“LATERAL LOCATION OF PLACENTA AS PREDICTOR OF PRE-ECLAMPSIA IN PREGNANT WOMEN, A HOSPITAL BASED PROSPECTIVE STUDY.”

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ABBREVIATIONS

PE	-	Preeclampsia
PlGF	-	Placenta associated growth factor
PAPP-A	-	Pregnancy associated plasma protein A
sFlt-1	-	Soluble fms-like tyrosine kinase1
SBP	-	Systolic blood pressure
DBP	-	Diastolic blood pressure
ACOG	-	American College of Obstetricians and Gynecologists
AHA guidelines	-	American Heart Association guidelines
BMI	-	Body mass index
WHOMCS database	–	World health organization multi-country survey on maternal and newborn health
NAMPT	-	Nicotinamidephosphoribosyltransferase
H2S	-	Hydrogen sulphide
NO	-	Nitric oxide
HLA-G	-	Human Leucocyte Antigen class G
MHC	-	Major Histocompatibility complex
SEPS1	-	Selenoprotein S
PPV	-	Positive predictive value
NPV	-	Negative predictive value
CI	-	Confidence interval

FGR	-	Fetal growth restriction
OR	-	Odds ratio
USG	-	Ultrasonography
LSCS	-	Lower segment cesarean section
APH	-	Antepartum hemorrhage
PPH	-	Postpartum hemorrhage
LDL	-	Low density lipoprotein
PIH	-	Pregnancy induced hypertension
HCG	-	Human chorionic gonadotropin
DM	-	Diabetes Mellitus
WHO	-	World health organization
RCT	-	Randomized controlled trial
KAHER	-	KLE Academy of Higher Education and Research center
KLE’s	-	Karnataka Lingayat Education Society
JNMC	-	Jawaharlal Nehru Medical College
DNA	-	Deoxyribonucleic acid
Sl.No.	-	Serial Number
LMP	-	Last Menstrual Period

ABSTRACT

Background and objectives

Preeclampsia (PE) is a disorder of pregnancy involving multiple systems of the body.Systolic blood pressure more than or equal to 140mm Hg and diastolic of over or equal to 90mm Hg recorded on two separate occasions 4hours apart, beyond 20 weeks period of gestation with proteinuria 300mg or more per 24 hour urine defines pre eclampsia. The objective of the present study was to study whether lateral location of placenta can be used as predictor of preeclampsia.

Methodology

This one- year cross-sectional study was conducted from January 2019 to December 2019 on singleton pregnant women between 18 to 24 weeks gestationattending antenatal clinic at KAHER Dr. Prabhakar Kore Charitable Hospital, Belagavi. Ultrasonography was performed on these women and location of placenta was determined. The women were reassessed at delivery and looked for preeclampsia. Pregnancy outcomes in terms mode of delivery, baby weight were also assessed.Data were analyzed by the Chi-square test.

Result

490 women were screened. 468 women were recruited for the study and 22 women were excluded due to lethal fetal anomalies. Ultrasonography was performed on 468 women and placental location was determined. The placental location was classified as lateral and central placenta. 74 (15.8%) women had lateral placenta and 394 (84.2%) had central placenta. Women recruited for the study were reassessed at delivery for development of preeclampsia, mode of delivery, baby weight. 431

women were reassessed at delivery. Out of the women with lateral placenta, 28(38.4%) developed preeclampsia and 45 (61.6%) were normotensive. Among the women with central placenta, 32(8.9%) developed preeclampsia and 326(91.1%) were normotensive. Out of women with lateral placenta, 25(7.0%) developed mild preeclampsia and 7 (2.0%) developed severe preeclampsia. Among the women with central placenta, 21(28.8%) developed mild preeclampsia and 7(9.6%) developed severe preeclampsia. Mode of delivery had no association with placental location. Also, baby weight at delivery had no significant relation with placental location.

Conclusion

Location of placenta can be used as a safe, reliable, non-invasive method of determining preeclampsia and help in early diagnosis of the disease.

Keywords

Location of placenta, preeclampsia.

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INTRODUCTION

Preeclampsia (PE) is an ailment of pregnancy involving multiple systems of the body.Systolic blood pressure more than or equal to 140mm Hg and diastolic of over or equal to 90mm Hg recorded on two separate occasions 4hours apart, beyond 20 weeks period of gestation with proteinuria 300mg or more per 24 hour urine defines preeclampsia.[1]

The incidence of preeclampsia among the pregnant women is about 28% in developed world and 5-8% in developing world.[2] It is the 2nd most significant cause contributing to maternal mortality of pregnant women in the world, after hemorrhage.[2]The incidence of the disease in India is approximately 8-10% in the year 2019[3]**.** The burden of preeclampsia is reported to be 8% in KAHER JNMC in 2019. In primigravida, the prevalence of syndrome is 6-7% as compared to 3 -4% in multigravida.[4]

76,000 women and 5,00,000 babies succumb to pre eclampsia every year. The life span of women developing preterm preeclampsia is decreased by 10 years on an average.[5]

Preeclampsia can further be categorized as early and late onset based on gestational age. 34 weeks being the guide for distinction between early onset and late onset PE. Preeclampsia before 34 weeks gestation is associated with more unfavorable outcomes.This exemplifies the need of screening in early period of gestation .[6] Screening the large sections of pregnant women in pursuit of disease is a logistic approach of preventive medicine.[7]

Preeclampsia is a malady of Placenta(Greek: ‘plakous’ meaning ‘flat cake’). The etiology of preeclampsia is imprecise, whereas several theories have been proposed for development of preeclampsia. The pathogenesis of PE is

multifactorial.Early onset preeclampsia is attributed to defect in placentation whereas the pathogenesis of late onset preeclampsia revolves around the placental aging and predilection of maternal genes to metabolic and cardiovascular ailments [8]

NEED FOR THE STUDY:

There are tests for prediction of pre eclampsia based on a number of pathologieslike cold pressor test, isometric hand grip test and the roll over test.[9]Several biochemical markers form the basis of screening of pre eclampsia. Decreased levels of Placenta associated growth factor (PlGF) and maternal PAPP-A, elevated soluble fms-like tyrosine kinase1 (sFlt-1) are important biochemical entities describing the disordered placentation.[6]

Ultrasound findings also form the basis of prediction of the disease. The presence ofdiastolic notch in the mid trimester is the earliest analystof the disease. Doppler ultrasound ofthe uterine arteries in the 2nd trimester with abnormal waveform reveals the abnormal placentation and high resistance of uterine vessels involved in the pathology of the disease.

The mid trimester sonography at 18-24 weeks gestation describing the placenta location is a non-invasive, safe method for detection of preeclampsia at an early gestation. Bilateral uterine arteriesare the source of placental intervillous space. Unilateral placental implantation acquires adequate blood flow from ipsilateral uterine artery with the aid of collateral arteries from the contralateral side.[10]

This sonological determination of placental location which further envisages the diagnosis of preeclampsia is cost effective, innocuous, reliable technique in contrast to other predictors of the disease.

The study aims at contributing the proactive reliable tool for prediction of preeclampsia and its outcomes, and minimizes the morbidities and mortalities contributed by the deadly disease sequence. Adequate antenatal management, screening, presumption, diagnosis and timely treatment would help fight threatening disease and aid deliver healthy mother and healthy baby.

OBJECTIVES

To study whether lateral location of placenta can be used as predictor of preeclampsia.

REVIEW OF LITERATURE

Pregnancy is a physiologic process with alteration in every system of the body contributed by stimuli from fetus and placenta. This involves cardiovascular remodeling. Pregnancy is characterized by hypervolemic state. Systemic vascular resistance decreases by approximately 21% during pregnancy. There is fall of 5-10% in diastolic and mean arterial pressure.[11]

Pregnancy being a dynamic process can bring a phenomenal change in blood pressure. Hypertensive disorders remain the intriguing mysterious hurdle in obstetrics. The syndrome is a multifaceted complex process contributing to the toll of maternal and neonatal morbidities and mortalities.

Epidemiology:

Hypertensive disorders with hemorrhage and infection form the deadly trio taking millions of lives worldwide.[11] Hypertensive disorder of pregnancy accounts to 5-10% of the maternal health burden.[12] 10million women in the world are affected by preeclampsia, which is 7fold higher in the developing countries[13]. The number of cases of gestation hypertension in India was 7.5%, preeclampsia 5.7%, chronic hypertension 0.6% in the year 2019. General approximation of pregnancy hypertension in India in 2019 was 14.0%.[14]

Pregnancy induced hypertension paramount to maternal and infant mortality. Every3 minutes a women succumbs to this deleterious malady.[15] Maternal deaths due to this deadly syndrome amounts 12% in the developing nations.[16] Infant mortality

among females with severe hypertensive disorders is 5 times greater than the normotensive women.[7]

Definition and classification:

Classification of hypertensive disorders in pregnancy[17]:

1. Gestation hypertension
2. Preeclampsia
    - Mild
    - Severe
3. Eclampsia
4. Chronic hypertension before pregnancy
5. Chronic hypertension with superimposed gestation hypertension
    - Superimposed preeclampsia
    - Superimposed eclampsia

Gestation hypertension : It is defined as systolic blood pressure(SBP) greater than or equal to 140mm Hg and diastolic blood pressure(DBP) of more than or equal to 90mm Hg, or both, on two occasion 24 hours apart beyond 20 weeks period of gestation in a formerly normotensive women.

