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A PROSPECTIVE STUDY ON HISTOPATHOLOGICAL CHANGES IN PLACENTAS OF HIGH-RISK PREGNANCY AT A TERTIARY CARE HOSPITAL

Dr.N.Bhavana[1], Dr.C.Sushma*[2], Dr.Md.Khader Faheem[3], Dr.C.A.Vishali[4], Dr.G.Indrani[5]

[1]Assistant Professor, Dept. of Pathology, Sri Venkateswara Institute of Medical Science, Tirupati
[2*]Associate Professor, Dept. of Pathology, S.V.Medical College, Tirupati
[3]Associate Professor, Dept. of Pathology, Govt. Medical College, Kadapa
[4]Assistant Professor, Dept. of Pathology, Anna Gowri Medical College & Hospital, Puttur
[5]Professor & Head, Dept. of Pathology, S.V.Medical College, Tirupati

***Corresponding Author:** Dr.C.Sushma
*Email: rjkf38@gmail.com

Abstract

Introduction: Placenta serves as a mirror of intrauterine maternal and fetal environment, and its histopathological examination provides valuable insight into adverse pregnancy outcomes and also aids in understanding underlying pathophysiological processes.

Objective: To evaluate the spectrum of gross and microscopic histopathological changes in placentas of high-risk pregnancies.

Method: A prospective observational study for a period of 6 months was conducted on 50 placentas obtained from high-risk pregnancies at a tertiary care hospital. Gross morphological parameters, including placental weight, thickness, and diameter, were recorded. Histopathological findings like syncytial knots, villous fibrosis, villous hyalinization, fibrinoid necrosis, infarcts, calcification, chorioamnionitis, intervillous hemorrhage, cytotrophoblastic proliferation, and perivillous fibrin deposition were studied.

Results: The most common high-risk groups encountered were gestational hypertension (26%), severe anemia (20%), and gestational diabetes mellitus (14%). Mean maternal age was highest in GDM pregnancies (30.4 ± 3.4 years). Overall mean gestational age was 36.5 ± 1.7 weeks in high risk pregnancies.

Placentas in GDM showed the highest mean placental weight (564 g), diameter (18.2 cm), and thickness (3.8 cm), while preterm placentas had the lowest values (mean weight 217 g). Syncytial knot formation was most marked in GDM (64.2 ± 15.3/100 villi) and GHTN (62.3 ± 10.4/100 villi). Calcifications were most frequent in IUGR (3.5 ± 0.9/10 LPF), followed by hypertensive and anemic cases. Villous stromal fibrosis, fibrinoid necrosis, and intervillous hemorrhage were significantly associated with hypertension and IUGR. Chorioamnionitis was observed predominantly in GDM and preterm cases.

Conclusion: Placentas from high-risk pregnancies show a distinct spectrum of histopathological changes, varying with the underlying maternal condition. Thus placental examination serve as a valuable adjunct in explaining adverse maternal and perinatal outcomes and guiding future obstetric care.

INTRODUCTION:
Placenta forms a vital link between mother and fetus. Status of both maternal and fetal health is reflected in placenta[1]. Any pregnancy can turn into a high risk one anytime during its course. A high-risk pregnancy is defined as one which is complicated by factor or factors that adversely affects the pregnancy outcome - maternal, perinatal or both[2]. The examination of placenta may provide information about various lesions in placenta and their association with various complications of pregnancy like Gestational diabetes, hypertensive disorders in pregnancy, hypothyroidism, Rh incompatibility, Intrauterine growth restriction, severe anemia, preterm, IUD, placenta previa[3].Pathological changes in the placenta of high-risk groups include infarction, calcifications, diffuse placental thrombosis, inflammatory placental vasculopathy, abnormal trophoblastic proliferation, increased syncytial knots, hypovascularity of the villi, obliterative enlarged endothelial cells in the fetal capillaries and fibrin plaque formation[4]. The present study is designed to observe the histopathological changes in the placenta of various high-risk groups.

AIM & OBJECTIVES
Aim: To evaluate the spectrum of histopathological changes in placentas of high-risk pregnancies.

Objectives:
To study the gross morphology of placenta in high-risk pregnant groups.
To assess different histopathological alterations in placentas of high-risk pregnant groups.

MATERIAL AND METHOD:
Study Design: Prospective study.
Study Setting: Department of Pathology, Sri Venkateswara Medical College, Tirupati, Andhra Pradesh
Study Period: six months from the date of Institutional Scientific committee and Institutional Ethics Committee approval.

Study Subjects/units:
Placenta of high-risk pregnant women sent to the department of pathology are studied and examined for histopathological alterations.

