

Maternal Soluble Endoglin (sEng) at 14-20 weeks as a predictor of pre-eclampsia

Dr. Most. Arifa Sharmin, MCPS, FCPS (OBGYN), FCPS (Feto-maternal Medicine)
Junior consultant (Gynae & Obs), Satkhira Medical College Hospital, Satkhira, Khulna

Introduction:

Pre-eclampsia (PE) has remained a significant public health threat in both developed & developing countries contributing maternal & perinatal morbidity and mortality globally and complicates 5-10% of pregnancy worldwide^{1,2}. Eclampsia causes 20% maternal death in Bangladesh³. Several predictive markers for pre-eclampsia, including placental growth factor, soluble fms-like tyrosine kinase-1 (sFlt-1), plasma protein 13, and pregnancy-associated plasma protein-A (PAPP-A) have been evaluated, but none is recommended in routine clinical use⁴. It was observed that preeclamptic placentas over express Endoglin mRNA as well as Eng protein. Various studies have indicated the role of soluble endoglin (sEng), an anti-angiogenic factor, in the pathogenesis of PE.⁵

Aim:

To evaluate the relationship of maternal serum soluble endoglin (sEng) as a predictor of pre-eclampsia (PE) in early second trimester (14-20 weeks) of pregnancy and to improve the maternal, fetal and perinatal outcome by intervening treatment like oral aspirin which will decrease the angiogenic imbalance and to prevent the complex syndrome or adverse effect of PE.

Study Design:

Prospective cohort

Methodology:

Study was carried out on 92 pregnant women over a period of 6 months from June 2019 to November 2019 at 14-20 weeks, having no evidence of PE.

Procedure:

Demographic profile, medical & family history was recorded. Blood pressure measured with ideal criteria. 3 ml of blood sample was collected, stored at -20°C and the level of sEng was measured as ng/ml and converted to MOM using unpaired t-Test. Chi-squared (χ^2) was done to see the association between high level of sEng and development of PE. ROC was used to the best cut off point of sEng values.

Results and Observations:

Prevalence of Pre-eclampsia was 4.3%. Significant association was found in education & monthly income in both group ($p=.005$ & $.002$ respectively). Severe PE developed in < 34 weeks & 50% were primigravid. High level of sEng was found in PE. ($p=.001$). Test result shows an AUC of .906 at a cut-off value of sEng 9.5ng/ml, the Sensitivity was 75%, Specificity was 95.45%, positive predictive value was 42.86%, negative predictive value 98.82% and accuracy was 94.57%. Three patients with high level of sEng and one with normal level developed Preeclampsia. So, there is a significant association($p<.001$) found with a risk ratio of 24.60.

Table-1: Comparison of sEng (ng/ml) between normotensive and preeclampsia group (n=92)

	Non-preeclampsia/ Normotensive (n=88)		Preeclampsia (n=4)		p-value
	N	Mean±SD	n	Mean±SD	
15 weeks	13	6.20±0.83	1	25.20	
16 weeks	20	6.30±1.28	0		
17 weeks	15	6.54±1.74	1	26.10	
18 weeks	9	5.94±0.82	1	30.10	
19 weeks	13	6.33±1.28	1	6.20	
20 weeks	18	6.62±2.11	0		
Total	88	6.36±1.46		21.90±10.68	<0.001*
sEng MoM		1.08±0.25		2.01±0.81	<0.001*