It is deliberated as severe when systolic blood pressure reaches up to 160mm Hg and diastolic up to 110mm Hg or both.[17]

- Proteinuria and end organ damage are excluded from the definition of gestation hypertension.
- The blood pressure should normalize within 12 weeks after delivery.[18]

- On an average about 50% women advance to develop preeclampsia.
- The likelihood of progression to preeclampsia is when high blood pressures are recorded before 32 weeks pregnancy.[1]

Pre eclampsia:

Pre eclampsia is characterized by:

- Pregnancy >20weeks of gestation
- Proteinuria 2+ on dipstick or >300mg/24 hour
- Arterial hypertension ≥140/90 mm Hg

"The ACOG practice bulletin number 202 in January 2019" defined preeclampsia as pregnancy complication beyond 20 weeks with combination of proteinuria and/or symptoms and signs of end organ dysfunction.

The new cut off for blood pressure to define preeclampsia according to AHA guidelines is changed from 140/90mm Hg to 130/80mm Hg.[19]

Preeclampsia can further be distinguished as mild and severe.

Severe features include:

- Blood pressure recordings more than 160mm Hg systolic and more than 110mm Hg diastolic.
- Thrombocytopenic (platelets <1lakh/dL)
- Compromised liver function – doubling of liver enzymes, right upper quadrant pain not relieved with medication
- Renal insuffiency (serum creatinine>1.1mg/dL)
- Pulmonary edema

- Visual disturbances
- Headache not subsiding with medications, not accounted to alternate diagnosis.[1]

Atypical Preeclampsia – gestation hypertension or gestation proteinuria with symptoms of Preeclampsia and /or features of hemolysis, raised liver enzymes, falling trend of platelets.[18]

Eclampsia – (eklampsis - "lightening"):Features of preeclampsia complicated with seizures or coma distinct from other cerebral conditions.[18] Features of headache, blurring of vision, nausea/ vomiting, epigastric pain, oliguria constitute imminent eclampsia. Imminent eclampsia predisposes eclampsia.

Other causes of seizure include:

1. Epilepsy

2. Metabolic causes

3. Thrombotic thrombocytopenic purpura

4. Cerebrovascular accidents

5. Encephalopathy/ encephalitis

6.Tumors.[18]

Chronic hypertension-

Hypertension in women prior to conception or development of hypertension <20weeks of gestation.

Chronic hypertension superimposed gestation hypertension:

Inception of proteinuria >2+ before 20weeks gestation.

Risk factors of hypertensive disorders of pregnancy:

- Modifiable
- Non modifiable

Modifiable risk factors:

1. Body mass index (BMI): overweight and obese women are directly associated with development of pregnancy induced hypertension.
2. Anemia : anemia predisposes to Preeclampsia
3. Smoking and alcoholism : direct correlation with hypertensive disorders of pregnancy

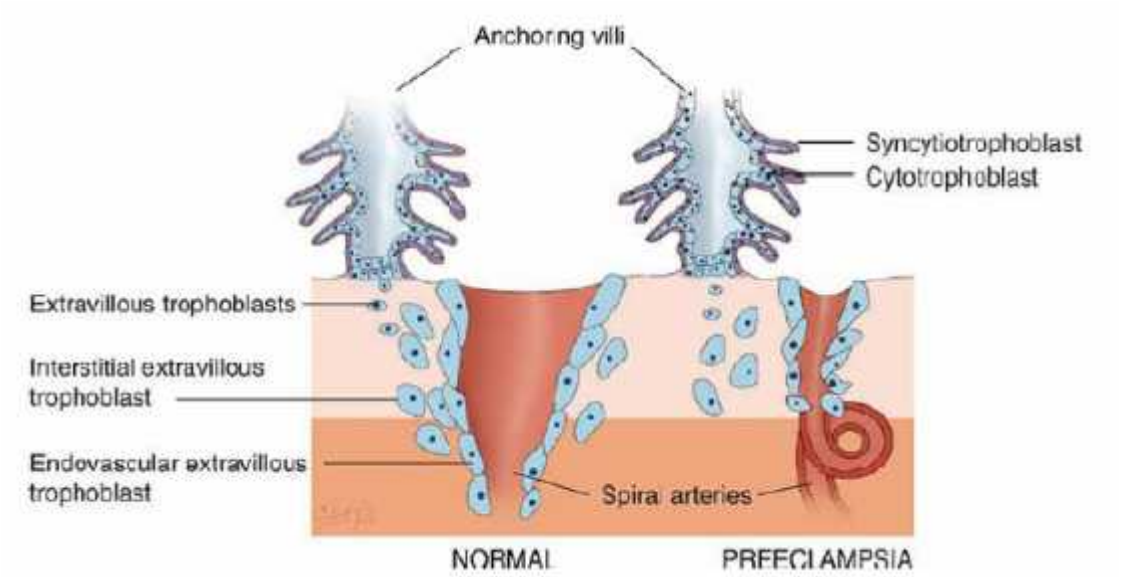
Non modifiable risk factors:

1. Maternal age: There is positive association of higher maternal age and Preeclampsia. Age >35 are linked with development of hypertension.
2. Parity: Primigravida are at high risk of Preeclampsia – eclampsia syndrome.
3. Multiple gestations: There is 2.25 times higher risk of Preeclampsia in multiple gestation in contrast to singleton pregnancy according to WHO MCS (World health organization multi-country survey on maternal and newborn healthWorld health organization multi-country survey on maternal and newborn health) database.
4. Other medical conditions: Diabetes and hypertension are positively related.

5. Previous history of Preeclampsia: In contrast to normotensive women in prior gestation, women with Preeclampsia in a preceding pregnancy had a 7.61-fold escalated risk of PE in case–control studies and 7.19-fold increased threat to development of PE in cohort studies.[20]
6. Genetic predisposition : The genes like angiotensin gene , endothelial nitric oxide synthase, nicotinamidephosphoribosyltransferase (NAMPT)gene are linked with evolution of Preeclampsia.[21]

Etiopathology:

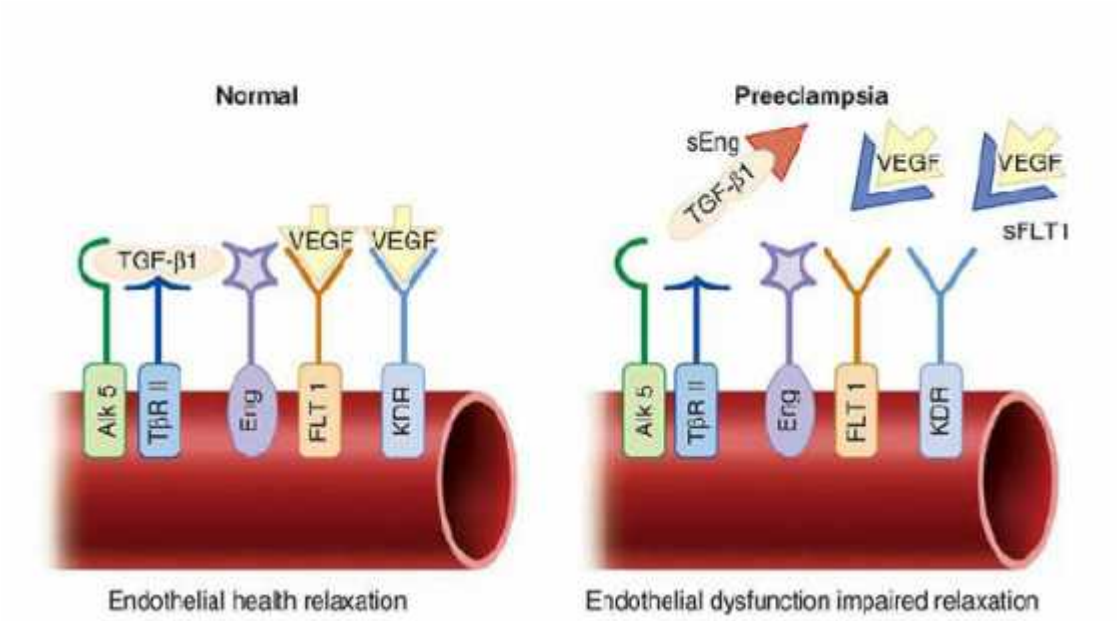
Placenta remains the important determinant of Preeclampsia. During implantation, cytotrophoblast invasion into spiral arterioles converts the vessels into low resistance, high flow system. The defect in this trophoblast invasion has been the hypothesis for inception of Preeclampsia. Defective remodeling of spiral arterioles at endo-myometrial interface add to decrease in placental blood flow → release of antiangiogenic mediator → endothelial damage.[22]



Angiogenicand Anti-angiogenic protein:

Several angiogenicfactor abnormalities have been noted in preeclampsia, but the factors studied most extensively are the anti-angiogenic proteins - soluble forms–like tyrosine kinase 1 (sFlt-1) and the pro-angiogenic protein- placental growth factor (PlGF).

