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Introduction

- ❖ Pre-eclampsia (PE) affects 2-8 % of pregnancies.
- ❖ Major cause of perinatal and maternal morbidity and mortality.
- ❖ Emerging biomarkers are placental growth factor (PIGF) and serum FMS like tyrosine kinase(sFlt)

sFlt1

PIGF

Material and Methods

- ❑ Prospective cohort study
- ❑ Population : Southeast Asian population , Queen Mary Hospital, tertiary care Centre in India
- ❑ Inclusion criteria : Preeclampsia ≥20 weeks to ≤ 34weeks
- ❑ History, demographic details, blood pressure
- ❑ Blood testing for sFlt and PIGF : on Roche platform in collaboration with metropolis laboratory.
- ❑ Admitted, biochemical test, maternal and fetal surveillance .
- ❑ Antenatal steroid coverage for lung maturity and Mgso4 seizure prophylaxis and neuroprotection if required.
- ❑ Fetomaternal outcomes were recorded
- ❑ Maternal and fetal adverse outcomes were recorded

Maternal

- Severe Hypertension (requiring intravenous antihypertensives)
- Seizures
- Placental abruption
- pPH
- ICU admission
- Ventilatory support
- Mortality
- Acute kidney injury
- DIC
- HELLP
- ARDS
- Cortical blindness
- Retinal Detachment

Fetal / neonatal

- Preterm births < 34weeks
- NICU admission
- Respiratory distress syndrome
- NEC
- SGA< 10th centile
- Mechanical ventilation
- CPAP
- Stillbirth
- IUD
- Neonatal death

Result

- ❑ Total number of women analyzed after inclusion and exclusion criteria = 91.
- ❑ Mean age of the pregnant women at recruitment was 28.29±5.01 years
- ❑ Mean period of gestation at the time of presentation was 30.63±2.86 weeks (22weeks 3 days – 34weeks 4 days)
- ❑ Primiparity was present in 47 (51.6 %) women while 44 (48.4 %) were multigravida.
- ❑ Medical disorders (Chronic hypertension, GDM, type 2 diabetes, hypothyroidism, cholestasis, previous history of PE and CKD.) were prevalent (but were not significantly different between women who had adverse outcome versus who had normal fetomaternal outcome .
- ❑ Mean duration of raised blood pressure = 9.32 ± 10.61 days
- ❑ Mean systolic blood pressure was 166.31± 15.3 mm Hg , mean diastolic blood pressure was 108.54±10.86 mm Hg.
- ❑ Mean level of sFlt in our population was 9400.24 pg/ml and PIGF was 160.90 pg/ml.
- ❑ Mean ratio of sFlt/PIGF in this study was 439.78 with the minimum value of 1.27 and maximum value of 1080.

SIGNIFICANT RELATIONSHIP BETWEEN BIOMARKERS AND ADVERSE FETOMATERNAL OUTCOMES

	Maternal adverse event						p-value	
	Yes			No				
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75		
MAP (mmHg)	130.00	124.65	137.35	123.30	118.00	130.00	<0.001	
sflt (pg/ml)	11500	5438.00	18431.50	3051.50	1548.00	7998.00	<0.001	
plgf (pg/ml)	44.88	16.75	91.40	148.50	52.20	273.00	<0.001	
ratio	306.22	126.62	862.33	30.63	5.40	90.21	<0.001	

Applied Mann Whitney U test for significance. Consider highly significant.

	Neonatal adverse event						p-value	
	Yes			No				
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75		
MAP	130.00	124.00	137.30	124.35	120.00	130.00	0.004	
sflt (pg/ml)	12100	8055.00	19053.00	3051.50	1481.00	7467.00	<0.001	
plgf (pg/ml)	27.20	16.30	57.00	148.50	59.90	232.00	<0.001	
ratio	378.45	242.00	873.76	30.63	5.59	78.35	<0.001	

Applied Mann Whitney U test for significance. Consider highly significant

Nonsignificant correlation between markers an period of gestation at presentation