Unpaired student t-test, *significant

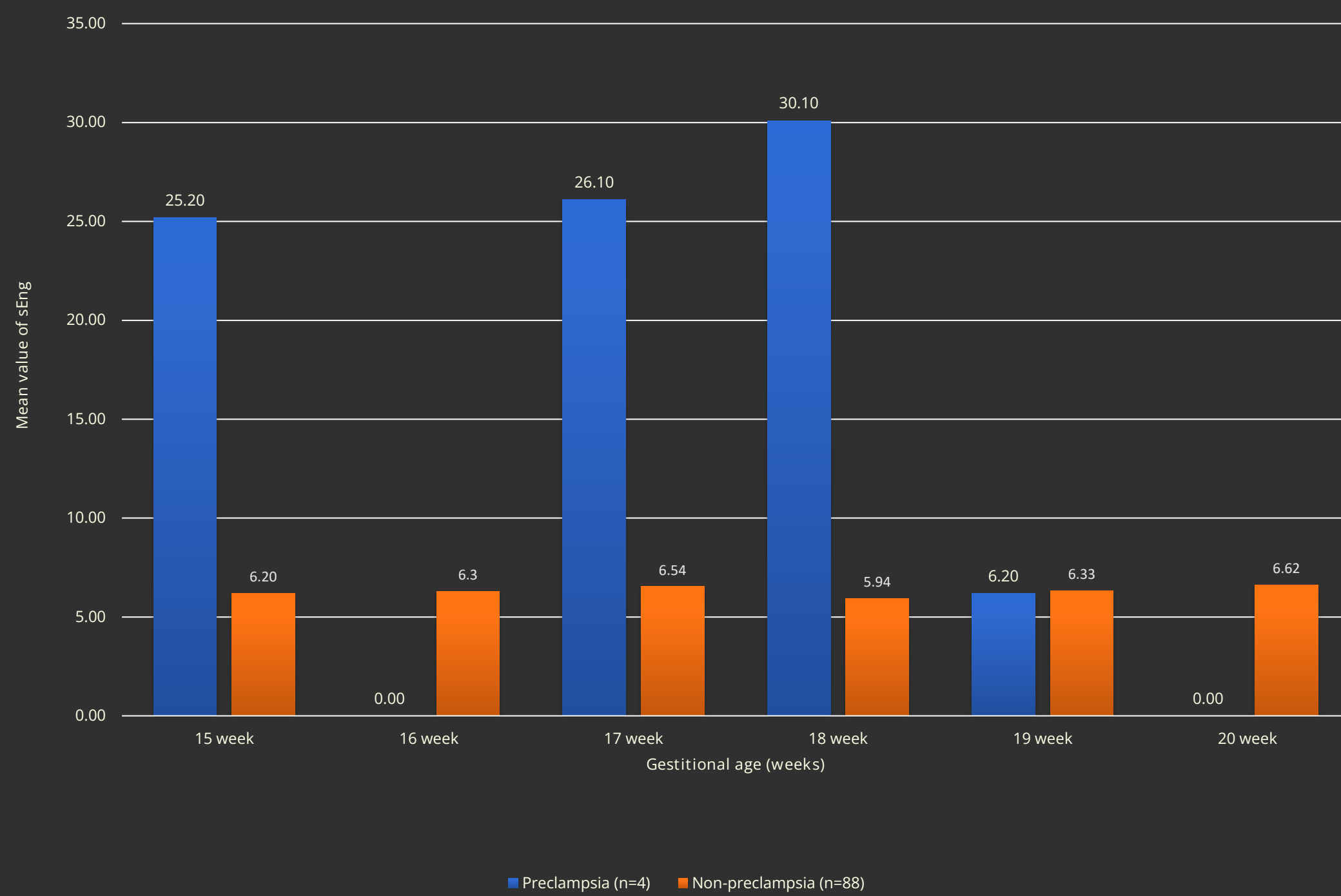


Figure-1: Mean values of sEng in specific gestational age

Table-2: Association of sEng level in preeclampsia and non-preeclampsia patients (n=92)

Level of sENG	Preeclampsia (n=4)	Non-Preeclampsia (n=88)	RR 95% CI	p-value
High (MoM >1.87)	3(75.0%)	7 (8.0)	9.42/24.60	<0.001*
Normal (Mom >1.87)	1(25.0)	81(92.0)	(3.80-23.39)	
Total	4 (100.0%)	88 (100.0)		