Sample Size: 50
Inclusion Criteria:
All complete placenta specimens along with umbilical cord and membranes of the following groups will be taken for study after taking written informed consent.
 Severe anemic pregnant women with < 7mg/dl of hemoglobin.
 Gestational diabetic mother's that either commence or first diagnosed in pregnancy.
 Mothers with Gestational hypertension showing systolic blood pressure of ≥ 140mmHg and/or diastolic blood pressure ≥ 90 mmHg confirmed on atleast 2 occasions 4 to 6 hours apart but within a week period.
 IUGR babies whose birth weights are disproportionately low for gestational (10th percentile) or 2 SD.
 Preterm with Gestational period of < 37 weeks.
 Mothers with low lying placenta/ placenta previa.
 Mothers with Hypothyroidism
 Rh negative pregnancy
 IUD
 Multiple pregnancy
Exclusion Criteria:
 Autolysed specimens
 Mothers with HIV infection

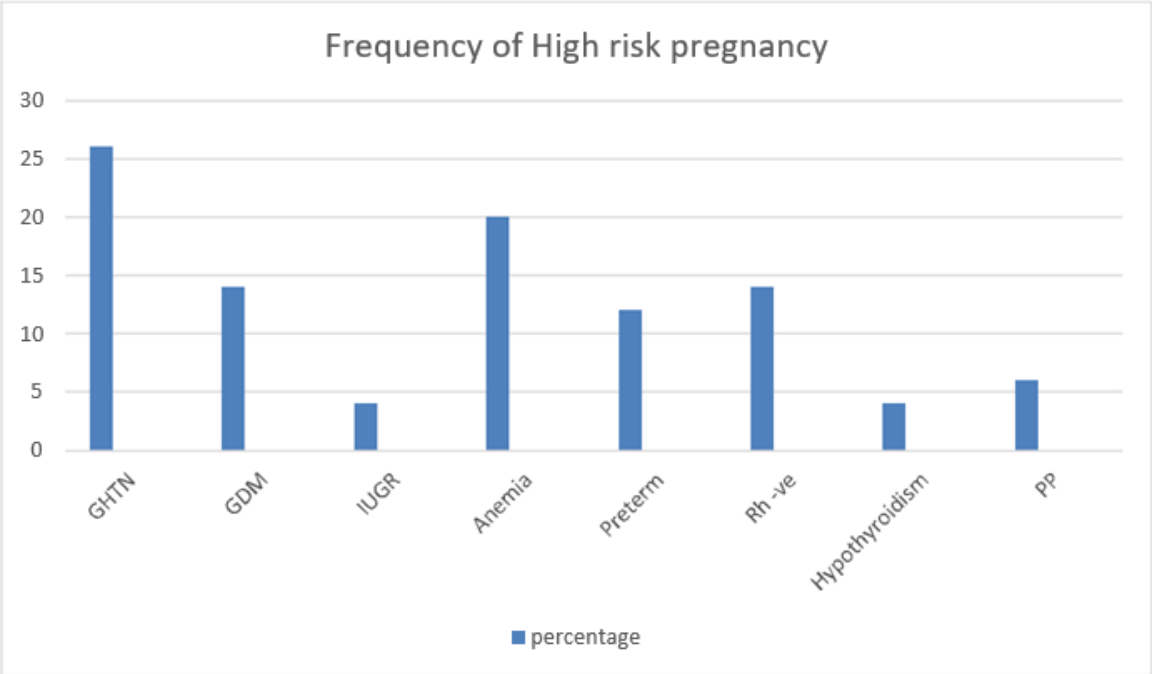
METHODOLOGY:
This study is designed as a prospective study, will be conducted in department of pathology, SVMC, Tirupati, over a period of 6 months.
Placental specimens received to the pathology department are categorised based on the clinical diagnosis into following high risk groups: Gestational Hypertension, Gestational Diabetes Mellitus, Intra Uterine Growth restriction, preterm pregnancy, severe anemia in pregnancy, Rh negative pregnancy, hypothyroidism, multiple pregnancy, mothers with low lying placenta and IUD.
For macroscopic examination, placenta received in 10% formalin are weighed after 24 hrs fixation and gross examination is done.

For microscopic examination, 5 cm of tissue strips are taken from the following areas: umbilical cord, central portion of the placenta, peripheral portion of the placenta, any gross lesion or representative area, extraplacental membranes. Sections of the tissues are taken for routine paraffin embedding. After embedding, sections of 4-5 micron thickness are cut with the microtome and stained with hematoxylin and eosin stain. Slides are studied under the compound microscope for Placental villi, size of villi, syncytial knot formation, hyalinization, fibrinoid necrosis, cytotrophoblastic proliferation, Stromal pathology, stromal fibrosis, calcification, hyalinization and intervillous hemorrhage etc.

RESULTS AND ANALYSIS:
The collected data will be entered in MS Excel spreadsheet. All categorical variables will be represented in the form of rates and percentages. Mean and standard deviations will be used to describe the continuous variables. Data thus collected is analysed using EPIINFO 7.2.5.CDC ATLANTA and MS Excel, Microsoft office 365 software.

