Section: Obstetrics and Gynaecology

Original Research Article

ROLE OF PLACENTAL GROWTH FACTOR AT 13 TO 16 WEEKS IN PREDICTING PRE-ECLAMPSIA AND FETAL GROWTH RETARDATION IN SOUTH KARNATAKA POPULATION

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Received : *07/09/2024*
Received in revised form : *25/10/2024*
Accepted : *09/11/2024*

Keywords:
Pre-eclampsia, PAPP-A, CR length, false positive rates, HDP.

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DOI: 10.47009/jamp.2024.6.6.8

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (6); 34-37

Abstract

Background: Determination of placental growth factor (PIGF) for predicting hypertensive disorders of pregnancy (HDP) will enable prevention of preeclampsia and morbidity and mortality of neonates and mother. **Materials and Methods:** 80 pregnant women with HTN were compared with 80 controlled (healthy) pregnant women. BMI, MAP, and BP were recorded. USG measurements included CR length by using the Neimo X.G. ultrasonic ultra sound Machine and pulsation of uterine artery recorded by color Doppler imaging. The biomarkers included PIGF and a free PAPP-A and β-hCG analysis chemiluminescent enzyme-linked immune-absorbent assay. **Result:** In 80 cases, pregnant women's parameters of clinical manifestation were compared with normal (controlled) women, and the p value was highly significant ($p<0.001$). Various HTN markers were also compared with controlled pregnant women, and the p value was highly significant ($p<0.001$). predictive values of markers of HTN disorder of pregnancy when used alone or in combination were also analyzed, and false predictive rates were 10% in alone and varied from 4.5% to 34.6% in combined analysis. **Conclusion:** The roles of placental growth factor concentration along PAPP-A and pulsation of artery indexation have remarkable prediction of PE and fetal growth retardation in the first trimester of pregnancy.

INTRODUCTION

The placental growth factor (PIGF) is an angiogenic protein produced by the placenta and is implicated in trophoblastic invasion of the maternal spiral arteries.[1] Maternal serum levels at 11–13 weeks gestation are decreased in the pregnancies with impaired placentation that develop preeclampsia and in those that deliver birth of a small gestation age (SGA) emanates.[2]

Hypertensive disorders of pregnancy (HDP) occur among 10% of all pregnancies globally and make a major contribution to maternal and morbidity.[3] The four subcategories of HDP are pre-eclampsia (PE) and eclampsia chronic hypertension, gestational hypertension, and superimposed PE. Early identification of women at risk for preeclampsia (PE) remains a major challenge in antenatal care.[4] Few studies have focused on evaluating the screening performance of PIGF. Hence, an attempt is made to study the placental growth factors at 13 to 16th weeks in prediction of PE and fetal growth retardation.

MATERIALS AND METHODS

80 pregnant women regularly visiting the obstetrics and gynecology department of Srinivas Institute of Medical Sciences and research center Mukka, Suratkal, Mangaluru-574146 were studied.

Inclusion Criteria

The singleton pregnancies between 13 weeks to 16 weeks who gave their consent for study were selected.

Exclusion Criteria

Patients having acquired or inherited thrombophilia, usage of asprin, and immune compromised pregnancies were excluded from the study.

Method: All the pregnancies were dated from the last menstrual period. (If consistent with measurement of the crown-rump length), socio-economic status, habits, HTN in previous pregnancy, BMI, MAP, BP were recorded. USG measurements were taken by the same sonographer (MK) using the Nemio X. G. ultrasound machine (Toshiba, Tokyo, Japan). These measurements included crown-rump length (C-R length) and uterine artery droppier imaging

ISSN (O): 2687-5365; ISSN (P): 2753-6556

(resistance index, plurality index, and systolic/diastolic rate) were recorded.

Levels of various biomarkers studied in serum samples taken during the first trimester and stored at 80 OC before use. The concentrations of PIGF, PAPP-A, and free B-human chorinic gonadotrophin (β-hCG) are analyzed by chemiluminescet enzyme-linked immune-sorbent assay in an Immoiate 1000 analyzer (Siemens, excellent reliability (0.90). Row dates are collected with no corrections made for maternal factors.

80 pregnant women with PIGF and HTN were compared with 80 normal (controlled) pregnant women. All the participants were followed up by periodic check-up unit delivery. The developments of any complications, such as HDP, intrauterine growth restrictions, LBW, pre-term birth, or intrauterine death, were noted.

