"Association Between Maternal First Trimester Serum Analytes (PAPP-A, BETA hCG, PLGF) And Adverse Pregnancy Outcomes"
A One Year Observational Study at Kaher's Dr. Prabhakar Kore Hospital and Medical Research Centre

By

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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ASSOCIATION OF FIRST TRIMESTER MATERNAL SERUM ANALYTES (PAPP-A, BETA HCG, PLGF) WITH ADVERSE PREGNANCY OUTCOMES 1 YEAR OBSERVATIONAL STUDY AT KAHER'S DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE"** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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LIST OF ABBREVIATIONS

PAPP-A	**:**	Pregnancy Associated Plasma Protein A
hCG :	**:**	Human Chorionic Gonadotropin
PLGF	:	Placental Growth Factor
PROM	:	Prelabour Rupture Of Membranes
FGR	:	Fetal Growth Restriction
GDM	:	Gestational Diabetes Mellitus
PE	:	Pre Eclampsia
NICU	:	Neonatal Intensive Care Unit
APH	:	Antepartum Haemorrhage
FPR	:	False Positive Rate
OPD	:	Out Patient Department
MoM	:	Multiples Of Median
TSH	:	Thyroid Stimulating Hormone
LH	:	Luteinizing Hormone
FSH	:	Follicular Stimulating Hormone
IGFBP	:	Insulin-like Growth Hormone Binding Proteins
IGF	:	Insulin-like Growth factor
UTPI	:	Uterine Artery Pulsatility Index
VEGF	:	Vascular Endothelial Growth Factor
HUVE	:	Human Umbilical Vein Endothelial Cells
sFlt-1	:	Soluble Fms- Like Tyrosine Kinase 1
NT	:	Nuchal Translucency

SGA : Small For Gestational Age

UA : Umbilical Artery

AFP : Alpha Feto Protein

AREDV : Absent Reverse End Diastolic Velocity

BMI : Body Mass Index

LBW : Low Birth Weight

HPL : Human Placental Lactogen

uE3 : Unconjugated Estriol

LR : Likelihood Ratio

IVF : In-Vitro Fertilization

ABSTRACT

Introduction

The prevention and prognosis of adverse pregnancy outcomes are of great significance. The management of high risk pregnancy is particularly challenging because of the risk of the associated adverse pregnancy outcomes. Emphasis is on early detection and prevention for individuals likely to undergo complications in pregnancy. Screening tests are important to identify such high risk patients in early pregnancy, i.e first trimester 9 weeks to 13 weeks of gestation. Dual markers is routinely done in the first trimester irrespective of the risk categorization. In low resource setting, addition of placental growth factor to first trimester serum analytes PAPP-A and beta hCG can pick up more cases of pregnancies at risk of developing complications.

Objective

To determine association of 1st trimester PAPP-A, BETA HCG and PLGF with adverse pregnancy outcome.

Material and Methods

A ll antenatal women between 9 weeks and 13 weeks 6 days period of gestation attending the out patient department, and meeting the inclusion and exclusion criteria presenting at KAHER's Dr. Prabhakar Kore Hospital, Belagavi were included in the study. 3ml of venous blood was taken in a plain vacutainer, provided by the laboratory and it was processed by – Time Resolved Fluroimmunoassay on Auto-Delfia. The Software used for analysis-Lifecycle software from PerkinElmer Life and Analytical Sciences. These pregnancies were followed up at delivery and the results were noted. Pre-Eclampsia, fetal growth restriction, preterm delivery, oligohydramnios, low birth weight, placental abruption,

gestational diabetes mellitus, chromosomal anomalies like trisomies and missed abortion.