Correlations						
Spearman's rho	POG at presentation	Correlation Coefficient	POG at presentation	sflt (pg/ml)	plgf (pg/ml)	ratio
			p-value			
				.807	.008	.076
			N	91	91	91

** . Correlation is significant at the 0.01 level (2-tailed).

Significant correlation between POG at delivery and markers

Correlations						
Spearman's rho	POG at delivery	Correlation Coefficient	POG at delivery	sflt (pg/ml)	plgf (pg/ml)	ratio
			p-value			
				.615**	.745**	-.799**
			N	91	91	91

** . Correlation is significant at the 0.01 level (2-tailed).

Significant inverse correlation between interval between presentation and delivery.

Correlations						
Spearman's rho	interval in days	Correlation Coefficient	interval in days	sflt (pg/ml)	plgf (pg/ml)	ratio
			Sig. (2-tailed)			
				.638**	.570**	-.714**
			N	90	90	90

** . Correlation is significant at the 0.01 level (2-tailed).

Discussion

- ❑ H Zeisler et al, *N Engl J* 2016;374: 13-22 (PROGNOSIS study) sFlt-1/PIGF < 38 has a NPV of 99.3% to rule out PE.
- ❑ Area under receiver operator curve shows sFlt and PIGF to emerge as best biomarkers compared from other biochemical markers to predict adverse fetomaternal outcomes in PE.
- ❑ Maternal adverse outcomes : (AUC (95% CI) for sFlt-1/PIGF ratio was 0.81 (0.72–0.90) , PIGF 0.25 (0.15–0.35) and sFlt-1 0.79 (0.70–0.88)
- ❑ Neonatal adverse outcomes : (AUC (95% CI) for sFlt-1/PIGF ratio was 0.88 (0.80–0.96) , PIGF 0.18 (0.09–0.27) and sFlt-1 0.83 (0.74–0.91)

Adverse maternal outcomes

Adverse neonatal outcome

- ❑ Reddy et al , *Ultrasound Obstet Gynecol* 2022; 59: 596–605 women with suspected or confirmed PE, individual markers of sFlt-1/PIGF ratio and EFW perform well in predicting adverse perinatal outcomes. AUC (95% CI) for sFlt-1/PIGF ratio was 0.69 (0.59–0.78) , PIGF 0.65 (0.55–0.75) p= 0.19 and sFlt-1 0.69 (0.60–0.79) p= 0.68
- ❑ Elisa Simon et al, *Pregnancy hypertension* 2020;22: 17-23. AUC for sFlt-1/PIGF ratio were 0.59 (95%CI 0.42–0.75) and 0.75 (95%CI 0.62–0.88) for maternal and perinatal complications.
- ❑ Relative risk for delivery within 48 h for a sFlt-1/PIGF ratio > 655 was 5.3 (95% confidence interval 2.7–10.6) p<0.01

Conclusion

- sFlt/PIGF ratio has a potential role in triaging of patients who actually need monitoring and delivery compared to those who can still be left with follow up.
- This could limit the risk of prematurity upon the fetus.
- There was a significant correlation between the levels of sFlt/PIGF ratio and the number of weeks the time of delivery could be prolonged
- Lower levels were followed up and delivery could be delayed till 36 to 37 weeks which is a remarkable .

Symptoms in patients which mimicked severe PE like headache (due to pituitary adenoma), visual blurring due to retinal problem, epigastric pain due to gastritis, fits due to old tuberculoma, deranged biochemistry due to any other respective causes.

These patients were having element of non severe PE also, but due their associated features they were labelled as severe PE. These patient sFlt/PIGF levels were lesser than 100 and they were followed up till 36 to 37 weeks which significantly helped to lessen the stress of iatrogenic prematurity. This also helps in reducing ICU / HDU admission since women with lower levels can be monitored in wards. Along with this it gives confidence to the treating team that they are not doing any harm by not delivering a woman labelled to have severe PE. .

This test has a outstanding potential benefit to be used for women lesser than 34 weeks pregnancy with preeclampsia in triaging for hospital admissions. Levels appear higher in south Asian women compared from Caucasians and large scale study could give better results