Blood pressure measurement of 140/90 mm Hg or more on at least two occasions when taken more than 4 hours apart at any time during pregnancy was used to define the group of women with HDP. Early onset of HDP was defined as the development of hypertension (HTN) before 34 weeks, while late onset HDP was defined as the development of HTN after 34 weeks.

Duration of study was from February 2022 to February 2023.

Statistical Analysis: The HTN disorder results in variables of biomarkers, biophysical markers, and BMI. Uterine artery plurality index and cut values of both controlled and cases were compared with the z test. The statistical analysis was carried out in SPSS software.

RESULTS

[Table 1] Comparison of clinical manifestations of Hypertensive pregnant women –

- Maternal age: 23.3 (± 4.2) in controlled, 25.4 (± 3.5) in cases, t test 3.4 and p<0.001
- Duration of marriage >1 year: 19.6 (± 1.57) in controlled, 33.6 (± 2.5) in cases, t test 43.7 and p<0.001
- Parity: 0.8 (± 0.2) in controlled, 0.6 (± 0.3) in cases, t test 4.9 and p<0.001
- History of HTN disorders is pregnancy: 30 (± 2.6) in controlled, 26 (± 10.2) in cases, t test 3.3 and p<0.001
- BMI: 20..3 (± 2.3) in controlled, 24.6 (± 3.7) in cases, t test 8.6 and p<0.001
- Mean arterial pressure (MAP) mm/Hg: 79.2 (± 7.5) in controlled, 90.6 (± 10.4) in cases, t test 7.9 and p<0.001
- Length of pregnancy at the time of screwing week: 11 (± 0.5) in controlled, 13 (± 0.7) in cases, t test 20.7 and p<0.001
- CR length (mm): 60.3 (± 10.8) in controlled, 68.2 (± 9.6) in cases, t test 3.1 and p<0.001
- Length of pregnancy at delivery week: 40 (± 1.2) in controlled, 36.2 (± 3.5) in cases, t test 9.1 and p<0.001
- birth weight of fetus: 29 (± 1.4) in controlled, 27 (± 1.6) in cases, t test 8.4 and p<0.001

[Table 2] Comparison of various markers in hypertensive pregnancy and controlled group –

- Biochemical markers (PIGF pg/ml): 30.3 (± 8.2) in cases, 38.2 (± 10.2) in controlled, t test was 2.3 and p<0.001.
- PAPP-A (MIU/ml): 5.8 (± 1.30) in cases, 6.24 (± 1.80) in controlled, t test was 1.77 and p<0.001.
- Uterine artery pulsatility Index: 1.58 (± 0.45) in cases, 1.40 (± 0.50) in controlled, t test was 2.39 and p<0.001.

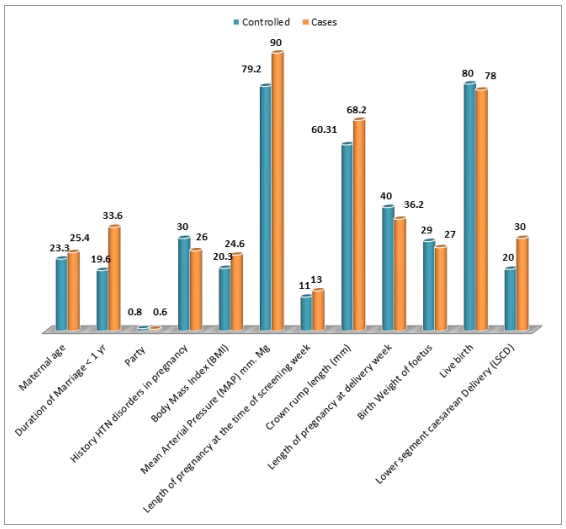

Figure 1: Comparison of clinical Manifestation of HTN pregnant women with controlled pregnant women

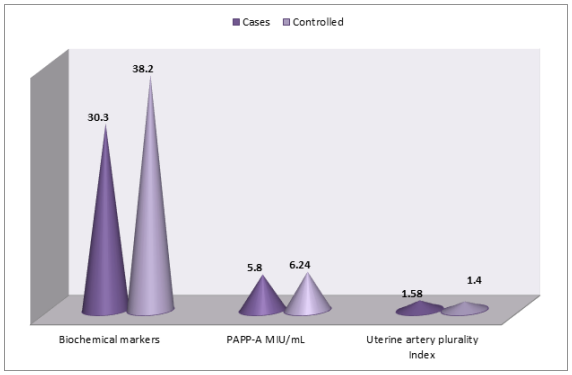

Figure 2: Comparison of various markers in Hypertensive pregnancy and controlled pregnant women