Table 1: Distribution of high risk pregnancy cases

High risk category	Frequency	Percent
Gestational HTN	13	26
Gestational diabetes	7	14
IUGR	2	4
Severe Anemia	10	20
Preterm	6	12
Rh negative	7	14
Hypothyroidism	2	4
Placenta previa	3	6
Total	50	100



In the present study, among 50 high risk pregnancies, majority of the cases belonged to Gestational HTN(26%) followed by severe anemia (20%), Gestational Diabetes mellitus (14%) and Rh negative pregnancies (14%), Preterm (12%), Placenta previa (6%), Hypothyroidism (4%) and IUGR (4%).

Table 2: Maternal age wise distribution of study subjects

Age group	G HTN		GDM		IUGR		Severe anemia		Preterm		Rh -ve		Hypothyroidism		Placenta previa		Total	
(In years)	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
≤20	3	23	0	0	1	50	1	10	1	17	0	0	0	0	2	67	8	16
21-25	6	46	1	14	0	0	6	60	4	66	6	86	1	50	0	0	24	48
26-30	4	31	2	28	1	50	3	30	0	0	1	14	1	50	0	0	12	24
31-35	0	0	4	58	0	0	0	0	1	17	0	0	0	0	1	33	6	12
> 35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	**13**	**100**	**7**	**100**	**2**	**100**	**10**	**100**	**6**	**100**	**7**	**100**	**2**	**100**	**3**	**100**	**50**	**100**

In our study increased mean maternal age observed in Gestational Diabetes Mellitus – 30.4 ± 3.4, followed by Hypothyroidism -25.5 ± 4.9, Rh negative pregnancy – 23.8 ± 1.6, Gestational Hypertension – 23.7 ± 2.5, Placenta previa – 23.6 ± 10.2, IUGR – 23.5 ± 6.8, Anemia – 23.4 ± 1.9 and Preterm – 23.3 ± 4.

The overall mean age of high-risk pregnant women is 24.6 ± 1.3.

Table 3 : Gestational age wise distribution of study subjects

Gestational age(wks)	G HTN		GDM		IUGR		Severe anemia		Preterm		Rh -ve		Hypothyroidism		Placenta previa	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
≤37	1	8	0	0	1	50	4	40	6	100	0	0	0	0	0	0
38	1	8	1	14	0	0	2	20	0	0	1	14	0	0	1	33
39	11	84	4	57	0	0	4	40	0	0	6	86	2	100	2	67
40	0	0	2	29	1	50	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	13	100	7	100	2	100	10	100	6	100	7	100	2	100	3	100

In the present study, the mean gestational age in Gestational Diabetes mellitus is 39.1 ± 0.5 followed by Hypothyroidism – 39 ± 0, Rh negative pregnancy – 38.8 ± 0.3, Gestational Hypertension – 38.7 ± 0.4, Placenta previa – 38.6 ± 0.6, Anemia – 37.8 ± 0.7, IUGR – 23.5 ± 6.9 and Preterm – 22.6 ± 6.6.

Overall mean gestation age for high-risk pregnant women is 36.5 ± 1.7

Table 4 : Gross findings of study subjects

Parameter	Gestational hypertension	Gestational diabetes	IUGR	Severe Anemia	Preterm	Rh -ve	Hypothyroidism	Placenta Previa
Mean Placental weight (gm)	438	564	350	459.5	217	494	490	500
Placental weight in gms								
<400	4	0	2	3	6	0	0	0
401 – 500	7	0	0	4	0	6	2	2
501 - 600	2	7	0	3	0	1	0	1
> 601	0	0	0	0	0	0	0	0
Mean Placental diameter	15	18.2	14.5	15	12.5	18	16.5	17
Mean Placental	2.5	3.8	2	2.2	1.8	1.9	1.7	2.5

thickness								
Infarcts								
Absent	8	3	0	4	4	4	1	3
Present	5	3	2	6	2	3	1	0

In the present study, mean placental weight, mean placental diameter and means placental thickness in Gestational Diabetes mellitus is 564.3 ± 9.4gms, 18.2 ± 0.8cm and 3.8 ± 0.5cm followed by placenta previa – 500 ± 11.3gms, 17 ± 1.1cm and 2.5 ± 0.6cm, Rh negative pregnancy – 494.3 ± 8.4gms, 18.1 ± 2.9cm and 2 ± 0.3cm, Hypothyroidism – 490 ± 19.6gms, 16.5 ± 0.9cm and 1.75 ± 0.5cm, Anemia – 459.5 ± 52.7gms, 15 ± 0.7cm and 2.15 ± 0.3cm, Gestational Hypertension – 437.7 ± 44.2gms, 15.4 ± 1cm and 2.5 ± 0.3cm, IUGR – 350 ± 19.6gms, 13.5 ± 0.9cm and 2 ± 0cm and Preterm – 216.6 ± 36gms, 12.5 ± 1.9cm and 1.8 ± 0.2cm.
Increased number of infarcts is seen in IUGR - 100%, Anemia - 60% cases followed by Gestational DM- 50%, Hypothyroidism – 50%, Rh negative pregnancies - 43%, Gestational hypertension - 38% cases, Preterm – 33% and none of the placenta previa cases showed any infarcts.

