non-Consanguinous	25 weeks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No

91	36	26/F	Primigravida	Non-Consanguinous	27 weeks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
92	42	23/F	Primigravida	Non-Consanguinous	34 weeks	Spontaneous	No	Yes	No	Yes	No	No	No	No	No	Yes (Hb 10.4 mg/dl)	No
93	43	22/F	Primigravida	Non-Consanguinous	23 weks 2 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
94	44	28/F	G2P1	Non-Consanguinous	28 weeks 6 days	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
95	45	22/F	Primigravida	Non-Consanguinous	28 weeks 2 days	Spontaneous	No	No	Yes (TSH 6.12 Iu/ml)	No	No	No	No	No	No	No	No
96	46	25/F	G2A1	Non-Consanguinous	26 weeks	Spontaneous	No	Yes	No	Yes	No	No	No	No	No	Yes (Hb 10.1mg/dl)	No
97	47	27/F	G2P1	Non-Consanguinous	26 weeks 4days	Spontaneous	No	Yes	No	Yes	No	No	No	No	No	No	No
98	48	21/F	Primigravida	Non-Consanguinous	32 weeks 1 day	Spontaneous	yes (HbA1c 6.5%)	No	No		No	No	No	No	No	Yes (Hb 10 mg/dl)	No
99	49	33/F	Primigravida	Non-Consanguinous	26 weeks	Spontaneous	No	No	No	No	No	No	No	No	No	No	No
100	50	23/F	Primigravida	Non-Consanguinous	30 weeks	Spontaneous	No	Yes (160/102 mmhg)	No	Yes	No	No	No	No	No	No (Hb 12.0 mg/dl)	No

SR NO	AUTOPSY NO	INFARCTION	AVM	DV	DVH	HEMATOMA	VFN	VILLITIS	AVASCULAR VILLI	VSK	IFD	DVM	THROMBI	DECIDUITIS	CHORANGIOSIS	CALCIFICATION	TYPE OF LESION
1	11	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	MIXED (MVM+ FVM)
2	12	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	FVM
3	14	NO	YES	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+ FVM)
4	16	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	FVM
5	17	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	MIXED(MVM+FVM)
6	21	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	FVM
7	22	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
8	23	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	CALCIFICATION	MVM
9	27	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	CALCIFICATION	MVM
10	31	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
11	33	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	YES	NO	YES	NO	NO	FVM
12	34	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	MIXED(MVM+FVM)
13	42	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(FVM+MVM)
14	43	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
15	44	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
16	46	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)
17	47	YES	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+ FVM)
18	49	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	MIXED(FVM+MVM)
19	50	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
20	55	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	FVM
21	57	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	MIXED(FVM+MVM)
22	58	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)
23	60	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM

24	63	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+ FVM)
25	66	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
26	67	NO	YES	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	CALCIFICATION	MIXED(FVM+MVM)
27	68	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	FVM
28	69	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	CALCIFICATION	MVM
29	71	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	CALCIFICATION	MIXED(FVM+MVM)
30	73	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
31	77	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	FVM
32	80	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
33	81	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	CALCIFICATION	MIXED(MVM+FVM)
34	86	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	YES	NO	FVM
35	87	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
36	90	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)
37	91	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	YES	NO	MIXED(FVM+MVM)
38	92	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
39	93	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
40	94	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+ FVM)
41	98	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
42	101	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
43	102	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	YES	NO	MIXED(MVM+FVM)
44	103	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	FVM
45	104	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO	FVM
46	105	YES	NO	YES (FIBRINOID NECROSIS)	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	CALCIFICATION	MVM
47	109	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
48	110	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
49	113	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+ FVM)
50	115	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
51	116	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	FVM

52	117	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	YES	CALCIFICATION	FVM
53	123	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	MIXED(MVM+FVM)
54	124	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+ FVM)
55	125	YES	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	MVM
56	126	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	FVM
57	129	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
58	130	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	MIXED(MVM+FVM)
59	131	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
60	132	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)
61	145	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	NO	MVM
62	148	YES	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	MIXED(MVM+ FVM)
63	151	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
64	156	YES	YES	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	MIXED(MVM+FVM)
65	157	NO	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	MIXED(MVM+ FVM)
66	158	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
67	161	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+FVM)
68	162	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	NO	MIXED(MVM+ FVM)
69	164	YES	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	MIXED(FVM+MVM)
70	165	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
71	166	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	FVM
72	169	YES	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)
73	173	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	FVM
74	174	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
75	179	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	FVM
76	181	YES	YES	YES (FIBRINOID NECROSIS)	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	CALCIFICATION	MVM
77	1	NO	YES	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)
78	2	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
79	6	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	CALCIFICATION	MIXED(MVM+FVM)

80	10	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
81	11	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	YES	NO	MIXED(MVM+FVM)
82	12	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	YES	NO	MIXED(MVM+FVM)
83	19	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	FVM
84	22	YES	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
85	24	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	FVM
86	25	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
87	27	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
88	28	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	MVM
89	29	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	FVM
90	30	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+FVM)
91	36	NO	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	FVM
92	42	YES	YES	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+ FVM)
93	43	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+ FVM)
94	44	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(MVM+FVM)
95	45	YES	YES	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	MIXED(MVM+ FVM)
96	46	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES	YES	YES	YES	MIXED(MVM+FVM)
97	47	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	YES	NO	FVM
98	48	YES	NO	NO	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	FVM
99	49	YES	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	YES	NO	NO	MIXED(FVM+MVM)
100	50	YES	NO	NO	NO	NO	YES	YES	NO	NO	NO	NO	NO	NO	NO	NO	NO	MIXED(MVM+FVM)