[Table 3] Predictive values of markers of Hypertension disorders of pregnancy when used alone or in combination –

- FPR 10% for in dividual variables (a) 23.2 PIGD cut value, 0.5 cut value of MOM, 32.2 HDP, 36.2 early onset of HDP 30.2 late on set of HDP 10% FPR

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- (b) PAPP-A MIU/ml: 2.2 cut of value, 0.3 cut of early of MOM, 32.0 HDP, 26.4 early onset of HDP, 33.2 late in set of HDP 10% of FPR.
- (c) MAP (mm/Hg): 89.2 cut of value, 1.1 cut off value of MOM, 51.6 HDP, 65.2 early onset of HDP, 38.2 late in set of HDP 0%.
- (d) BMI: 25.2 cut off value, 1.1 cut of value of MOM, 41.2 HDP, 47.4 early onset of HDP, 41.6 late in set of HDP 10% of FPR.
- Combined BMI MAP, PAPP-A and PIGF 90 HDP, 71.2 early onset of HDP, 62.4 late on set of HDP, 34.6% of FPR.

Table 1: Comparison of clinical Manifestation of HTN pregnant women with controlled pregnant women.

Sl. No	Clinical Manifestation	Controlled (80)	Cases (80)	t test	p value
1	Maternal age	23.3 (± 1.7)	25.4 (±3.3)	3.4	P<0.001
2	Duration of Marriage < 1 yr	19.6 (± 1.7)	33.6 (± 2.3)	43.7	P<0.001
3	Party	0.8 (± 0.2)	0.6 (± 0.3)	4.9	P<0.001
4	History HTN disorders in pregnancy	30 (± 2.6)	26 (±10.2)	3.3	P<0.001
5	Body Mass Index (BMI)	20.3 (± 2.5)	24.6 (± 3.7)	8.6	P<0.001
6	Mean Arterial Pressure (MAP) mm. Mg	79.2 (± 7.5)	90.0 (± 10.4)	7.9	P<0.001
7	Length of pregnancy at the time of screening week	11 (± 0.5)	13 (± 0.7)	20.7	P<0.001
8	Crown rump length (mm)	60.31 (± 10.8)	68.2 (± 9.6)	3.1	P<0.001
9	Length of pregnancy at delivery week	40 (± 1.2)	36.2 (± 3.5)	9.1	P<0.001
10	Birth Weight of fetus	29 (± 1.4)	27 (± 1.6)	8.4	P<0.001
11	Live birth	80	78	--	--
12	Lower segment caesarean Delivery (LSCD)	20	30	--	--

Table 2: Comparison of various markers in Hypertensive pregnancy and controlled pregnant women

Sl. No	Markers	Cases (80)	Controlled (80)	t test	p value
1a	Biochemical markers PIGF pg/mL	30.3 (± 8.2)	38.2 (± 10.2)	5.3	P<0.001
b	PAPP-A MIU/mL	5.8 (± 1.30)	6.24 (± 1.80)	1.77	P<0.001
2	Uterine artery plurality Index	1.58 (± 0.45)	1.40 (± 0.50)	2.39	P<0.001

Table 3: Predictive values of markers of HTN disorders of pregnancy when used alone or in combination

Sl. No	Variables	Cut off value	Cut of value if MOM	Detection rate			FPR
				HDP	Early onset of HDP	Late onset of HDP	%
1	FPR 10% for individual variable						
a	PIGD pg/mL	23.2	0.5	32.2	36.2	30.2	10
b	PAPP-A MIU/mL	23.0	0.3	32.0	26.4	33.2	10
c	MAP, mm Hg	89.2	1.1	52.6	65.2	38.2	0
d	BMI	25.2	1.1	41.2	42.4	41.6	10
e	PI	2.0	1.2	17	21.8	12.9	10
f	Controlled BMI, MAP, PI, PAPP-A	--	--	90	71.2	62.4	34.6
2	FPR-10% for combined variable						
a	PIGF pg/mL	22.0	0.5	17.7	16.6	12.7	7.0
b	PAPP_A mm Hg	1.5	0.3	26.4	13.2	23.2	6
c	MAP, mm Hg	26.0	1.2	26.4	13.2	23.2	3.2
d	BMI	26.0	1.2	24.6	21.6	24.6	4.5
e	PI	2.2	1.5	22	14.2	4.2	4.4
f	Combined BMI & MAP	--	--	46.2	58.2	43.2	7.4
2	Combined BMI, MAP &PAPP-A	--	--	62.9	67	55.2	9.1
3	Combined PAPP-A & PIGE	--	--	34	32.1	34.2	7.5
4	Combined BMI, MAP & PAPP-A	--	--	62	67	53.7	9.3
5	Combined BMI, MAP, PAPP-A	--	--	67.2	70.7	62.8	10
6	Combined MAP, PAPP-A PIGF	--	--	71.1	74.1	63.2	10.2

