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A prospective study for the prediction of pre eclampsia with serum prolactin level

Dr. KL Malarvizhi, Dr. M Kavitha, Dr. M Indhuja and S Padmanaban

Abstract
Background: Pre eclampsia is a multi-system disorder specific to pregnancy and puerperiumwhich manifest by hypertension and proteinuria after 20weeks of gestation andresolves by 12 weeks after delivery. Preeclampsia is a multisystem disorder of pregnancy whose aetiology remains unknown. Although management is evidence based, past hypotheses and scientific contributions have influenced the understanding of pathophysiology of preeclampsia and guided its management.
Aims & Objectives
1. To find if prolactin has a role in pathogenisis of pre eclampsia.
2. To estimate serum prolactin during 14-20 weeks of pregnancy.
3. To correlate serum prolactin levels during 14 -20 weeks of pregnancy as a predictor for pre eclampsia

Materials & methods
Type of study: Prospective observational study
Period of Study: 6 months
Place Of Study: Antenatal outpatient department& Antenatal Ward. Labour ward**.** Dept of Obstetrics & Gynaecology. Govt Kilpauk Medical College &Hospital, Chennai 10.
Results: In my study mean prolactin level is 297.47 in pre eclampsia and 139.46 in healthy pregnant. This study shows statistically significantincrease in prolactin level in pre eclamptic women compared to healthy pregnant women. When the serum prolactin is 196 mg /dl sensitivity is .829 and 1- specificity is 000 and the youden index is maximum at that point .829. hence 196mg /dl is cut off value for predicting pr eclampsia. Based upon the statistical analysis sensitivity of the test is 82.85% and specificity is 100% and positive predictive value is 100% and negative predictive value is 92.11%. Coefficient of the agreement is .865671642 which is an excellent agreement.
Conclusion: This study revealed raised level of prolactin in women with pre eclampsia compared to healthy pregnant. Still large number of study is required to conclude prolactin as marker of pre eclampsia.

Keywords: Key words-proximal tibia fracture, MIPPO, knee stiffness, wound dehiscence

Introduction
Pre eclampsia is a multi-system disorder specific to pregnancy and puerperiumwhich manifest by hypertension and proteinuria after 20weeks of gestation andresolves by 12 weeks after delivery. Preeclampsia is a multisystem disorder of pregnancy whose aetiology remains unknown. Although management is evidence based, past hypotheses and scientific contributions have influenced the understanding of pathophysiology of preeclampsia and guided its management [1, 2, 3].

DIAGNOSIS OF HYPERTENSION
- Systolic BP > 140mmHg
- Diastolic BP > 90 mmHg

At least two measurements, should be taken, in the same arm, 6 hours apart but within a week period and the average should be considered. High systolic and diastolic BP have been associated with adverse foetal and maternal outcome [4, 5].
Identifying increase in blood pressure from booking or preconception blood pressure, instead of relying on absolute value, was considered useful in diagnosing [7, 8].

Measurement of Proteinuria
All pregnant women must be checked for proteinuria. Urinary dipstick testing might be used for screening patients for proteinuria (due to easy availability, convenience and low cost.)
Grading for proteinuria is

Trace -0.1mg/dl
1+ - .3mg/dl
2+ -1mg/dl
3+ -3mgdl
4+ - 10mg/dl

There may be inter observer variations with visual dipstick assessment. This can be alleviated by the use of automated dipstick readers, which can reduce both false positive and negative rates. If the woman has hypertension, a proteinuria of 1+ is diagnosed as pre eclampsia

Diagnosis of Clinically Significant Proteinuria
Urinary excretion of 300mg or more of protein in 24 hours urine collection or persistent 30mg/dl in random clean catch sample on atleast 2 occasions collected 6 hours apart is defined as clinically significant protein uria, this corresponds to urine protein/creatinine ratio of 30mg/mmol after ruling out urinary tract infection [6, 7].

Urine Spot Pcr
This is an alternative to 24 hours urine protein, spot protein to creatinine ratio of more than .3 indicates significant protein uria.

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Inclusion Criteria
Patients with known gestational age between (14-20) week will be selected irrespective of parity. Those who develop pre eclampsia will be the cases and others will be control.