Rana et al. proposedthe elevatedsFltt -PlGF ratio is detrimental to Preeclampsia than the lower ratio.[23] The multicenter trial in 2013 involving 14 countries conducted a study on high risk pregnant women in mid and third trimester showed that sFLt-PlGF ratio of >38 at 24-37weeks can be used to anticipate preeclampsia and need follow up.



Hemeoxygenase pathway:

Hemeoxygenase converts heme into byproduct of carbon monoxide. Carbon monoxide acts as vasodilator causing dilation of placental vessels. This

hemeoxygenase is expressed by trophoblast. The levels of hemeoxygenase are decreased in hypertensive women, which contribute to placental insufficiency.

Hydrogen sulphide pathway:

Hydrogen sulphide (H2S) has a vasodilator, cytoprotective and angiogenic function. "H2S" is fostered by three enzymes, cystathionine b-synthase, cystathionine g-lyase and 3-mercaptopyruvate sulfurtransferase, with the substrates cystathionine, homocysteine, cysteine, and mercaptopyruvate. The H2S levels are decreased in hypertensive women.

Nitric oxide pathway:

Nitric oxide is another vasodilator and has a role in physiological spiral arterial remodeling. Lowe DT et al proposed that relative deficiency of NO and a surge in peroxynitrite and arginase contribute to metabolic derangements in the process of the disease.

Oxidative stress:

Maternal mesothelium and leucocytes on the maternal surface of placenta are the source for generation of excess free radical general. These amplified levels of free radical contribute to endothelium damage of Preeclampsia disease process.

Misfolded proteins:

Buhimschi et al. recommended the theory of misfolded placental proteins in etiopathology of pre eclampsia.[24]Congophilia- marker of protein instability and misfolding, has been elevated in urine of Preeclamptic women. Such misfolded protein aggregates are on upraise in fluids of preeclampsia women.

Immunological theory:

The cells of trophoblast exhibit a special HLA-G enclosed class-I MHC molecule that enables cells of trophoblast to permeate the spiral arterioles. This invasion is resisted by patients of preeclampsia resulting in inadequate spiral artery remodeling.[25]

- T lymphocytes secrete cytokines which activate the neutrophils. The activated neutrophils cause the endothelial damage -the fundamental pathology in preeclampsia.
- The hypertensive disorders of pregnancy are linked with SEPS1 -an inflammatory response gene accounting for the increase in inflammatory mediators.
- The phospholipase A2, C reactive proteins,activin A are some of the cytokine mediators which areincreased in preeclampsia.
- Austgulen et al. expressed the role of adhesion molecules in preeclampsia which are hoisted in hypertensive women[26].
- Toll like receptors,member of innate immunity, activation of which secretes cytokines, triggering the pathological sequelae of preeclampsia.[27]

Screening:

Screening is an essential step in prevention of disease process. It helps in knowing the occurrence of the disease and controlling it well before its onset.

Non Laboratory:

Parity and family history:

Preeclampsia is the disease of primigravida with the incidence of 5-6% as compared to 0.25-0.5% in multigravida.

Preeclampsia is more common in first degree relatives.[22]

Roll over test:

Gant et al reported the significance of roll over test in 1973. The surge in diastolic BP of >20 when women is made to roll over from left lateral to supine at 28-32weeks of gestation would help anticipate the incidence of the disease[28].

Angiotensin infusion test:

Talledo et al studied the role of angiotensin and preeclampsia. The quantity of angiotensin <8ng/Kg/m^2 increases the diastolic blood pressure by 20mm Hg would stipulate the occurrence of preeclampsia[29].

Hand grip test:

Isometric hand grip is based on principle of surge in sympathetic activity and subsequent elevation of blood pressure in healthy adults. Degani et al made substantial efforts to portray that a rise in blood pressure of >20mm Hg during isometric hand grip test at 28-32weeks was positively related to prediction of the disease[30].

Uterine artery Doppler study as tool for preeclampsia:

YasminCasmod et al revolutionized the role of Doppler velocimeter in prediction of preeclampsia. The study was conducted on 144 participants at 11-14weeks gestation. Doppler study was re-analyzed at 22-24weeks and 28-32weeks. The presence of diastolic notch and pulsatility index >1.5 in first trimester were evaluators of increased resistance to blood flow in placental bed. This test was safe, noninvasive and promising[31].

Location of placenta:

VandanaAmbastha et al conducted a prospective study in the year 2016 – 2017 on 250 uncomplicated primigravida women. All the enrolled women were subjected to ultrasound at 18-24 weeks and 32-36 weeks. Women were analyzed for development of PE which was terminal point of the study. Women were also looked for the pregnancy outcomes. There is 5 times greater prevalence of PE among women with lateral placentation[2].

PaiMuralidhar et al performed a similar study in the Kasturba hospital, Manipal on 426 women. The women were categorized into the groups with central and lateral placenta. The maternal features were analogous in both groups. A remarkable number of women with lateral placenta developed PE in the consequent low and high risk pregnancies[45].

Another enormous study by Shivamurthy et al, demonstrated similar findings on a cohort of 5730 women in Davangere over a year. Ultrasonography was performed on all the women and the placenta position was described. The women were followed up and development of the disease was looked for. Those with PE were

further evaluated at term. Shivamurthy et al concluded that preeclampsia has substantial association with position of placenta[47].

ParveenaFareed et al described comparable conclusions on a total of 200 pregnant individuals, equally distributed in the cohort of 100 each of central and lateral placentation. Patients with lateral placenta had higher occurrence of the threatening disease. Further the frequency was greater in the high risk women in contrast to low risk women[49].

Kannamani et al examined 300 women for placental location and its association with hypertensive disorders of pregnancy. 72 women had lateral placentation and 228 had central placentation. 34 women (80.9%) of the women with lateral placenta developed high BP according to ACOG guidelines and only 8 women (19.1%) developed hypertension. Thus, location of placenta can be used as reliable parameter for prediction of preeclampsia with sensitivity of 81%, specificity of 85.3%, positive predictive value (PPV) of 47.2% and negative predictive value (NPV) of 96.4%[7].

Keshavarz et al piloted a retrospective case control study in 2017. 379 women were involved in the study, 121 with PE were assigned the group of “cases” and 258 with no PE belonged to the group of “controls”. This study similarly concluded that lateral placentation was common in women whose antenatal period was complicated with hypertension. The study emphasizes that prediction of preeclampsia by usual ultrasound at mid trimester helps in early diagnosis of the disease and help ameliorate the complications of the disease[53].

Singh et al pioneered a similar case control study on 592 women. Lateral placenta determined by ultrasound at 18-24 weeks gestation had association with hypertensive disorders complicating pregnancy with an odds ratio of 2.578 and 95% confidence interval (CI). They also proposed the positive association of lateral placental location with FGR with an odds ratio (OR) of 3.006[54].

Kaku et al proposedthe results of another prospective study performed on 350 women. 154 pregnant individuals had central placenta and 196 females had lateral placenta. 131 women (70%) of the lateral placenta developed PE and 56 (29.9%) of the central placenta developed PE. They found a two times greater incidence of PE among women with lateral placenta[15].

In a hospital based follow up study by Kore et al, study subjects were categorized to groups A and B with group A having central placenta and group B having lateral placenta. Among the group A, 13 women (40.62%) with central placentation developed the disease and 19 (59.38%) with lateral placenta developed PE. They proved a significant correlation between location of placenta and PE with sensitivity of 59.38%, specificity of 88.10%, PPV of 48.72% and a NPV of 91.93%[55].

Nandanwar et al validated similar results performed on cohort of 900 women. 365 women (66.4%) out of 549 women with lateral placentation developed PE and 128(36.4%) out of 351 women with central placentation developed PE. Hence, there is 3 fold greater incidence of PE in women with lateral placenta, determined by USG at mid trimester[56].

Pillay et al conducted another similar study on 100 pregnant women. 68 women had central placenta and among them 7 (25%) developed hypertension and 32

women had lateral placenta among which 21 (75%) developed PE. The team found a positive relation of placental location with development of PE with a p value of <0.001, sensitivity 75%, specificity 85%, PPV 62%, NPV 90%[57].