MOM=Multiple of Median HDP=Hypertensive disorder of pregnancy
FPR=False positive rate PIGF=Placental growth Factor
PAPP-A=Pregnancy associated plasma protein
MPA=Mean Artery pressure PI=Uterine artery plurality Index

DISCUSSION

Present study of role of placental growth factor at 13 to 16 weeks in predicting retardation in south Karnataka population. In comparison of clinical manifestation of HTN pregnant women controlled group, maternal age duration of marriage > 1 year parity, history of HTN disorders in pregnancy, BMI

ISSN (O): 2687-5365; ISSN (P): 2753-6556

MAP (mm/Hg) length of pregnancy at the week of screening at week CR length, length of pregnancy at delivery week. Birth weight of fetus live birth LSCD had significant p value ($p<0.001$) [Table 1]. In comparison of various markers in HTN pregnancy, the controlled group had a significant p value ($p<0.001$) [Table 2]. In the study of predictive values of markers of HTN disorder of pregnancy, when used alone, they had a 10% false predictive rate (FPR), and in the combined value, the false predictive value (FPR) varied from 3.2 to 34.6 [Table 3]. These findings are more or less in agreement with previous studies.[5-7]

The alleviation of biochemical parameters and variation in biophysical parameters are due to multi-factorial causes. The medical history included chronic HTN, DM, anti-phospholipids, syndrome, thrombophilla, human immune deficiency virus infection, and sickle cell disease. Medication (including and hypertensive antidepressant, anti-epileptic, anti-inflammatory, asprin, β-mimetec insulin, steroids thyroxin), parity (parous or nuiliparous, if no delivery beyond 23 weeks). Obstetric history (including previous pregnancy with PE) and family history of PE (another).[8]

It is also reported with PIGF that PAPP-A increases with fetal CR length and decreases with material BMI.[9] The raised artery pulsation is due to impaired placental function during the first trimester of pregnancy and is correlated with alleviation of PIGF and PAPP-A factors. These factors have increased the risk of perinatal mortality and morbidity and both short-term and long-term maternal complications.[10] Hence, early screenings of PE have a significant contribution to make to rule out pre-ectampsia and fetal growth retardation.

Such alleviation parameters as PFGR, PAPP-A, and raised diffusion indexation were also useful in down syndrome screening because reduction of such parameters may result in down syndrome of the fetus.[11] Implantation and trophoblastic invasion of the placenta play a crucial role in its development as an organ for transport of nutrition and oxygen to the fetus. Placental remodeling occurs in two stages. In the first stage, between 8 and 12 weeks, there was a loss of smooth muscle and elastic from the spiral arteries, which converted the utero-placental circulation into low resistance. Second remodeling occurs at 16–18 weeks of gestation. Defective placental implantation leads to hypoperfusion, hypoxic reperfusion injury, and oxidative stress.[12] A derangement in trophoblastic differentiation is thought to underlie the pathophysiology of gestational HTN, preeciampsia, and fetal growth retardation (FGR).

CONCLUSION

The present studies of the role of PIGF at 13 to 16 weeks have altered PIGF, PAPP-A, and increased arterial pulsation index. Identification of the values or levels of these parameters and the risk of maternal and fetal outcomes can be predicted and monitored as early diagnosis of clinical signs of the disease and associated fetal growth restriction and avoid development of serious complications through such interventions as administration of anti-HTN medication and early delivery. But this study demands further pathophysiological, genetic, pharmacological, hormonal, and nutritional studies because the exact mechanism and role of placental growth factors are still unclear.

Limitation of study: Owing to the tertiary location of the study institution, a small number of patients, lack the latest techniques, we have limited findings and results.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556