Exclusion Criteria
- Chronic hypertension
- Type 1&2 Diabetes mellitus
- Multiple pregnancy
- Any chronic illness
- Thyroid disorders
- Patients with H/O galactorrhea
- Patients with H/O drug intake which affect serum prolactin such as neuroleptics, prokinectics, PPIs, H2 blockers.

Results

Table 1: Distribution of age in the study group

	Frequency	Percent
<= 20 Years	5	4.8
21-25 Years	36	34.3
26-30 Years	44	41.9
31-35 Years	12	11.4
>= 36 Years	8	7.6
Total	105	100.0

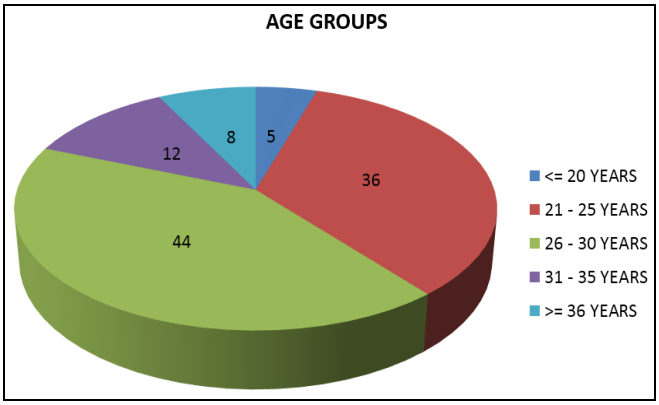

Chart 1

In study group 4.8% were in the age group less than 20 years and 34.3% were in the age group 21to 25 years 41.9 in the age group between 26 to 30 years 11.4% were in the age group between 31 to 35 years 7.6% were above 36years.

Pre Eclampsia

Table 2

	Frequency	Percent
Yes	35	33.3
No	70	66.7
Total	105	100.0

Among the study group 33.3% developed pre eclampsia remaining 66.7% remain normotensive.

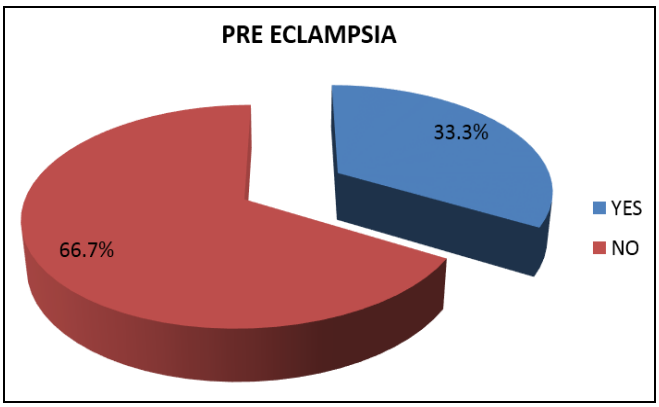

Chart 2

Table 3: Mild & Severe Pre Eclampsia

	Frequency	Percent
NO	70	66.7
MILD	23	21.9
SEVERE	12	11.4
Total	105	100.0

Among the study group 66.7% remain normotensive 21.9% developed mild pre eclampsia and 11.4% developed severe pre eclampsia.

Chart 3

Table 4

Prolactin * Preeclampsia Crosstabulation						
			Preeclampsia			Total
			No	Mild	Severe	
Prolactin	UPTO 209	Count	70	6	0	76
		% within Preeclampsia	100.0%	26.1%	0.0%	72.4%
		% of Total	66.7%	5.7%	0.0%	72.4%
	210-300	Count	0	11	1	12
		% within Preeclampsia	0.0%	47.8%	8.3%	11.4%
		% of Total	0.0%	10.5%	1.0%	11.4%
	>300	Count	0	6	11	17
		% within Preeclampsia	0.0%	26.1%	91.7%	16.2%
		% of Total	0.0%	5.7%	10.5%	16.2%
Total		Count	70	23	12	105
		% within Preeclampsia	100.0%	100.0%	100.0%	100.0%
		% of Total	66.7%	21.9%	11.4%	100.0%

Chi square= 11.582 P=0.000<0.001 significant.