Jyoti et al performed the study on 130 individuals. 93 women had central and 37 women had lateral placenta. 28 developed PE with the incidence of PE to be 21.5%. Out of the women who developed PE, 19(51.3%) had lateral placenta and 9 (9.7%) had non lateral placenta. Thus, the study established an association between location of placenta and PE. Further, they found that majority of normotensive women had vaginal delivery in contrary to preeclamptic women who had to undergo emergency LSCS due to various causes. Perinatal outcome was nearly identical among the groups.[58]

Bhalerao et al steered a study recruiting 463 women. 71 developed PE, among which 52(73.23%) had laterally implanted placenta and 19(26.76%) had centrally implanted placenta. They reported a 2.7 times higher risk of developing preeclampsia in women with lateral placenta. However, they found no significant association between location of placenta and mode of delivery/birth weight of the baby[59].

In a follow up research by Kakkar et al, 150 pregnant individuals were enrolled. 84(56%) individuals had lateral placenta and 66(44%) had central placentation. Among 84 women with lateral placentation, 56(66.6%) developed PE in contrary to which only 24(36.3%) out of the 66 women with central placenta developed PE. They perceived a 5 fold higher risk of PE among women with lateral placentation and opined that location of placenta can be used as a safe, reliable tool for prediction of the disease[10].

Magann et al conducted an extensive study on 3336 pregnant females. They performed a prospective study to look for location of placenta and various pregnancy outcomes. 10 different placental locations were determined in mid trimester sonography. Outcomes considered were "placenta previa, abruption placenta, antepartum hemorrhage (APH), preterm labor, abnormal presentation, fetal growth restriction (FGR), PE, preterm delivery, 1-min and 5-min Apgar scores (<7) and postpartum hemorrhage (PPH)". The study proposed no substantial correlation between location of placenta and hypertensive disorders of pregnancy. Also, birth weight of the babies at delivery was independent of placental location determined at mid trimester[60].

Similarly, Pai et al piloted a research on 426 females. 324 had central placentation and 102 had unilateral implantation of placenta. 71 females developed PE, among whom 52(74%) had unilateral placenta which was statistically significant. They opined that the sensitivity of using placental location as a predictor for preeclampsia was 73%, specificity was 86%, PPV was 51% and NPV was 94%[61].

Laboratory parameters:

Lipid parameters and Preeclampsia-

Elisabeth BalstadMagnussen et al, conducted a population based prospective study on 3494 women to reveal a positive correlation between lipid parameters – cholesterol, low density lipoprotein (LDL) cholesterol,triglycerides, non-high density lipoprotein cholesterol and risks of hypertension in pregnancy[32].

Quadruple markers in PIH prediction:

Emma J Davidson et al, studied the role of maternal serum activinA, inhibin, human chorionic gonadotropin, α fetoprotein as mid trimester predictors of pregnancy induced hypertension. Activin A and HCG have linear association with preeclampsia as compared to inhibin, and alpha fetoprotein which are insignificant[33].

Urinary albumin and preeclampsia:

P Ekbom critically evaluated the role of urinary albumin as indicator of eclampsia in type 1 diabetes. Microalbuminuria (30-300mg/24hr urine) is the single most essential marker of eclampsia in type 1 DM[34].

Urine calcium excretion:

L Sanchez-Ramos et al proposed that women with hypertension excreted less calcium in urine which persisted throughout gestation. The threshold value being 195mg/24hours. This is because of increased calcium reabsorption from distal tubules[35].

Urine calcium creatinine ratio and preeclampsia:

P J Saudan et al – hypocalciuria is feature of preeclampsia. The calcium/creatinine ratio of 0.10 is predictive for onset of preeclampsia with 68% sensitivity and 70% specificity[36].

Protein-creatinine ratio in prediction of preeclampsia:

OyaDemirci et al advocated that protein-creatinine ratio can be used as alternate to 24hour protein assessment as quick diagnosis of eclampsia. Correlation

co-efficient of 0.758 p/c ratio and 24our protein excretion reveals the result with 91% sensitivity, 95.4% specificity, 95.2% positive predictive value (PPV), 91.2% negative predictive value37.

Uric acid and preeclampsia:

Chun Lam et al have been credited for the establishment of relation between uric acid and preeclampsia. Hyperuricemia is pathognomic of severity of the maternal syndrome of preeclampia[38].

Fibronectin and hypertensive syndrome:

Fibronectin is generally ameliorated in pregnancy which is further exaggerated in hypertensive disease.

Prevention:

Pharmacological:

- **Aspirin**: The imbalance between vasoactive substances and thromboxane paves its way for pathogenesis of preeclampsia. Aspirin has the ability to stabilize this imbalance and counteract aggregation of platelets. Also, the anti-inflammatory function of aspirin prevention of the disease[39]. Aspirin started in first trimester helps in prevention of hypertensive disorders of pregnancy. This has been strengthened by the meta-analysis of over 30,000 women.[40]
- **Low molecular weight heparin** and **dalteparin** are other drugs which help in conditions of placental dysfunction.The research work of Rey et al testified a substantial bargain in the frequency of recurrent preeclampsia[39, 41].

- **Calcium supplementation**: The body has inherent mechanism of secreting parathyroid hormone in conditions of low serum calcium. The women with low dietary calcium are at particular risks of developing the disease, indirectly by stimulating parathyroid hormone release which in turn increases intracellular calcium in the smooth muscle cells causing smooth muscle in the vessel wall to contract. Inception of supplementation of calcium during mid-trimester thus combats the rise in blood pressure. Calcium intake of approximately 1.5g/day is advised to all pregnant women[39].

Non pharmacological preparations:

- Women with low dietary calcium are recommended to take calcium (1.5-2g) during mid and third trimester of gestation according to WHO[42].
- Vitamin E and C, magnesium may help in preclusion of the disease but significance has not been effectively studied.
- Vitamin D deficiency has been associated with induction of pregnancy eclampsia. The effectiveness of vitamin D supplementation in pregnancy eclamptic women has been analyzed by one RCT which is makes it insignificant to generalize the use of vitamin D in pregnancy to prevent the disease.
- Nitric oxide is potentially known to cause vasodilation and this can be used to relieve the hypertension. This also explains the relative decrease in incidence of hypertension in smokers. Meher S, Duley L. have pioneered the effectiveness of nitric oxide in amelioration of the disease[43].

MATERIALS AND METHODS

This was a prospective study conducted on antenatal women attending the antenatal clinic of KAHER Dr. Prabhakar Kore Charitable Hospital, Belagavi.

Method of collection of data

a) STUDY DESIGN:

Hospital based prospective study

b) STUDY SETTING:

KLE's Dr Prabhakar Kore Charitable Hospital attached to KAHER's JNMC, Belagavi

c) STUDY PERIOD:

This study was conducted during interval between January 2019 and December 2019.

d) STUDY DURATION:

One year

e) STUDY POPULATION:

All pregnant women attending outpatient services at the hospital. The women are screened. Eligible women meeting the selection criteria enrolled for the study.

f) SAMPLE SIZE:

According to reference article

With the confidence level and 90% Power,

$N = Z_a^2 PQ / d^2$

Where $Z_a = 1.96$ at 95% confidence level

d = 10% of p (90% power)

p = 44%

Hence, N ~ 450

g) SELECTION CRITERIA:

INCLUSION CRITERIA:

All pregnant women attending antenatal clinic at 18 to 24 weeks of gestation in the KAHER Dr. Prabhakar Kore Charitable Hospital, Belagavi were recruited for the study.

EXCLUSION CRITERIA:

Patients with following conditions were disqualified from the study:

1. Chronic hypertension
2. Twin gestation
3. Patients with uterine anomalies
4. c/o Diabetes mellitus
5. c/o renal disease.

h) **ETHICAL CLEARANCE**:

Before instigation of the study, ethical clearance was acquired from "the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belagavi".

i) METHODOLOGY:

1. All pregnant women attending antenatal clinic in the KAHER Dr. Prabhakar Kore Charitable Hospital, Belagavi were screened for the study. 490 women were screened for the study.
2. Those with lethal fetal anomalies were barred from the study. 22 women out of 490 had lethal fetal anomalies and were omitted from the study.
3. Written informed consent was taken from women afore recruiting for the study.
4. Women meeting the above inclusion criteria, without the conditions mentioned in the exclusion criteria, were recruited in the study. 468 women were recruited for the study.
5. Detailed history was taken from the women recruited for the study.
6. Routine general physical examination was done and recorded.
7. Blood pressure measurement: Blood pressure was measured in the sitting posture. The disappearance of Korotkoff sound V was taken as diastolic blood pressure.
8. Obstetric scan was performed on all women hired for the study at 18-24 weeks gestation. The location of placenta was determined in the scan. Scan machine: Voluson S8 was used for the obstetric scan.

9. Determination of location of placenta: The location of placenta was classified as central and lateral.

LATERAL LOCATION OF PLACENTA: Probe of the scan machine was moved in the center of the abdomen from above downwards – placenta was classified as lateral, when edge was seen in the center of the uterus. Major bulk of the placenta was seen to occupy the left or the right side of the uterus.