Results

123 participants were enrolled in the study and 119 participants were followed up as per the exclusion criteria and loss to follow up. Among the outcomes measured, 8 (6.72%) of the participants had preeclampsia, 5 (4.24%) had preterm delivery, 5 (4.24%) had oligohydramnios, 3 (2.50%) had gestational diabetes mellitus ,4 (3.36%) had prelabour rupture of membranes (PROM) and 4 (3.40%) showed fetal growth restriction (FGR). Increased risk for Down's syndrome, was seen in 1 participant, 0.84% and the remaining participants were screened as low risk for Down's, Edward's and Patau's Syndrome. Beta- hCG mom, PAPP-A mom, and PLGF mom levels were statistically significant (p value- 0.01) for predicting preeclampsia, according to the findings of multivariate analysis. The optimum cut-off point for predicting preeclampsia, according to the ROC curve, was 0.74 mom. 5.08% of population underwent NICU admission.

Conclusion

First Trimester serum analytes PLGF and PAPP-A are equivocal as per the multivariate analysis for the association with pre eclampsia. However addition of PLGF to the Dual markers in the 1st trimester helps to increase the prediction of Pre Eclampsia. Routinely Dual markers (PAPP-A and beta Hcg) is being advised with NT scan in the 1st trimester genetic screening program. We can detect women at risk of pre eclampsia early in the first trimester so that such women can be subjected to preventive strategies like aspirin therapy.

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INTRODUCTION

Adverse pregnancy outcome is an umbrella term covering the complications that occur to the mother, the new born, or both during pregnancy, labor ,and the postpartum period. Some of the common pregnancy complications include hypertensive disorder of pregnancy, antepartum haemorrhage (APH) , stillbirth, low birth weight, prematurity prelabour rupture of membranes (PROM) , pre eclampsia, fetal growth restriction (FGR), GDM , and preterm delivery are major contributors to maternal and perinatal mortality and morbidity. They adversely affect the long-term cardiovascular health of the affected women and children . For example, preeclampsia increases a female's risk of myocardial infarction, stroke or diabetes mellitus by two to eight fold in the next two decades of life. Moreover, FGR fetuses have a two to eight fold increased risk for hypertension, cardiovascular disease, diabetes mellitus or renal disease during their lifetime extra utero.Adverse pregnancy outcomes also have a major psychological impact for the family as well as result in an increased cost for the healthcare system.[1,2]

Previous research has highlighted that the origin of underlying pathology of pre-eclampsia, FGR and preterm delivery lies in the early gestation, in the first trimester itself. [3] Also abnormal concentration of first trimester serum markers like PLGF ,beta HCG and PAPP-A during first trimester, is related to the onset of preeclampsia, small for gestational age and preterm delivery. [4] This has led to introduction of assessment of maternal serum biomarkers in first trimester to identify the individuals who need preventive measures and intense surveillance to improve the pregnancy outcomes. Results from recent studies have shown that about 65% of early-onset PE can be predicted using first trimester maternal serum placental growth factor (PlGF),

pregnancy-associated plasma protein-A (PAPP-A) and maternal demographics and history at a false positive rate (FPR) of 5%. [5]

With the increased use of first-trimester screening using PAPP-A and beta HCG for Downs syndrome and fetal aneuploidy, there is an opportunity to tow other biomarker screening tests for preeclampsia, FGR and preterm delivery and other APOs onto existing commonly performed tests .Lower serum PAPP-A and β-hCG levels were found to be associated with more frequent obstetric complications whereas PLGF is studied extensively for its association with pre eclampsia. There is dearth of literature on association of serum PLGF, Beta hCG and PAPP-A serum analytes with overall adverse pregnancy outcomes. Hence we aimed to identify the association of PAPP-A and free β-hCG ,and PLGF with adverse pregnancy outcomes.

AIMS AND OBJECTIVES

The aim of the study was to find the association between maternal first trimester serum analytes (PAPP-A, Beta Hcg, PLGF) and adverse pregnancy outcomes.