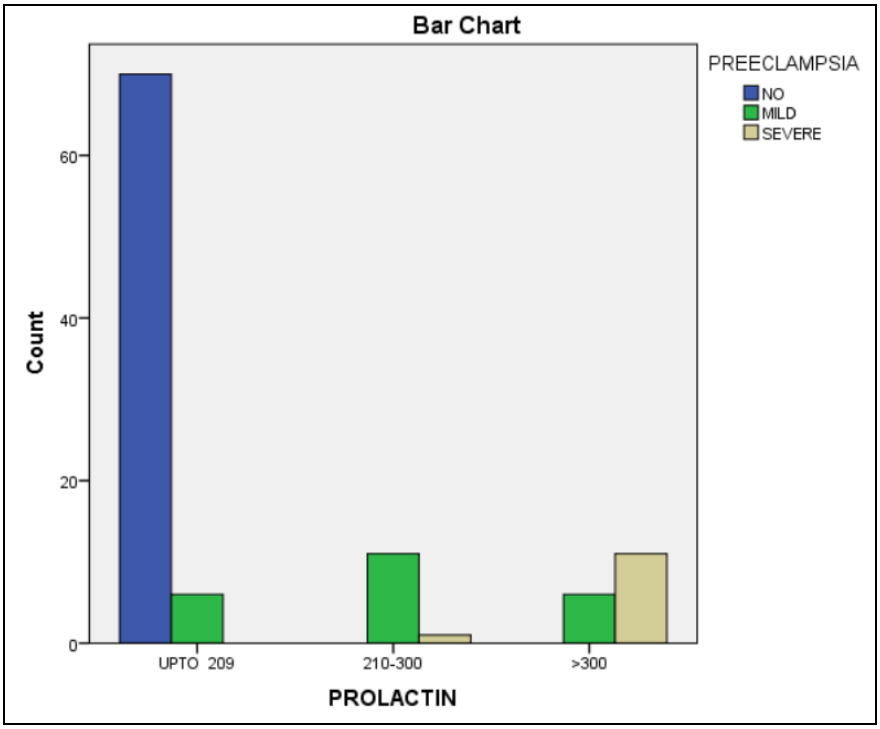

Chart 4

Table 5

Ga At Which Prolactin Taken * Outcome Crosstabulation						
			Outcome			Total
			No	Mild	Severe	
Ga At Which Prolactin Taken	13	Count	2	0	0	2
		% of Total	1.9%	0.0%	0.0%	1.9%
	14	Count	1	2	0	3
		% of Total	1.0%	1.9%	0.0%	2.9%
	15	Count	6	5	3	14
		% of Total	5.7%	4.8%	2.9%	13.3%
	16	Count	14	3	3	20
		% of Total	13.3%	2.9%	2.9%	19.0%
	17	Count	18	2	4	24
		% of Total	17.1%	1.9%	3.8%	22.9%
	18	Count	10	6	1	17
		% of Total	9.5%	5.7%	1.0%	16.2%
	19	Count	15	4	1	20
		% of Total	14.3%	3.8%	1.0%	19.0%
	20	Count	4	1	0	5
		% of Total	3.8%	1.0%	0.0%	4.8%
Total		Count	70	23	12	105
		% of Total	66.7%	21.9%	11.4%	100.0%

Chi square= 15.441 P=0.349 Not significant.