Fisher exact test was done, *significant

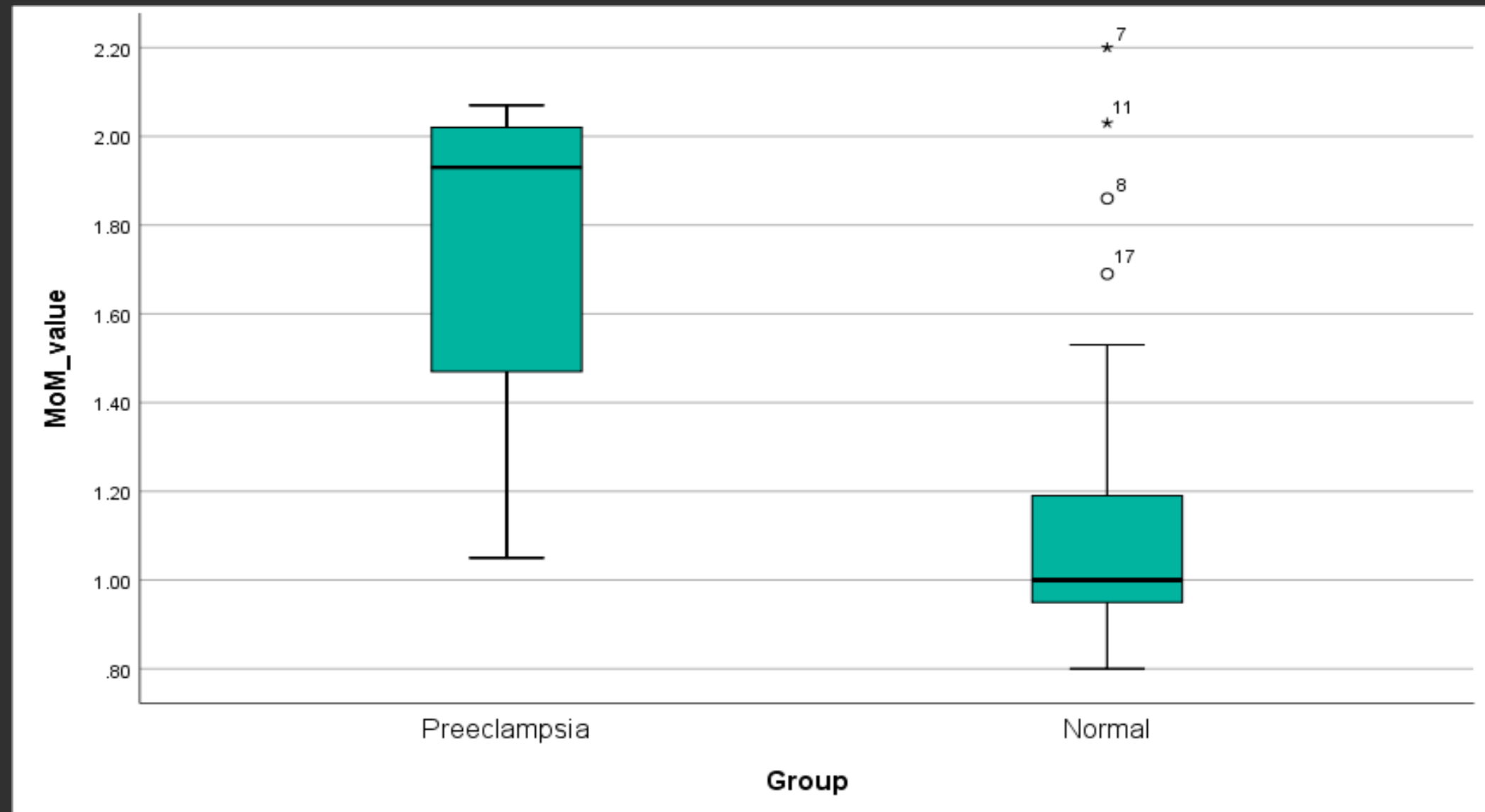


Figure-2: Box plot showing the median, interquartile range and range of Mom of sEng in preeclampsia and non-preeclampsia group