When more than 75% of placental mass is to one side of the midline, it is classified as lateral placenta.

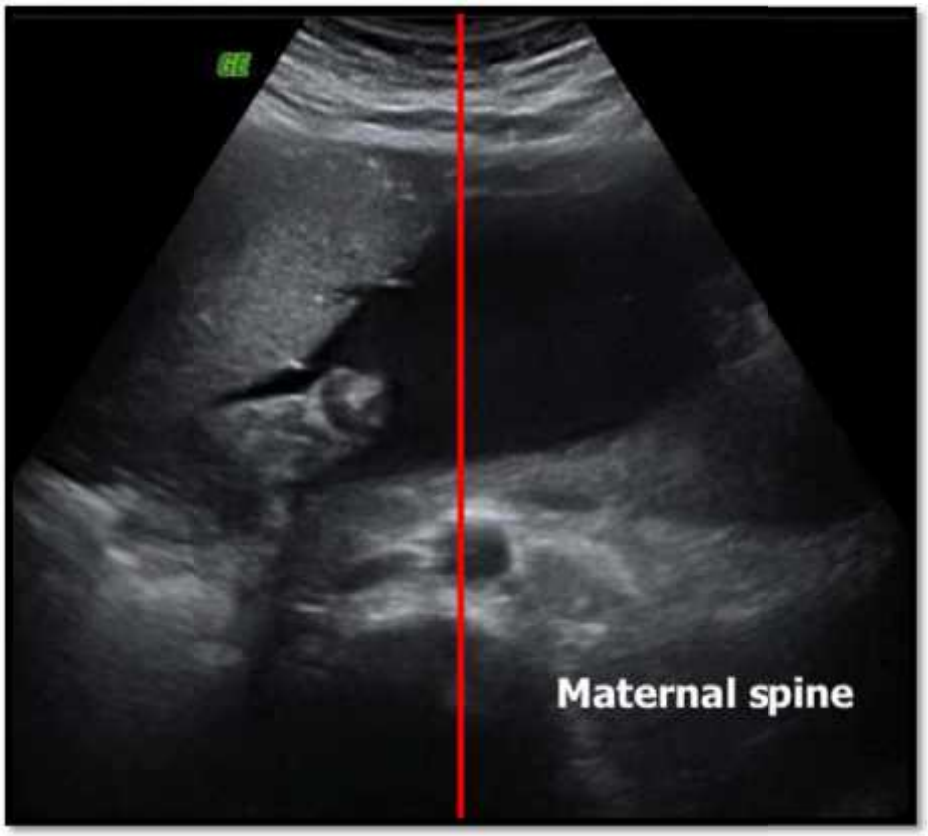


Fig 1. USG image of unilateral placenta

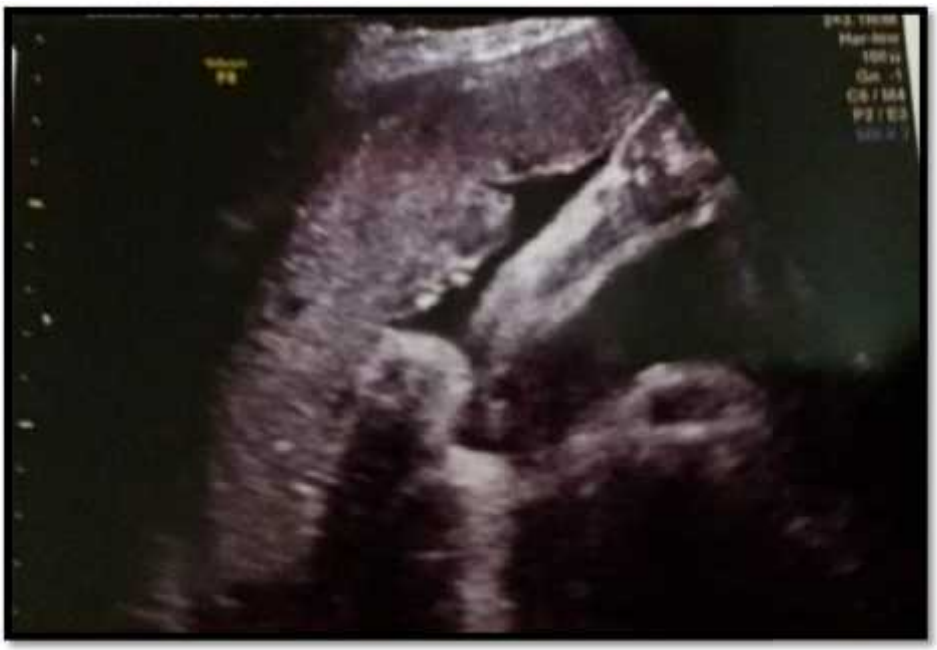


Fig 2: Lateral placentation

CENTRAL LOCATION OF PLACENTA:

On moving the probe from above downwards, when major bulk of placenta was seen at midline, it was classified as central placenta.

The placenta is categorized as central when it is correspondingly distributed between the right and left side of the uterus irrespective of anterior, posterior or fundal position.

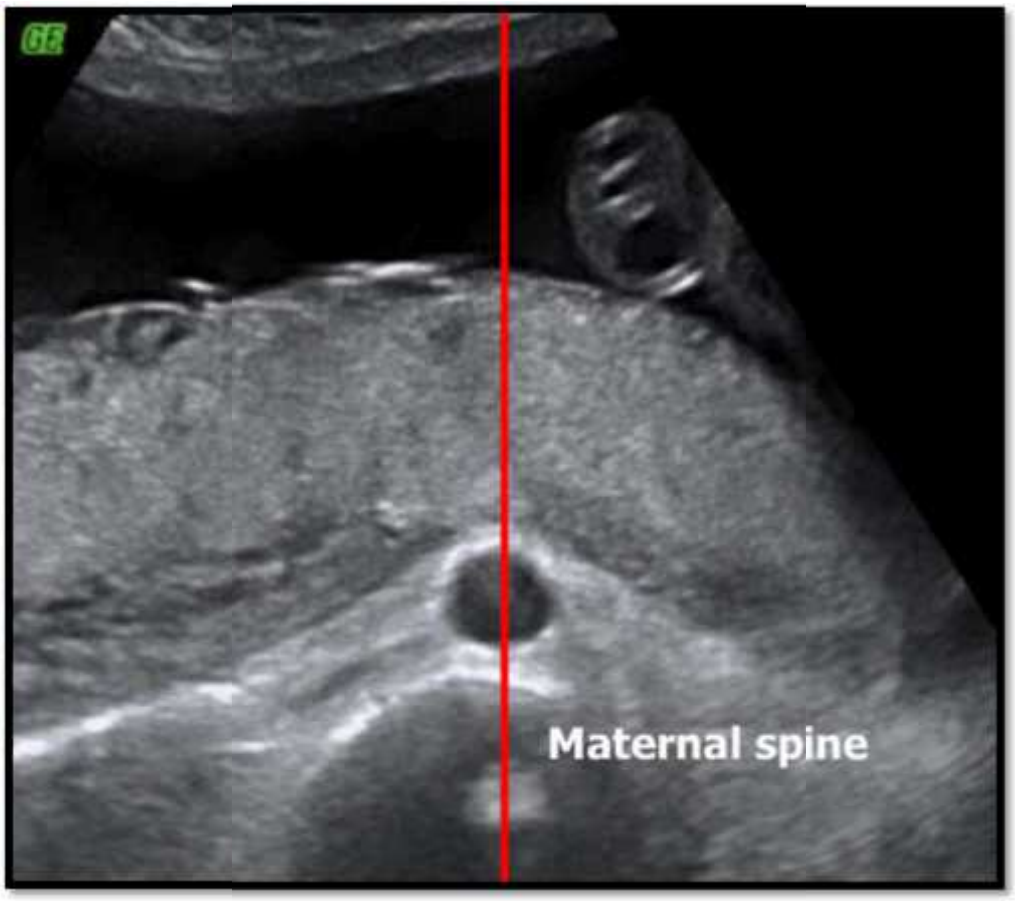


Fig 3.Mid trimester ultrasound picture of central placentation.