Table 5 : Various histopathological changes in study subjects

Microscopic features	**Gestational Hypertension N=13**	**Gestational Diabetes N = 7**	**IUGR N = 2**	**Severe anemia N=10**	**Preterm N = 6**	**Rh - ve n = 7**	**Hypothyroidism N = 2**	**Placenta previa N = 3**
No. of Syncytial knots per 100 villi								
0-30	2	1	2	5	5	5	0	2
31-60	8	4	0	3	1	2	2	1
61-90	3	2	0	2	0	0	0	0
91-120	0	0	0	0	0	0	0	0
No. of Calcified areas/ 10 Lpf								
0	5	1	0	2	2	4	2	1
1	2	3	0	3	1	1	0	2
2	1	1	0	1	2	0	0	0
3	1	1	1	2	0	1	0	0
4	1	1	1	1	0	0	0	0
5	3	0	0	1	1	1	0	0
No. of areas of fibrinoid necrosis/ 100 villi								

0 - 5	5	2	0	3	3	3	2	3
6-10	7	2	2	4	3	3	0	0
11-15	1	2	0	2	0	1	0	0
16-20	0	1	0	1	0	0	0	0
21-25	0	0	0	0	0	0	0	0
No. areas of Cytotrophoblastic proliferation								
1-5	3	0	0	3	4	0	2	3
6-10	0	1	1	5	1	1	0	0
11-15	1	0	1	2	1	4	0	0
16-20	2	2	0	0	0	2	0	0
21-25	7	4	0	0	0	0	0	0
Hyalinised villi per 10 Lpf								
1-5	2	5	1	4	1	2	0	2
6-10	1	2	1	2	2	2	0	0
11-15	3	0	0	0	0	1	1	0
16-20	3	0	0	2	3	2	0	1
21-25	4	0	0	2	0	0	1	0
Perivillous fibrin deposition								
Present	4	1	1	4	3	6	0	2
absent	9	6	1	6	3	1	2	1
Villous stromal fibrosis								
Present	8	5	2	5	3	5	0	0
absent	5	2	0	5	3	2	2	3
Chorioamnioni								