The above box plot shows that the value of sEng MoM among normal subjects is very close to 1 and but in preeclampsia group it is on 2

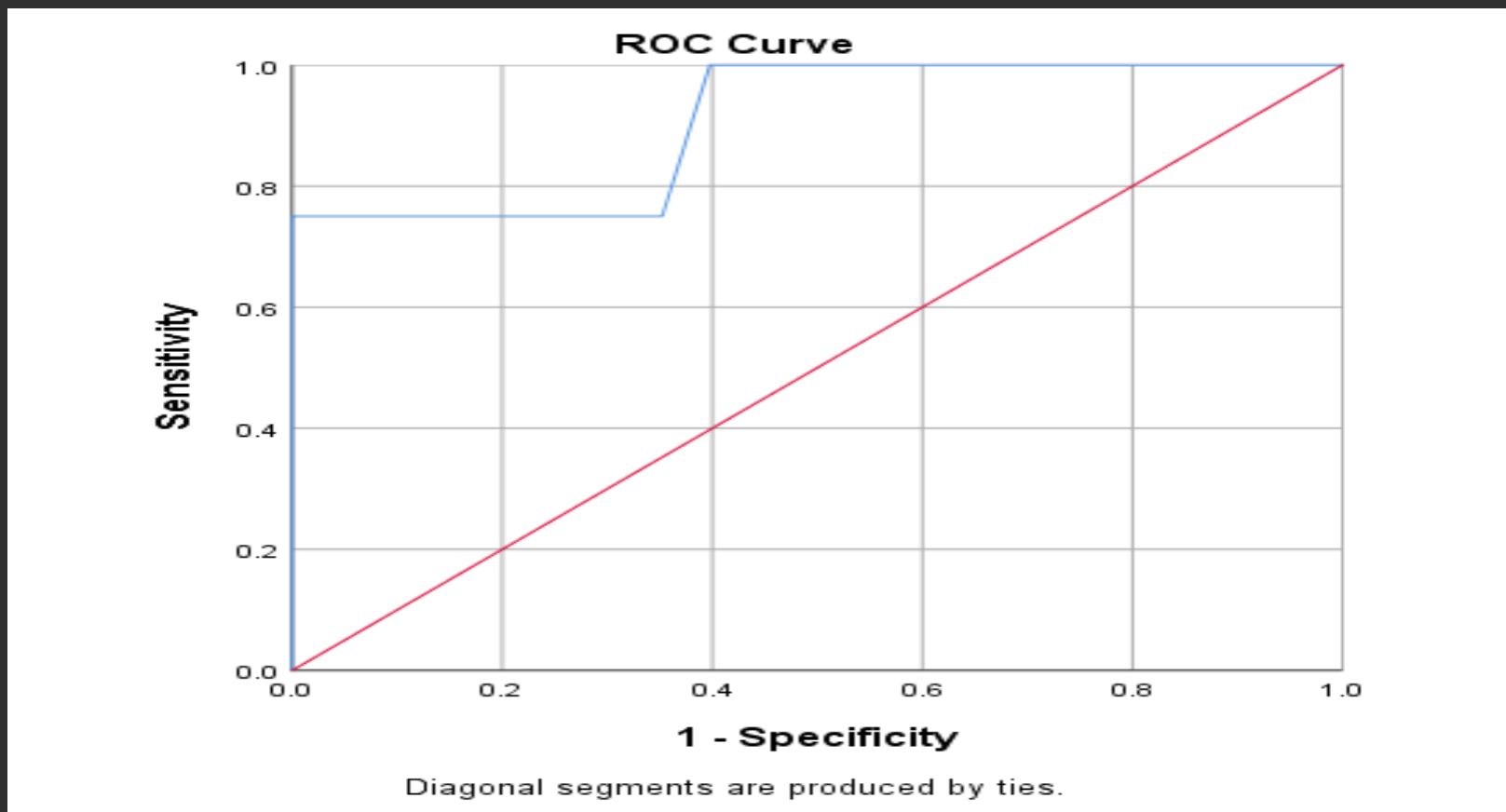


Figure-3.: ROC curve, AUC is .906

Table-3: Diagnostic Validity Test Result

	Values	95%CI
Sensitivity	75.00%	19.41% to 99.37%
Specificity	95.45%	88.77% to 98.75%
Positive Predictive Value	42.86%	9.90% to 81.59%
Negative Predictive Value	98.82%	93.62% to 99.97%
Accuracy	94.57%	87.77% to 98.21%

Test result shows an AUC of .906 at a cut-off value of sEmg 9.5ng/ml, the Sensitivity, was 75%, Specificity was 95.45%, positive predictive value was 42.86%, negative predictive value 98.82% and accuracy was is 94.57%

Discussion:

In our study prevalence of preeclampsia is 4.3%. However Rekha sachan et al reported 10.2% prevalence of PE in their study.⁶ The mean age of non-preeclampsia patients were 27.13 ± 4.54 year and PE patients were 26.75 ± 8.99. Rekha Suchan et al, showed in their study that mean age of non-preeclampsia patients were 27.5 ± .57 and PE were 25.56 ± .58.⁶ Young age and primigravida are proven risk factor for PE. which corresponds with our study. In the present study serum soluble endoglin (sEng) level of Preeclampsia group was significantly high ($p<0.001$) and this findings directly matched with the study by Rekha sachan showed that the mean levels were significantly higher in PE group compared to controls (5.60 ± 0.19 ng/ml) ($p<0.001$).⁴ In our study frequency of early onset preeclampsia was more(3 out of 4 patients) than late onset preeclampsia and it is also supported by the study done by Chaiworapongsa T et al.They showed that the median sEng in early onset of PE was higher than late onset P($p,.001$)⁷

Conclusion:

