Angiogenic and anti-angiogenic marker expression in hypertensive placentas: correlation with placental morphology, doppler findings, and foetal outcome.

Dr.Ruthra ,Dr. Umamaheshwari.G , Dr. Divya. R , PSG Institute of Medical sciences and Research, Tamilnadu, India.

BACKGROUND

Hypertensive disorders of pregnancy (HDP), affecting 10–15% of pregnancies worldwide, remain a major cause of maternal and fetal morbidity, with a multifactorial pathogenesis involving dysregulated angiogenesis. An imbalance between angiogenic factors (VEGF, PlGF) and anti-angiogenic factors (sFlt-1) plays a key role, though the precise mechanisms in hypertensive pregnancies are not fully understood. This study aims to evaluate placental morphology and the expression of VEGF and sFlt-1, and to correlate these findings with Doppler parameters and fetal outcomes in normal and hypertensive pregnancies.

AIMS & OBJECTIVES

- To evaluate VEGF and sFlt-1 expression in placental tissue
- To compare placental morphology in normal and hypertensive pregnancies
- To correlate histomorphology and IHC findings with Doppler parameters and fetal outcome

MATERIALS AND METHODS

Prospective study done in a tertiary-care centre with placentas from of 30 HDP and 30 control placentas. Clinical details, Doppler findings, and foetal outcomes were recorded. Placentas underwent gross, histopathological, and VEGF/sFlt-1 IHC evaluation with clinico-radiological correlation

RESULTS

TABLE 1: CLINICAL DETAILS

Study Population	Age		Gestational age			Gravidity		Mode of Conception		Doppler Findings		Foetal outcome	
	20-30 yrs	31–40 yrs	26- 32 weeks	33 -36 weeks	37-40 weeks	Primi	Multigravida	ART	Spontaneous	AEDF	PI (>95th percentile)	IUD	Live birth
Cases (n=30)	19	11	13	12	5	17	13	10	20	3/30	15/30	4	26
Controls (n=30)	29	1	0	5	25	24	6	0	30	Not done	Not done	0	30

TABLE 2: PLACENTAL GROSS MORPHOLOGY

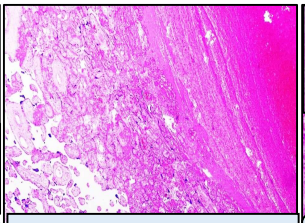
Parameters	Cases(n=30)		Controls(n=30)		P values
	Mean	SD	Mean	SD	
Placental Weight(gm)	288.8	115.13	401.57	55.01	<0.001
Fetal weight(kg)	1.63	0.50	2.92	0.39	<0.001
Foeto Placental Ratio	6.06	1.27	7.2	1.1	<0.001
Umbilical cord Diameter(cm)	0.84	0.2	1.33	1.46	<0.001

TABLE 3: MICROSCOPIC FEATURES

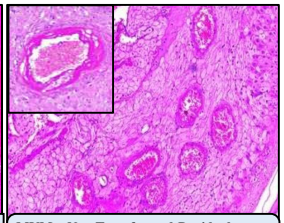
Microscopic features		Sub-categories	Cases	Controls
Maternal Vascular Malperfusion (MVM)	Infarcts	+	18	0
		-	12	0
	Decidual vasculopathy	+	11	0
		-	19	0
	Intervillous thrombus	+	13	0
		-	17	0
	Increased syncytial knots	+	7	4
		-	23	26
	Distal villous hypoplasia	+	3	2
		-	27	28
	Villous agglutination	+	7	18
		-	23	12
Fetal Vascular Malperfusion (FVM)		Low grade	7	3
		High grade	11	0
		Absent	12	27
Villitis of Unknown Aetiology (VUE)		+	7	0
		-	21	30
Perivillous fibrin deposition (PVFD)		+	3	8
		-	27	22
Acute Chorioamnionitis		+	3	13
		-	27	17
Villous Capillary lesion		+	12	Not seen
		-	18	Not seen

MICROPHOTOGRAPHS

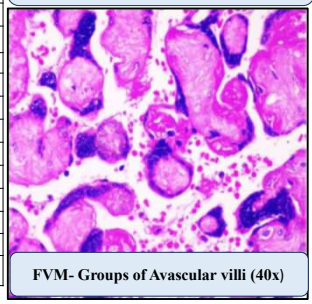
Gross: Placental parenchyma with multiple infarcts and thrombo-hematoma