tis								
Present	0	4	0	1	5	1	0	0
absent	13	3	2	9	1	6	2	3

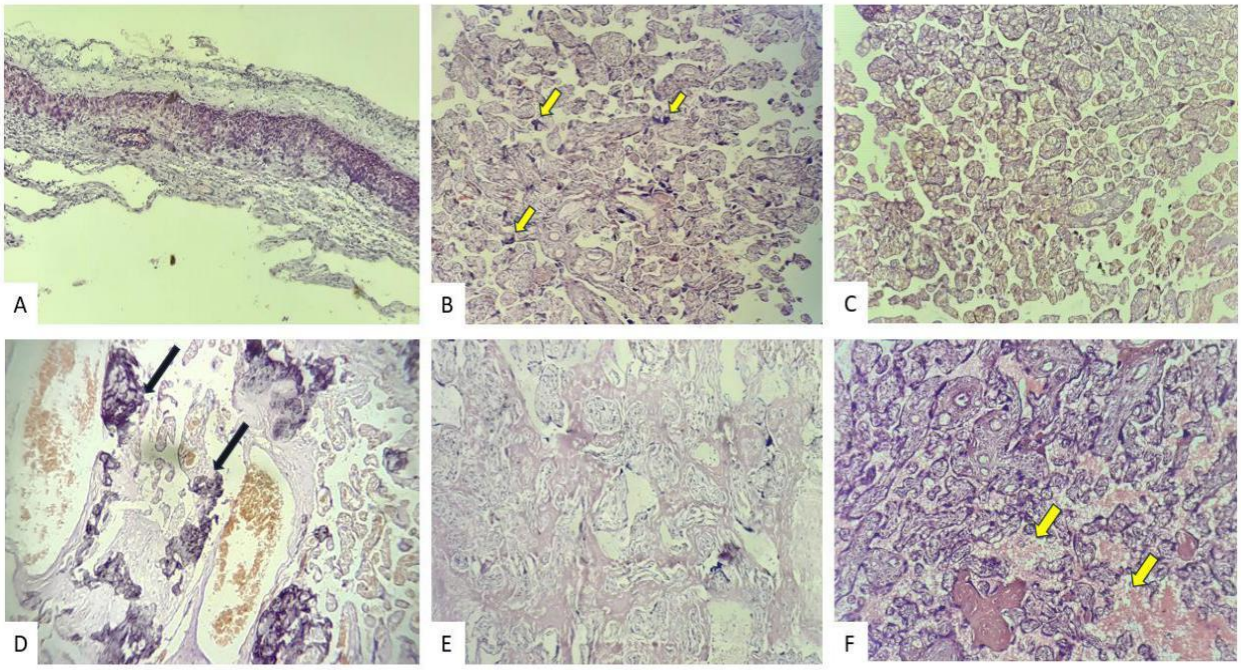
Intervillous hemorrhage

Present	7	1	1	3	0	6	1	1
absent	6	6	1	7	6	1	1	2

Syncytial knots: In the present study, the mean number of syncytial knots per 100 villi is 64.2 ± 15.3 in Gestational Diabetes mellitus, 62.3 ± 10.4 in gestational hypertension, 60 ± 0 in hypothyroidism , 51 ± 15.3 in Anemia, 40 ± 19.6 in placenta previa, 38.5 ± 10.8 in Rh negative pregnancy, 35 ± 9.8 in preterm and 30 ± 0 in IUGR.

Calcification: in the present study the mean number of calcified areas per10 Lpf is 3.5 ± 0.9 in IUGR, followed by 2 ± 1.1 in Gestational hypertension, 2 ± 1 in Anemia, 1.7 ± 1 in Gestational diabetes mellitus, 1.6 ± 1.4 in preterm, 1.2 ± 1.4 in Rh negative pregnancy, 0.6 ± 0.6 in placenta previa and none in Hypothyroidism.

Fibrinoid necrosis: In the present study, the number areas of fibrinoid necrosis per 100 villi is 11.4 ± 4.1 in Gestational diabetes mellitus, 10.5 ± 3 in Anemia, 10 ± 0 in IUGR, 8.5 ± 2.8 in Rh negative pregnancy, 8.4 ± 1.7 in Gestational hypertension, 7.5 ± 2.1 in Preterm, 5 ± 0 in Hypothyroidism and placenta previa.



A) Acute chorioamnionitis: Shows infiltration of neutrophils into the placental membranes H&E 10x; B) increased syncytial knots H&E 20X; C) chorangiosis- increased villous vascularity H&E 20X; D) multiple foci of calcification H&E 20x; E) picture showing fibrinoid necrosis and perivillous fibrin deposition H&E 20X; E) intervillous hemorrhage H&E 20X.

Cytotrophoblastic proliferation: In the present study, the number of areas of cytotrophoblastic proliferation per 100 villi is 21.4 ± 4 in Gestational diabetes mellitus, 18.3 ± 4.3 in Gestational

Hypertension,15.7 ± 2.5 in Rh negative pregnancy, 12.5 ± 4.9 in IUGR, 9.5 ± 2.2 in Anemia, 7.5 ± 3.3 in Preterm, 5 ± 0 in Hypothyroidism and Placenta previa.

Hyalinised villi: in the present study, Hyalinised villi per 10 Lpf is 20 ± 9.8 in Hypothyroidism, 17.3 ± 3.9 in Gestational hypertension, 14.2 ± 5.3 in Preterm, 13 ± 5.3 in Anemia, 12.1 ± 4.7 in Rh negative pregnancy, 10 ± 9.8 in placenta previa, 7.5 ± 4.9 in IUGR and 6.4 ±b1.8 in Gestational diabetes.

Perivillous fibrin deposition: In the present study, perivillous fibrin deposition is seen in 85.7 cases of Rh negative pregnancy followed by Placenta previa – 66.6%, IUGR – 50%, Preterm – 50%, Anemia – 40%, Gestational Hypertension – 30.8%, Gestational Diabetes mellitus – 14.2 % and none of the cases of Hypothyroidism.

Villous stromal fibrosis: in the present study, 100% cases of IUGR, followed by Gestational diabetes mellitus – 71.4%, Rh negative pregnancy – 71.4%, Gestational hypertension – 61.5%, Anemia – 50%, Preterm – 50%, and none of the cases showed villous stromal fibrosis in Hypothyroidism and Placenta previa.

Chorioamnionitis: In the present study, 83.3% of Preterm cases, 57% of Gestational diabetes mellitus cases and 14.2% cases of Rh negative pregnancy showed chorioamnionitis, remaining groups did not show any features of chorioamnionitis.

Intervillous Hemorrhage: In the present study, 85.7% cases of Rh negative pregnancy cases followed by 53.8% cases of Gestational Hypertension, 50% cases of IUGR and Hypothyroidism, 30% cases of Anemia, 14.2% cases of Gestational diabetes mellitus and none of the cases of preterm showed findings of intervillous hemorrhage.