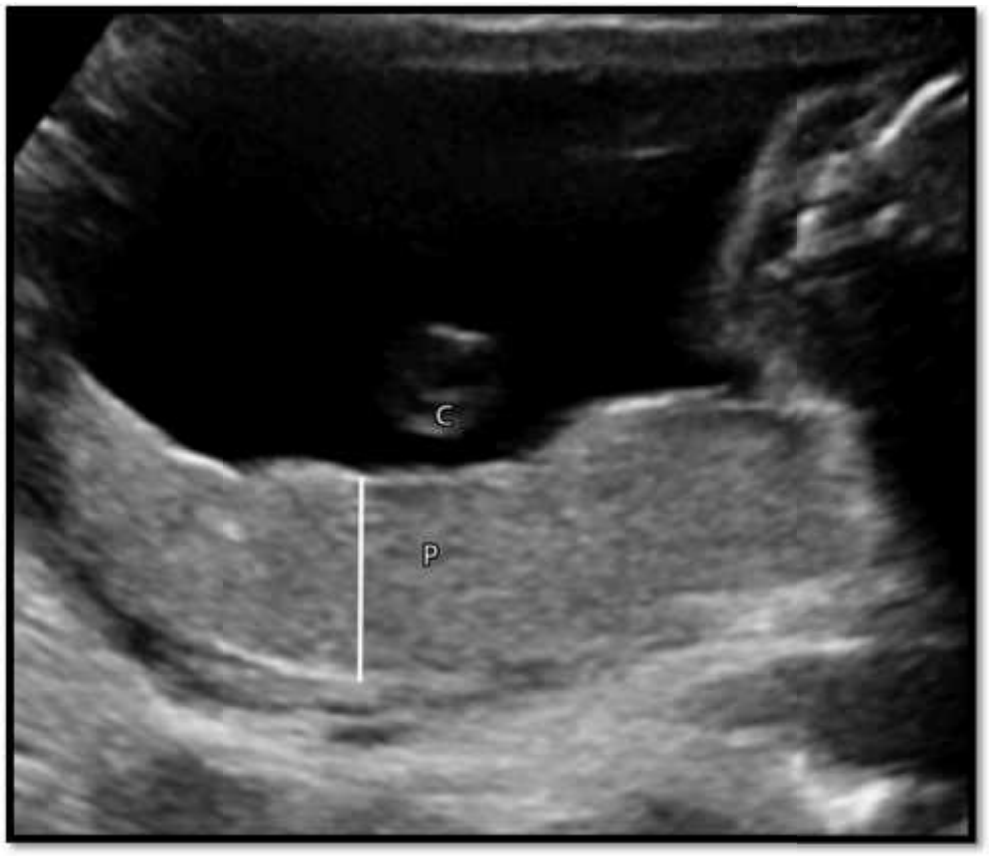


Fig 4: Central placentation

10. All the 468 women were reassessed at delivery. Out of 468 women, 37 women (7.9%) were lost to follow up.
11. Blood pressure was measured at admission on delivery.

    Blood pressure: the revised "ACOG criteria" was used to classify the blood pressure as normotensive and pre eclampsia.

    Women with pre eclampsia were further classified as mild and severe according to "ACOG criteria".
12. Mode of delivery, weight of baby and sex of baby were recorded.
13. Data was recorded in the Microsoft excel sheet and subjected to analysis.

DISCUSSION

- Preeclampsia is a pathological condition with multiple factors influencing the causation. Ever since, there have been various attempts in discovering newer modalities of its early diagnosis and prevention.

Serum markers as predictors of PE:

- Leona C Poon summarized that reduced PAPP-A concentration, expressed in terms of MoM (<0.4MoM) is a biochemical predictor of PE. The marker is evaluated in first trimester during the screening of aneuploidies. Never the less, the marker is influenced by factors such as period of gestation at screening, weight, race of the women, maternal habits, parity, and other comorbid condition[5].
- Women preordained to develop PE have higher concentration of plasma Fibronectin, a glycoprotein[50].
- The pathophysiology of PE directs towards the faulty placentation, which facilitates the trafficking of fetal cells and cell free fetal DNA[50].
- The levels of maternal HCG determined in 2nd trimester are elevated in women predisposed to PE[50].
- Serum uric acid is elevated in women predisposed to development of PE. Such women have placental insuffiency which progresses to placental ischemia, and increased breakdown of purines coupled with renal impairment (consequence of PE) is responsible for surge in serum uric acid levels[50]

Urine markers:

- Urine calcium excretion is dependent on glomerular filtration and tubular reabsorption. In women with PE, tubular reabsorption of calcium is increased, consequently leading to low urine calcium excretion, assessed at 24-34weeks[50].
- Munge et al reflected the low urinary calcium creatinine ratio among preeclamptic women in his study with a sensitivity of 63.63%, specificity of 94.87%, positive predictive value of 77.77%, and negative predictive value of 90.2% 52.

Ultrasound markers:

- First trimester uterine artery pulsatility index, expressed in terms of MoM, is substantially increased in pregnant females at risk of PE. The value of the predictor is inversely related to the gestation age at delivery. This index is modified by gestation age at screening, weight of the women, race of the women, pre-existing DM. This has been described by Leona C Poon[5]. First trimester early diastolic notch is the earliest predictor of the disease.

The present study aimed to ascertain a non-invasive method for prediction of the disease. As the etio-pathogenesis of preeclampsia centers to the placenta, this study endeavors to determine preeclampsia by knowing the placental location at 18-24weeks gestation.

Defective placentation and the resultant placental insufficiency is the key to the pathogenesis of preeclampsia. Human placenta is supplied by the bilateral uterine arteries, which are the branches of anterior division of internal iliac arteries. Blood supply to the placenta is influenced by the placental position in the uterus. The central situated placenta within the uterus, receives equal blood flow from both the uterine vessels. In contrast to this, the lateral placenta, receives adequate blood supply from ipsilateral uterine artery, whereas the blood flow from the contralateral uterine vessel

varies. This is compensated by the body's innate mechanism by development of collaterals. The blood supply by these collaterals is unpredictable. The resultant failure in trophoblast remodeling in these vessels initiates the disease process.[45]

Age of the patients:

In our study, patients were categorized into 4 groups - <20years, 21-25 years, 26-30 years, >31years. 13.25% belonged to age group of <20 years, 53.42% belonged to the group of 21-25years, 27.14% had age between 25-30years and 6.20% had age >31 years. Majority of the women belonged to the age group of 20-25years.

The results were similar to the study by Vandana Ambastha et al, the patients were distributed into 4 age groups- 16-20years, 21-25 years, 26-30years, >30years. 11.2% belonged to the age group of 16-20years, 54% had age groups between 21-25years, 28.8% belonged to the group of 26-30years and 6% had age >30 years. Majority of women belonged to group of 21-25 years[2].

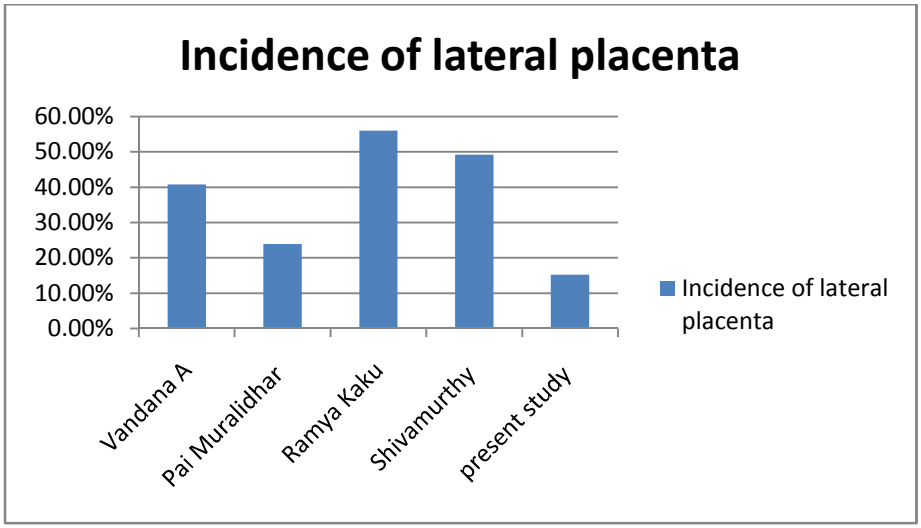
Shivamurthy et al conducted an extensive study, in which the study subjects were similarly divided into 4 age groups- <20years, 21-25 years, 26-30years and >30years. The study subjects were further classified as fundal and lateral group of placenta. <20years, there were 23.8% who had lateral placenta and 27.6% had fundal placenta. In age group of 21-25 years, 47.6% had lateral placenta and 55.3% had fundal placenta. Between 26-30 years of age, 24.1% had lateral placenta and 7.5% had fundal placenta. >30 years of age, 4.5% had lateral placenta and 9.5% had central placenta. Overall, majority of women – 246 study subjects belonged to the age group of 21-25 years[47].

Location of placenta:

In our study, 468 women were recruited. Out of the 468 women, 74 women had lateral location of placenta at 18-24weeks gestation. Incidence of unilateral placenta in the study was 15.4%. In the study conducted by Vandana Ambastha et al, incidence of lateral placenta was 40.8% among the total 250 women[2]. In another study by Pai Muralidhar et al, out of 426 women, 102 women developed pre eclampsia (23.9%) [45]. In a contemporary study by Ramya Kaku et al incidence of unilateral placenta was 56%[15]. In another prospective study by Dr N Sumathi et al, 123 out of 250 women had laterally located placenta[46]. In a large study by Shivamurthy H M et al, 59% had unilateral placentation as compared to 41% with central placentation[47].