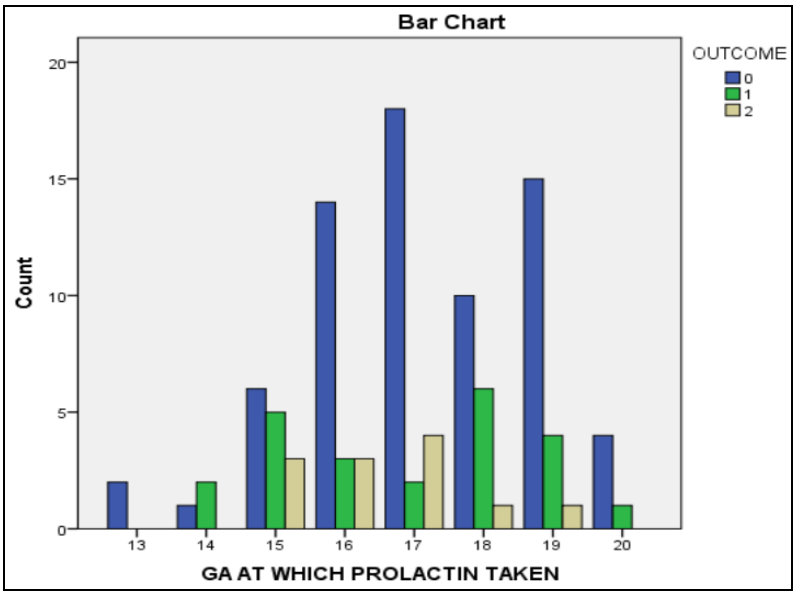

Chart 5

Table 6

Ga At Which Prolactin Taken * S. Prolactin (ng/ml) Group Crosstabulation						
			S. Prolactin (ng/ml) Group			Total
			1	2	3	
Ga At Which Prolactin Taken	13	Count	2	0	0	2
		% of Total	1.9%	0.0%	0.0%	1.9%
	14	Count	2	1	0	3
		% of Total	1.9%	1.0%	0.0%	2.9%
	15	Count	7	3	4	14
		% of Total	6.7%	2.9%	3.8%	13.3%
	16	Count	15	0	5	20
		% of Total	14.3%	0.0%	4.8%	19.0%
	17	Count	19	2	3	24
		% of Total	18.1%	1.9%	2.9%	22.9%
	18	Count	10	5	2	17
		% of Total	9.5%	4.8%	1.9%	16.2%
	19	Count	16	1	3	20
		% of Total	15.2%	1.0%	2.9%	19.0%
	20	Count	5	0	0	5
		% of Total	4.8%	0.0%	0.0%	4.8%
Total		Count	76	12	17	105
		% of Total	72.4%	11.4%	16.2%	100.0%

Chi square=18.117 P= 0.201 Not significant.

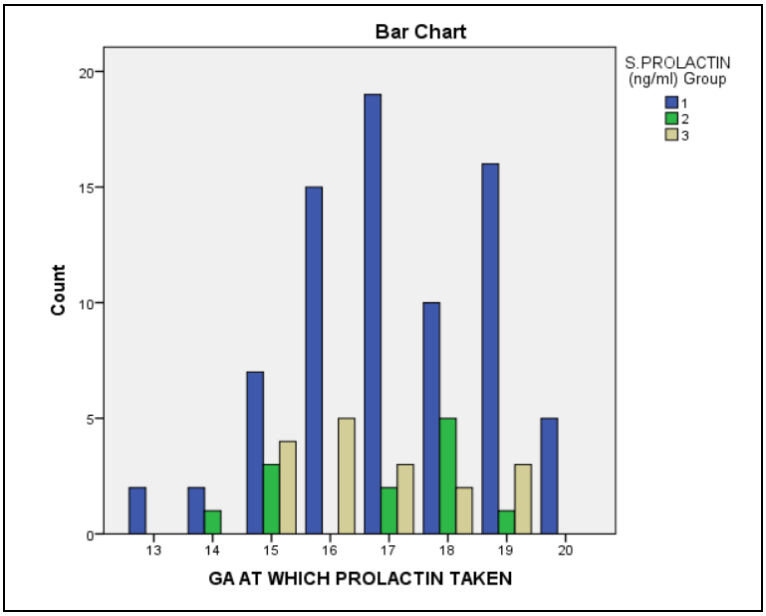

Chart 6

Table 7: Serum Prolactin Levels

Pre Eclampsia	N	Mean	Std. Deviation	P Value By 'T' Test
YES (Mild & Severe)	35	297.46	86.43	0.001
No	70	139.60	26.12	