DISCUSSION:

High-risk pregnancies are associated with an increased incidence of placental abnormalities. Histopathological examination of the placenta provides valuable insights into the underlying pathophysiology of adverse pregnancy outcomes, predicts the risk of possible recurrence, and provides useful information on treatment opportunities for future pregnancies.

In the present study, Gestational hypertension accounts for most of the cases - 26% , followed by severe anemia (20%), Gestational Diabetes mellitus (14%), Rh negative pregnancies (14%), Preterm (12%), Placenta previa (6%), Hypothyroidism (4%) and IUGR (4%), which is correlating with other study done by Parveen A et al[5] where Hypertensive disorders of pregnancy - (30%) are most common followed by gestational diabetes mellitus (22%).

In the current study, the mean maternal age is lower for Anemia (23.4 ± 1.9) and preterm (23.3 ±and higher for gestational diabetes mellitus (30.4 ± 3.4). According to numerous studies, women over 30 are more likely to develop GDM due to elevated insulin resistance, hormonal fluctuations, and an increased risk of being overweight.

The overall mean age of women linked to high-risk pregnancy is 24.6 ± 1.3 which is correlating with a study done by Parveen A et al[5] (28.7 ± 5.6 years).

In the present study, the mean gestational age is lower for IUGR (23.5 ± 6.9) and preterm (22.6 ± 6.6) and higher for Gestational Diabetes Mellitus (39.1 ± 0.5), followed by Hypothyroidism (39 0). According to a study done by Parveen A et al[5]., the average gestational age for high-risk pregnancies is 36.5 ± 1.7 weeks, which is consistent with the present study of 36.8 ± 3.4 weeks.

Gestational diabetes mellitus has the largest mean placental weight, placental diameter, and placental thickness in this study—564.3 ± 9.4 kg, 18.2 ± 0.8 cm, and 3.8 ± 0.5 cm—compared to other high-risk groups. These findings are consistent with those of earlier studies conducted by Pradnya S et al[6] and Soad A et al[7]. The compensatory hyperplasia of villous parenchyma to fetal hyperglycemia results in increased placental weight and fetal macrosomia.

In this study, the average placental weight, placental diameter, and thickness of overall high-risk pregnancies were 459.5 ± 52.7 gms, 15 ± 0.7 cm, and 2.15 ± 0.3 cm, respectively. These values are significantly lower than the normal pregnancy and are consistent with findings from prior studies by Mongia SM et al[8]. and Gunapriya R et al[9]. (476.8 ± 33.16 gm).

In cases of gestational hypertension, the average placental weight, placental diameter, and thickness are 437.7 ± 44.2 gms, 15.4 ± 1 cm, and 2.5 ± 0.3 cm, respectively. These values are consistent with earlier studies conducted by Parveen A et al[5]. (422.73±40.8) and Bhojwani K et al[10] (410±60gm) and Porwal V et al[11]. (409±88.69 g). The intra-cotyledonous vascular rearrangement that causes feto-maternal malperfusion is the cause of this reduced placental weight in gestational hypertension.

Only few studies on placental morphology in hypothyroid were available in the literature. In the present study mean placental weight in Hypothyroidism is found to be 490 ± 19.6gms, 16.5 ± 0.9cm and 1.75 ± 0.5cm which is correlating with a study done by Parveen A et al[5] (508.83 ± 32.13 gm). Kumari S et al[12] mentioned that hypothyroidism leads to increased apoptosis in placenta therefore might be playing a key role in reducing weight of placenta.
In the present study, lowest mean placental weight, placental diameter and placental thickness is observed in Preterm delivery - 216.6 ± 36gms, 12.5 ± 1.9cm and 1.8 ± 0.2cm. Because, Preterm infants are born before the placenta has fully matured and supported optimal fetal growth, resulting in a smaller placenta.
Current study showed increased number of infarcts in IUGR - 100%, followed by Anemia - 60%. Begum M et al[13] observed that in IUGR macroscopically identifiable placental infarcts occurred frequently, similar to present study.

Gestational Hypertension:
The current evidence points to Gestational hypertension being a multifactorial and a multisystem disorder. The primary mechanism in the pathogenesis of this condition has been determined to be abnormal placentation and the cytotrophoblast's defective invasion of the spiral arteries disrupting physiological vascular remodeling. Manifestations of reduced maternal blood flow in the form of infarction, cytotrophoblast hyperplasia and reduced fetal blood flow in the form of and syncytial knotting and villous fibrosis have been found in the previous studies.

Infarction – In the present study, 38 % cases (5/13) showed infarcts. Placental infarction denotes an area of ischemic villous necrosis secondary to thrombotic occlusion of the maternal uteroplacental blood vessels.

Cyto-trophoblastic hyperplasia – In the present study, the average number of areas of cyto-trophoblastic proliferation per 100 villi is 18.3 ± 4.3 and involvement of >20% villi is seen in 53 cases (7/13). Other study done by Kartheek BVS et al[13], recorded abnormal cyto-trophoblastic proliferation in 36.36% of hypertensive pregnancies as compared to normal ones. Studies have shown a positive correlation between the severity of hypertension and the percentage of abnormal cyto-trophoblastic proliferation.