Incidence of lateral placenta in different studies.

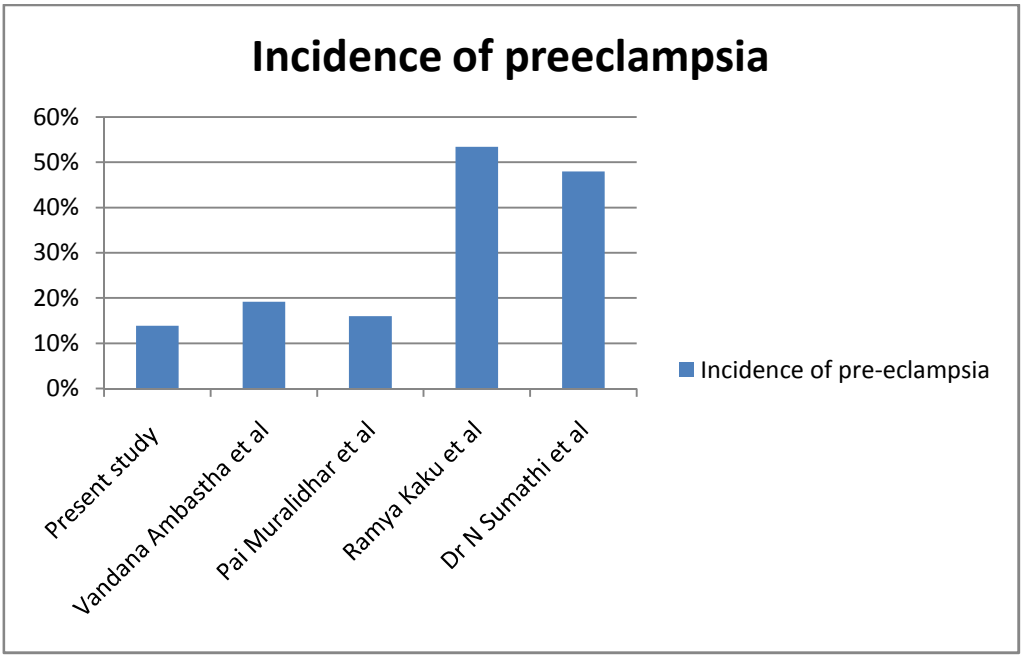
Vandana Ambastha et al	40.8%
Pai Muralidhar V et al	23.9%
Ramya Kaku et al	56%
Dr N Sumathi et al	49.2%
Shivamurthy H M et al	59%



In the present prospective study, incidence of PE among the 431 women assessed at delivery was 13.9% (60 out 431). In a study by Vandana Ambastha et al, new onset of preeclampsia was 19.2 %(48 out of 250)[2]. In a study Pai Muralidhar et al, new onset of preeclampsia was 16 %(71 out of 426)[45]. 53.4 %(187 of 350) of women developed preeclampsia as observed by Ramya Kaku et al[15]. Similarly, Dr N Sumathi et al, observed the overall incidence of preeclampsia to be 48% (120of 250) in the year2015-16[46].

Incidence of preeclampsia in various studies.

Present study	13.9%
Vandana Ambastha et al	19.2%
Pai Muralidhar et al	16%
Ramya Kaku et al	53.4%
Dr N Sumathi et al	48%



Association of location of placenta and preeclampsia

In the current study, out of 73 women with laterally situated placenta, 38.4 %(28) developed preeclampsia as compared to 61.6% (45) who were normotensive. Among the women with central placentation, only 8.9 %(32 of 358) developed preeclampsia and 91.1% (326 of 358) had normal blood pressure.

In a study by Vandana Ambastha et al, 39.2% (40 of 102 lateral placenta) developed preeclampsia and 60.7% were normotensive[2]. In another study by Ramya Kaku et al, similar results were obtained, in which among the total 196 women with unilateral placenta, 131(66.8%) developed preeclampsia and 39.9%(65/196) remained normotensive. In women with central placenta, 56/154 (36.3%) developed preeclampsia and 98/154(63.6%) remained normotensive[15].

In the Pai Muralidhar et al study, 195 high risks and 231 low risks women were observed. Out of the 195 high risk patients, 51(26%) developed preeclampsia, out of which 68.7% (35/51) had unilateral placenta. Among the women with low risks, 8.6% (20) developed preeclampsia, of which 60% (12/20) had unilateral placenta[45].

In contrast to the above, study by Rosanna Salama-Bello et al in 2014-2015, the relationship between placental location and hypertensive disorders was looked for in 464 pregnant women. 411 (88.57%) had central placenta and 53 (11.42%) had lateral placenta. The incidence of hypertensive disorders of pregnancy was similar in both groups (21% versus 19%; p value – 0.71). Thus, according to this study, there is no association of location of placenta and pregnancies complicated with hypertensive disorders.

In the current study, the p value obtained was <0.0001, which is statistically significant as comparable to other studies.

The value obtained was similar to another study by Shagufta Yousuf et al, which was conducted on 201 women, and resultant p value was ≤0.001[48].

In another study by Parveena Fareed et al, a prospective study was conducted on 200 pregnant individuals, with 100 women in group of lateral placenta and 100 in the group of central placenta. Out of 100 women with lateral placenta, 39(39%) developed as against the 11(11%) in the central placenta. The p value obtained was <0.001 which was analogous to our study[49].

Placental position and severity of preeclampsia

In our study, among the 28 patients with lateral placenta and preeclampsia, 21 women had mild preeclampsia and 7 patients had severe preeclampsia with BP ≥160/110 mm Hg. Amongst the 32 women of central placenta group, 25 pregnant women had mild preeclampsia and 7 had severe preeclampsia.

The study by Ramya Kaku et al, the women with lateral placentation were further classified as mild, moderate and severe. The BP measurements in mild group had range between 140/90 and 149/99 mm Hg with 84 women belonging to this sub group, moderate subset (150/100 – 160/109 mm Hg) and 27 women, severe sub group analysis (BP >160/110 mm Hg) having 20 pregnant individuals[15].

In the research of Priyadarshini et al in the year 2019 of 100 cases, the women were classified as 'PIH' (pregnancy induced hypertension) and 'no PIH'. 33 women of 68 lateral placental cases had PIH and 15 cases of 32 women with central placentation had PIH. Of the 33 women with lateral placenta, 25 had mild PIH and 8

had severe PIH as compared 14 of the central group PIH having mild PIH and 1 of central group having severe PIH[16].

Another study by Bhattacharjee AK et al, overall 200 cases were enrolled , cases were looked for preeclampsia with the severity into consideration. 50 women had mild preeclampsia, of which 26 (26/50) had lateral situated placenta and 24 (24/50) had placenta with central position. 52 cases of severe PE were examined, majority 40 (40/52) had unilateral placenta and the remaining 12 (12/52) had central located placenta[9].

Mode of delivery

In our study a total of 431 were reassessed at delivery for the maternal and fetal outcomes. Amongst the 73 with lateral placenta who were reassessed at delivery, 36(49.3%) were delivered by LSCS and 37(50.7%) delivered vaginally. In the central group of placenta, 139(38.8%) were terminated by LSCS and 219 (61.1%) delivered vaginally.

The results obtained were akin of the study by Vandana Ambastha et al, of the 250 women enrolled for the study, 102 had lateral placenta, 55 (54%) landed up undergoing LSCS and 47 (46%) delivered via the normal vaginal route. In the group of 148 with central placenta, 93 (62.8%) had vaginal delivery and 55(37.2%) had to be terminated by LSCS[2].

In the research by Sumathi et al, a total of 52 patients had vaginal delivery, of which 39 (75%) had lateral placenta and 13 (25%) had central placentation. 68 women underwent LSCS, with majority (59, i.e., 56.7%) had unilateral placenta and 9 (13.2%) had central placenta[46].

Strengths of the study:

- Placental location is determined by ultrasound during anomaly scan, done at 18-24 weeks gestation, which doesn't require any additional procedure or scan.
- Detection of placental location by ultrasonography is a noninvasive procedure which is reliable, cost effective, and safe.

Limitation of the study:

- Sample size is limited.
- In the present study, ultrasonography has been performed by more than individual.
- Uterine artery Doppler coupled with location of placenta has higher predictive value in diagnosis of hypertensive disorders of pregnancy, which has not been evaluated in our study.

CONCLUSION

Preeclampsia is a multifactorial disease. In the present study,we looked at the association between location of placenta and development of preeclampsia. The incidence of lateral placenta was determined. Overall incidence of preeclampsia was determined. Location of placenta was associated with development of preeclampsia.

Lateral location of placenta, due to placental insufficiency, predisposes to development of preeclampsia. Also, laterally located placenta at mid trimester scan has a positive association with severity of preeclampsia.

Location of placenta had no role in determination of mode of delivery. Also, weight of babies at delivery was independent with location of placenta.

Other factors, like age of the pregnant women and parity, were not associated with preeclampsia in our study.