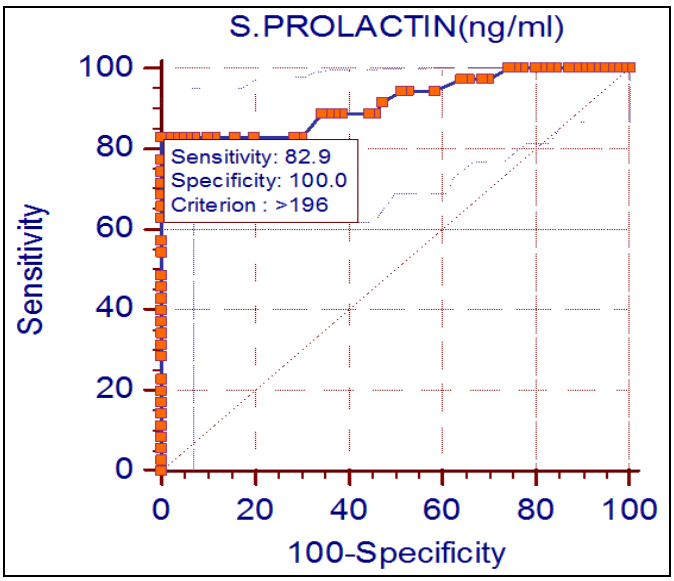

Chart 7

Discussion

This prospective was carried out at kilpauk medical college and hospital. After getting informed consent from the patients serum prolactin was taken from 195 women between 14 to 20 weeks and was asked to come for follow up. Only 105 came for follow up till delivery. Detailed history taken, proper clinial examination was done, blood pressure and urine albumin was checked in each ante natal visit.

In my study mean prolactin level is 297.47 in pre eclampsia and 139.46 in healthy pregnant. This study shows statistically significantincrease in prolactin level in pre eclamptic women compared to healthy pregnant women.

Pre eclampsia is a syndrome charecterised by hypertension and protein uria since from ancient times the etiology of pre eclampsia is unknown. This is due to incomplete invasion of trophoblast in muscular endothelial spiral arteries leading to decreased utreo placental blood flow and increased vaso pressor response. Since etiology is unknown many cross section study and case control study showed prolactin has a role in the patho physiology of pre eclampsia. Prolactin naturally elevated in pregnancy found to be raised more in pre eclampsia. Normal non pregnant women prolactin level is less than 35 micro grams and in each trimester it is found to be elevated.

In this study majority of the women were in the age group between 26 to 30 years. 60% were primi gravida. Majority has no abortions. 6% has one abortion 33.3% developed pre eclampsia. Among 33.3%, 22% developed mild pre eclampsia and 11% developed severe pre eclampsia. Median duration of serum prolactin measurement is 17 weeks 3 days and median duration pre eclampsia development is 33weeks and 6 days.

11% has one plus urine albumin and 11% has three plus urine albumin. Mean serum prolactin who developed pre eclampsia is 297.46 and the stand deviation is86.43and the mean serum prolactin who has not developed pre eclampsia is 139.60 and the standandard deviation is 26.12 and the p value is .001 which is statically significant. When the serum prolactin is 196 mg/dl sensitivity is .829 and 1-specificity is 000 and the youden index is maximum at that point .829. hence 196mg/dl is cut off value for predicting pr eclampsia. Based upon the statistical analysis sensitivity of the test is 82.85% and specificity is 100% and positive predictive value is 100% and negative predictive value is 92.11%.

K coefficient of the agreement is .865671642 which is an excellent agreement.

Limitations of the Study

Out of 195 patients only 105 came for follow up. When serum prolactin was less than 226ng/dl some patients develop pre eclampsia hence negative predictive value is less. We need to follow up the patient for long time and large number of patients and large number of study is needed to show that the serum prolactin is a predictor of pre eclampsia.

Conclusion

The statistically significant difference between the mean serum prolactin levels of the pre eclamptic patients and normal patients denotes a significant association of serum prolactin level with pre eclampsia.

Area Under the Curve				
Area	Std. Error	p value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.916	0.034	0.001	0.849	0.983

Based on the Youden index, the cut off value of serum prolactin for predicting eclampsia is 196 mg/dl. When sensitivy is higer and 1- specificity is lower cut off value is taken and the youden index is maximum at that level only that is 0.829.

This study revealed raised level of prolactin in women with pre eclampsia compared to healthy pregnant. still large number of study is required to conclude prolactin as marker of pre eclampsia.

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