Villous stromal fibrosis – In the present study, villous stromal fibrosis is observed in 61.5% cases (8/5) which may be due to reduced fetal blood flow through the villi resulting in stromal fibrosis. similar findings observed in a study done by Satosar A et al[14] (53%).

Calcification – In the present study, the mean number of calcified areas per 10 Lpf is 2 ± 1.1. Calcification is a sign of placental ageing or maturation. Other studies done by Goswami P et al[15]., and Dutta A et al[16]., showed calcification in 66% and 44.3% cases. It can be concluded that the incidence of placental calcification increases as the severity of the hypertension increases.

Syncytial knots - In the present study, the mean number of syncytial knots per 100 villi is 62.3 ± 10.4 and >30 syncytial knots per 100 villi is seen in 84 % cases (11/13). Increased syncytial knots (Tenney-Parker changes) are a by-product of accelerated villous maturation and reduced perfusion. In normal pregnancy, these are seen in about 25% of the villi at term. Increased knots on more than 30% of the villi may be regarded as increased. A cutoff value of 30% can be used to determine the increased density of syncytial knots on the section under one low power field at a given gestational age. This finding is supported by Pathiraja RP et al[17]., (88.2%), Nahar L et al[18]., (95%), and Dutta A et al[16]., (73.8%): all three studies reported a statistically significant presence of syncytial knots.

Similarly increased number of syncytial knots, villous stromal fibrosis, cytotrophoblastic proliferation and increased calcification is also noted in other studies done by Kumar S et al[4], Bhojwani K et al[10] and Sharma N et al[19]. Other studies also found significant association between Hypertensive disorders of pregnancy and fibrinoid necrosis which may be due to uteroplacental insufficiency and vascular damage.

Gestational Diabetes mellitus:

Fibrinoid necrosis – A condition where the villous stroma is replaced by fibrinoid - protein deposit, occurs in GDM placenta as a consequence of metabolic disturbances and vascular changes. In GDM, fetal hyperglycemia, creates an inflammatory state and associated vascular dysfunction contribute to the development of fibrinoid necrosis. In the present study the average number areas of fibrinoid necrosis per 100 villi is 11.4 ± 4.1 and >10% involvement of villi is seen in 42.8% (3/7) cases whereas other study done by Evers IM et al[20], showed Haretha A et al[21] (61.1%).

Syncytial knots – Increased syncytial knots in GDM indicates placental malperfusion and occurs as a compensatory response to hypoxic stress. In the present study, the mean number of syncytial knots per 100 villi in GDM is 64.2 ± 15.3 and >30% villi involved in 85.7% (6/7) cases correlating with the study done by Anjali R et al[22] (80%)., Akhlaq et al[23]., (70%) and Haretha A et al[21] (82%).

Cytotrophoblastic proliferation – Increased cytotrophoblast proliferation indicates placental dysmaturity which is highly typical in placentas of diabetic mothers. In the present study, the average number of areas of cyto-trophoblastic proliferation per 100 villi is 21.4 ± 4 and >20% involvement of villi is seen in 57.1% (4/7) cases correlating with other studies done by Parveen A et al[5] (50%) and Anjali R et al[22] (60%).

Stromal villous fibrosis – GDM can impair placental blood flow and oxygen delivery leading to ischemia and hypoxia in the villous stroma which further triggers fibrosis. In the present study, villous stromal fibrosis is observed in 71.4% (5/2) cases. Similar findings of increased incidence of villous fibrosis is also found in Kumar S et al[4] (100%) and Anjali R et al[22] (100%).

Chorioamnionitis – GDM associated inflammatory state and hyperglycemic state in the placenta can create a more favourable environment for microbial colonisation and infection, GDM can also affect maternal immune function, making susceptible to infections. In the present study, 57% (4/7) cases are associated with chorioamnionitis similar to Kumar S et al[4].

Anemia:

Severe anemia leads to reduced amount of oxygen carrying red blood cells available in the placenta. This hypoxia causes the placenta to adapt by increasing its vascularisation. This compromised blood flow can lead to damage and death of villous tissue causing infarction, followed by deposition of fibrin like material – Fibrinoid necrosis, other changes include increased syncytial knots, villous stromal fibrosis, calcification reflect placenta's struggle to cope with the effects of maternal anemia.

In the present study, infarction seen in 60% (6/10) cases, average number of areas of fibrinoid necrosis per 100 villi is 10.5 ± 3 and >10% involvement of villi is seen in 30% (3/10) cases, average number of syncytial knots /100 villi is 51 ± 15.3 and >30% villi is seen in 50% (5/10) cases, villous stromal fibrosis is seen in 50% (5/10) cases, average number of calcified areas/10 Lpf in 2 ± 1 and >1/10Lpf is seen in 80% (8/10) cases.