As our study population is less, the sensitivity and positive predictive value is comparatively less but specificity and negative predictive value is high that means, the test study has shown the usefulness of sEng as a potential marker with high accuracy for diagnosing Preeclampsia. So, Serum sEng level can be used an emerging biomarker for prediction of preeclampsia and by this it could help to improve pregnancy outcome in patient risk of developing PE.

References:

- McClure EM, Saleem S, Pasha O and Goldenberg RL. Stillbirth in developing countries; A REVIEW OF CAUSES, RISK FACTORS (small) and prevention strategies. Journal of Maternal-Fetal and Neonatal Medicine 2009;22(3): 183-90
- Cunningham FG, Leven KJ, Bloom SL, Spongy CY, Dashe IS, Hoffman Bt, et al. Hypertensive Disorders, In Williams Obstetrics. MCGraw Hill Education 2014; 728-19.
- National Institute of Population Research and Training (NIPORT) MEASURE Education, UNC-CH, USA, ICDDR, February 2011, "Bangladesh Maternal Mortality and Heath Care Survey 2010", preliminary Results.
- Bellamy L, Casas JP, Hingorani AD, Williams DJ. Preeclampsia and risk of cardiovascular disease and cancer in later life; systematic review and meta analysis. BMJ 2007;vol.335: pp.974 13.
- Aggarwal P, Chandel N, Jain V, Jha V. The relationship between circulating endothelin-1, soluble fms-like tyrosine kinase-1 and soluble endoglin in preeclampsia. Journal of human hypertension 2010;vol.6(4):pp.236–241. [PubMed] [Google Scholar]
- Sachan R, et al. Serum Soluble Endoglin as Predictor of Non Severe Preeclampsia and Severe Preeclampsia in early Second Trimester of Pregnancy. Ann Med Health Sci Res 2018; 8:179-183.
- Chaiworapongsa T et al. Ultrasound Obstet Gynecol.2010 Feb;35(2)155-162