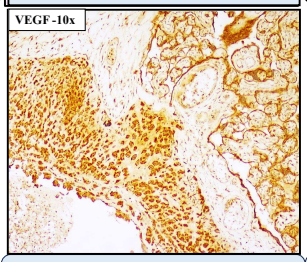
MVM-Central hematoma surrounded by infarcted villi



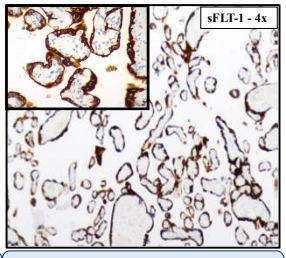
MVM – Non Transformed Decidual vessels(4 x) with fibrinoid necrosis of vessel wall & atherosis (insert)



FVM- Groups of Avascular villi (40x)



Villous & Extravillous trophoblasts exhibiting strong expression



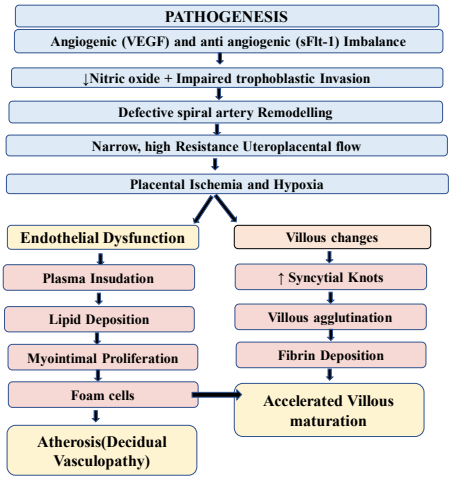
Villous trophoblasts exhibiting strong and diffuse expression

TABLE 4: IHC EXPRESSION OF VEGF & sFlt-1

	VEGF				sFlt-1		
Villous trophoblast	Staining	Cases	Control	p-value	Cases	Control	p-value
Strong and diffuse / patchy	Present/Absent	9/21	1/29	0.005	11/19	1/29	0.001
Moderate and diffuse /patchy	Present/Absent	21/9	9/21	0.001	12/18	2/28	0.002
Weak and focal /Non-specific	Present/Absent	0/30	20/10	<0.001	7/23	28/2	<0.001
ExtraVillous trophoblast	Staining	Cases	Control	p-value	Cases	Control	p-value
Strong and diffuse / patchy	Present/Absent	2/28	0/30	0.150	3/27	1/29	0.300
Moderate and diffuse /patchy	Present/Absent	17/13	10/20	0.069	18/12	3/27	<0.001
Weak and focal /Non-specific	Present/Absent	11/19	20/10	0.020	9/21	26/4	<0.001

*Statistical significance set at $p < 0.05$ (Fisher's exact test)

DISCUSSION



- In our study hypertensive placentas showed a significantly reduced placental weight, foeto-placental ratio, umbilical cord diameter along with a higher frequency of parenchymal lesions such as infarcts and thrombohematoma.
- Immunohistochemical analysis demonstrated a marked angiogenic imbalance in hypertensive placentas, characterized by increased VEGF expression and, more prominently, strong sFLT-1 overexpression compared to controls.
- The predominance of sFLT-1 suggests that anti-angiogenic dysregulation may play a more critical role than VEGF in the pathogenesis of hypertensive placental changes.

CONCLUSION

Placental dysfunction and angiogenic imbalance in hypertensive pregnancies are closely linked to adverse fetal outcomes, with pathologic placental examination playing a key role in identifying underlying vascular alterations and enabling early detection. These insights improve understanding of fetal risks and help guide clinical management, ultimately enhancing maternal and fetal outcomes.

ABBREVIATIONS

HDP: Hypertensive Disorders of Pregnancy, VEGF : Vascular Endothelial Growth Factor, sFlt -1: Soluble fms –like tyrosine kinase, PlGF : Placental like growth factor, FVM : Fetal vascular Malperfusion, MVM : Maternal vascular malperfusion, ART: Artificial Reproductive Technique, AEDF: Absent End diastolic Flow, PI: Pulsatility Index , IUD : Intrauterine death

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