Similar findings of increased frequency of infarction (60%), fibrinoid necrosis (60%), Syncytial knotting (40%), villous stromal fibrosis (90%) and calcification (30%) was found in a study done by Kumar S et al[4] and Kulandaivelu AR et al[24], Rangnekar et al[25]., found that, increased villous vascularity and decreased incidence of excess syncytial knot formation, suggest a possibility of an adequate compensatory capacity of patients.

Intrauterine growth restriction: Fetal Growth Restriction (FGR) is defined as a fetal weight below the 10th percentile for gestational age The common finding observed in placenta of IUGR was cytotrophoblastic hyperplasia and infarction, fibrinoid necrosis, increased syncytial knots and perivillous fibrin deposition.
In the present study, the average number of areas of cytotrophoblastic proliferation per 100 villi is 12.5 ± 4.9, the average number of areas of fibrinoid necrosis per 100 villi is 7.5 ± 2.1, the average number of syncytial knots per 100 villi is 30 ± 0 and is seen in 100% (2/2) cases but lower when compared to Gestational Hypertension, GDM and anemia.
Perivillous fibrin deposition is seen in 50% (1/2) cases. The mean number of calcified areas per 10 Lpf is 3.5 ± 0.9 and is seen in 100% (2/2) cases, which is higher than other high risk pregnancies.
Other studies have shown cytotrophoblastic hyperplasia in 44% Kaviya M et al[26], 62% Mehendale SS et al[27], 60 % Haretha A et al[21], increased calcification, fibrinoid necrosis (80%), increased syncytial knots (40%) and perivillous fibrin deposition (40%). Kotgirwar S et al[28] mentions fibrinoid necrosis is considered as hallmark of immune attacks on trophoblastic cells and syncytial knots are indicators of fetal circulation compromise. Bane AL et al[29] says the perivillous fibrin depositions might be acting as a barrier between fetal and maternal circulation is which reduces transfer of nutrients to fetus, leading to IUGR.
The association between IUGR and villous hypomaturity (44.4%; p=0.001) observed in the present study is supported by the findings of Vedmedovska N et al[30]., who reported villous hypomaturity in 36% of placentas from IUGR pregnancies.

Preterm:
preterm deliveries (defined as delivery at 20 weeks and <37 weeks of gestation) In the present study, significant association between Chorioamnionitis and preterm is observed with 83.3% (5/6) cases, which is correlating with other studies done by 6) (40%) and 10) (60%). In addition, 50% (3/6) cases showed perivillous fibrin deposition and villous stromal fibrosis which has no significance.

Rh negative pregnancy:
In the present study, increased cytotrophoblastic proliferation with mean number of 15.7 ± 2.5 seen per 100 villi, increased perivillous fibrin deposition in 85.7% (6/7) cases and increased villous stromal fibrosis is seen in 71.4% (5/7) cases.Similarly, increased cyto-trophoblastic hyperplasia seen in Narasimha A et al[31] (86%), Mehendale SS et al[27] (87.5%) and Haretha A et al[21] (62.5%), villous stromal fibrosis (81.8%) in Haretha A et al.

Hypothyroidism:
In the present study, pathological changes like increased syncytial knots with average number of 60 ± 0 per 100 villi and >30% involvement of villi is seen in 100% (2/2) cases, Hyalinized villi per 10 Lpf with a mean number of 20 ± 9.8 is seen in 100% (2/2) cases and Intervillous hemorrhage is seen in 50% (1/2) cases correlating with other study done by Haretha A et al[21] (83%).

Placenta previa:
In the present study, increased number of syncytial knots with a mean number of 40 ± 19.6 per 100 villi and >30% involvement of villi is seen in 33.3% (1/3) cases and increased perivillous fibrin deposition 66.6% (2/3) cases.

CONCLUSION:

In conclusion, this study highlights the importance of placental examination in the evaluation of high-risk pregnancies and provides a foundation for future research to improve maternal and fetal outcomes. The significant associations between specific high-risk conditions and histopathological findings underscore the need for further investigation into the pathophysiology of adverse pregnancy outcomes and the development of targeted interventions based on placental pathology.
However, the limitations of this study, including the relatively small sample size and the lack of a control group, should be acknowledged. Future research with larger, multicenter studies and the inclusion of normal pregnancies as a control group is needed to validate these findings and to explore the potential clinical applications of placental histopathology in high-risk pregnancies.

Ethical Consideration:
Written informed consent from the patients from whom placental samples are collected at Govt. Maternity Hospital and permission from the Professor & Head, Dept. of Pathology will be obtained for conducting the study.
All investigations are done free of cost and no financial burden on the patient will be levied related to the study.

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