SUMMARY

The current study was a prospective study conducted in the year 2020 for a period of one year at KLE's Dr Prabhakar Kore Charitable Hospital attached to KAHER's JNMC, Belagavi. The purpose of the study was to determine if location of placenta had a predictive role in diagnosis of preeclampsia. All antenatal attending the outpatient services undergoing obstetric scan at 18-24 weeks gestation were screened for the study. Women with lethal fetal anomalies and meeting the other exclusion criteria were precluded from the study. Women meeting the inclusion criteria, 468 in number, were enrolled for the study. Location of placenta, classified as central and lateral determined by scan at mid trimester was noted. All the women enrolled for the study were reassessed at delivery for development of preeclampsia, severity of preeclampsia, mode of delivery and baby weight. A total of 431 were re-examined at delivery.

- Majority of women belonged to the age group of 21-25 years with percentage of 53.42.
- The prevalence of parity of the women, classified as primigravida and multigravida, was comparable in the study.
- The incidence of women with lateral placentation was 15.8%.
- The overall incidence of PE in the study period of one year was 13.9%.
- The overall incidence of mild PE was 10.67% and that of severe preeclampsia was 3.24%.
- Of the women with lateral placentation, 38.4% women developed preeclampsia in contrast to 8.9% of preeclamptic women in the group of women with central placenta.

- Lateral location of placenta thus can be used as a noninvasive, inexpensive early determinant of preeclampsia.
- Location of placenta also has a role in determination of severity of preeclampsia.
- Location of placenta does not determine the mode of delivery.
- Location of placenta and baby weight at delivery is independent.

In our study, age of the pregnant women had no relation to development of preeclampsia.

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ANNEXURE I

ETHICAL CLEARANCE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/

Date: 24/11/2018

To,

REG.NO. BJ0118001

PG student in Obstetrics and Gynaecology,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"LATERAL LOCATION OF THE PLACENTA AS A PREDICTOR OF PRE ECLAMPSIA IN PREGNANT WOMEN, A HOSPITAL BASED PROSPECTIVE STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE II

INFORMED CONSENT

Purpose of the study:

The purpose of the study is to establish the association of lateral location of placenta and development of preeclampsia. This would help in early detection of patients with preeclampsia and prevent related complications.

Type of study:

This is a hospital based prospective study involving ultrasonography on pregnant women in the period of gestation 18-24 weeks to determine the location of placenta.

Participant selction :

All pregnant women at 18-24 weeks period of gestation undergoing scan at 18-24 weeks scan are recruited in the study.

Voluntary participation:

Your participation in research is voluntary .Your decision whether to participate in the study or not will not change present or future health care services offered to you and will not affect your relationship with J. N. Medical College

Information on the scan :

Ultrasound is done on women in the period of gestation 18-24 weeks to determine the location of placenta .

LATERAL LOCATION OF PLACENTA:

Probe of the scan machine will be moved above downwards in the center of the uterus –when the edge of the placenta is seen, when scanned in the center & major bulk of placenta is seen when probe is placed at right lateral or left lateral aspect of uterus – it is considered as right or left lateral location of placenta.

When more than 75% of placental mass is to one side of the midline, it is classified as unilateral right or left placenta.

CENTRAL LOCATION OF PLACENTA:

Whenmajority of placenta is seen in center of the uterus or posterior, it is considered as central location of placenta

The placenta is classified as central when it is equally distributed between the right and left side of the uterus irrespective of anterior, posterior or fundal position.

Procedure involved:

After selection of patients for the study and obtaining informed consent, patients will be evaluated as per history, general physical examination, routine antenatal investigations and ultrasonography. Location of placenta is determined in the scan done at period of gestation 18-24 weeks. These women will be followed for the development of signs and symptoms of preeclampsia. Outcome of pregnancy in terms of vaginal or cesarean delivery, outcome of baby in terms of baby weight are noted.

Side effects:

There are no known side effects of the study.

Risks:

There are no known risks associated with this study.

Benefits:

We want to let you know that there may be no benefits to you at present by participating in this study. By participating you will be helping to ensure that women in future.

Your participation being valuable contribution to medical research to predict preeclampsia in the early period of gestation and prevent related complications.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator. You will not be reimbursed for any expenses for participation in this research.

Privacy and Confidentiality:

The only people who will know that you are the research subject will be the members of the research team. No information about you or information provided by you during the research will be disclosed to others without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential. Results of the study will be used to improve maternal and perinatal outcome.

Withdrawal from study:

You can withdraw at any time from the study. There will be no penalty for withdrawal. You can be removed from the study if necessary.

Institutional/sponsor's policy:

In the event of any injury related to the study, treatment will be made available through KLE's Hospital & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact **REG.NO. BJ0118001,** Post graduate student, Department of Obstetrics and Gynecology, KLE's Hospital& MRC or by Ph. No: _____.

Contact details:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact **REG.NO. BJ0118001**, Post graduate student, Department of Obstetrics and Gynecology, KLE's Hospital and MRC, Ph. No: _____ or Dr._____, Professor, Dept. Of Obstetrics and Gynecology, KLE's Hospital and MRC, Belgaum, Ph. No: _____.

If you have any queries about your rights as a study participant, you may contact Dr. Roopa M Bellad, Prof. of Pediatrics as Chairman of J. N. Medical College

Institutional Ethics Committee on Human Subjects Research, Phone No.0831 2473777 ext-1527 at J. N. Medical College, Belgavi.

Consent statement:

I, _____ voluntarily agree for participating in this study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read form in my own vernacular language, including the risks and the benefits and having all my questions answered.

Participant Name : _____

Signature or the Left Thumb Print of Participant : _____

Investigators Name: _____ Signature: _____

Witness Name : _____ Signature: _____

Date: _____

ANNEXURE III

SCREENING PROFORMA

NAME
AGE
OP NO
DATE OF ENROLLMENT

H/O _____ months of amenorrhoea

Present complaints _____

Obstetric history:

Consanguinity:

Gravida _____ Para _____ Living

_____Abortion _____

Menstrual history:LMP : _____

EDD : _____ cEDD_____

GA : _____

Past history:

	YES	NO
H/O Hypertension		
H/O DM		
Renal disease		
Multiple pregnancy		

Family history:

General physical examination:

Pulse rate	
Blood pressure	
Pallor	
Edema	

Scan details:

Anomalies: _____

ANNEXURE IV

STUDY PROFORMA

PROFORMA

"LATERAL LOCATION OF THE PLACENTA AS A PREDICTOR OF PREECLAMPSIA IN PREGNANT WOMEN, A HOSPITAL BASED PROSPECTIVE STUDY"

NAME	
AGE	
ADDRESS	
PHONE NUMBER	
OP NO	
DATE OF ENROLLMENT	

H/O _____ months of amenorrhoea

Present complaints _____

Obstetric history: Gravida _____

Para _____ Living _____

Abortion _____

Menstrual history: LMP : _____

EDD : _____ cEDD_____

GA : _____

Past history:

	YES	NO
H/O Hypertension		
H/O DM		
Renal disease		
Multiple pregnancy		

General physical examination :

Pulse rate	
Blood pressure	
Pallor	
Edema	

Scan details :Location of the placenta

Lateral	
Fundal	
Anterior	
Posterior	

Gestational age at scan :_____ wks

BPD HC AC FL

SDVP:

Anomalies , if any : _____

Follow up :

Gestational age :_____ wks

Complaints : _____

BP: _____ mm Hg

Maternal outcome :

Gestational age at delivery :

PR: BP:

Pallor: Edema :

Abruption +/-

FHS :_____bpm

Mode of delivery :

	YES	NO
Vaginal		
Emergency LSCS		
Elective LSCS		
Instrumental		

Vaginal : Induced / not induced

Indication of LSCS :

Co-morbidities :

Complications :

Fetaloutcomes :

Live birth	
Still birth	

Birth weight : _____ kg

Sex of baby : Male / Female

NICU ADMISSION Yes / NO

Proteinuria -

ANNEXUREV

KEY TO MASTERCHART

SL. NO.	Serial number
OP/IP no.	Outpatient/inpatient number
LMP	Last menstrual period
EDD	Expected date of delivery
H/O HTN	History of hypertension
H/O DM	History of diabetes mellitus
PR	Pulse rate
BP	Blood pressure
BPD	Biparietal diameter
HC	Head circumference
AC	Abdominal circumference
FL	Femoral length
SDVP	Single deep vertical pocket
BP2	Blood pressure 2 (at delivery)
PE	Preeclampsia
GDM	Gestation diabetes mellitus
IGT	Impaired glucose tolerance
PPH	Postpartum haemorrhage
LSCS	Lower segment caesarean section
FGR	Fetal growth restriction
CPD	Cephalopelvic disproportion

MSL	Meconium stained liquor
CDMR	Caesarean delivery at maternal request
EDF	End diastolic flow
FSB	Fresh stillbirth
MSB	Macerated stillbirth