REVIEW OF LITERATURE

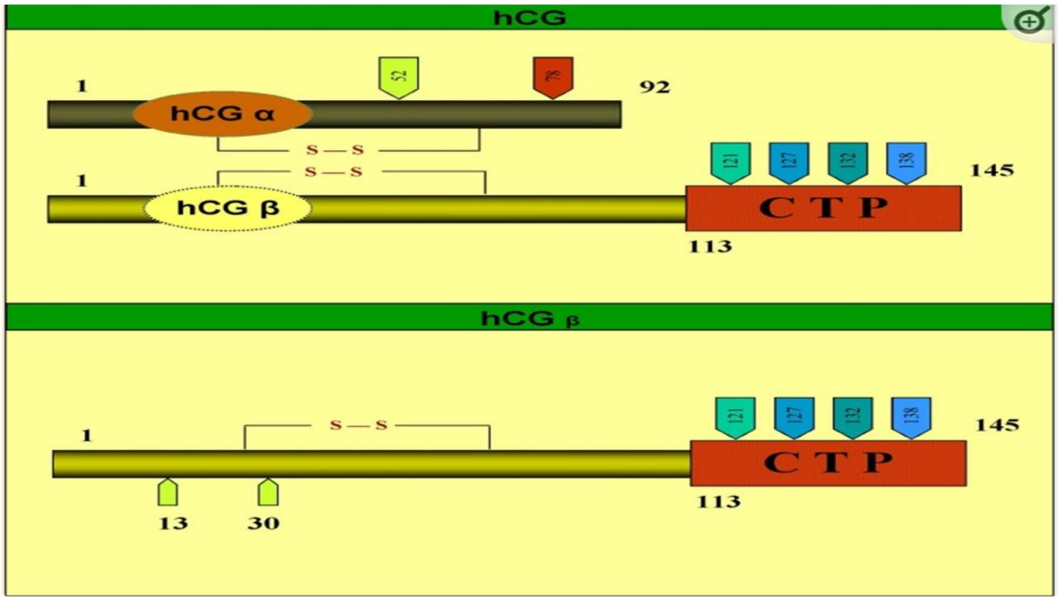
Despite appropriate antenatal care, unforeseen pregnancy complications still arise. Adverse pregnancy outcomes such as preeclampsia, fetal growth restriction and stillbirth may share the common basis of abnormal placentation [1, 2]. Placental development is facilitated by the coordinated and complex processes of vasculogenesis and angiogenesis, both prior to implantation and throughout gestation. Impairment of these processes may result in restricted blood flow to the fetus, increased maternal blood pressure and preterm delivery [1-3]. Biomarkers of angiogenesis are proposed as potential predictors of adverse pregnancy outcomes[4-6]. Angiogenic biomarkers have also been useful to explain the pathogenesis of related disorders of abnormal placentation such as intrauterine growth restriction, intrauterine fetal death, twin-to-twin transfusion syndrome, and fetal hydrops. In short, the discovery and characterization of angiogenic proteins of placental origin have provided clinicians a non invasive blood-based tool to monitor placental function and for early detection of disorders of placentation. Uncovering the mechanisms of altered angiogenic factors in preeclampsia and related disorders of placentation may provide insights into novel preventive and therapeutic options.

In many nations, prenatal trisomy screening based on the evaluation of biochemical markers in maternal serum has become a standard component of Obstetric practice. The first trimester has recently garnered the most attention for prenatal trisomy screening. Only maternal serum free hCG (free hCG) and pregnancy associated plasma protein-A (PAPP-A) have been proven to be useful among the biochemical indicators that have been studied. The purpose of first trimester maternal serum screening programmes is to identify women who will benefit from the testing and those who are

at higher risk of delivering a baby with Down's syndrome, Patau's syndrome, or Edward's syndrome.

Maternal serum free β-hCG hormone:

Only during pregnancy can you find human chorionic gonadotropin, a 39,500-Da glycoprotein hormone, in your blood and urine. Since [7] discovered, that Down's syndrome foetuses had higher levels of maternal serum hCG, most screening programmes now include hCG. hCG mediates a variety of placental, uterine, and foetal activities for the start and continuation of pregnancy. The expansion and differentiation of the endometrium during the mitotic phase, the targeted inhibition of the maternal immune system, the control of uterine shape and gene expression, and the coordination of complex signal transmission between the endometrium are a few examples [8].



Source:[Shiefa et a.,2013]

hCG in Pregnancy:

Recent studies employing placentas and maternal blood from PE patients further suggest that the placenta may have a role in the pathophysiology of PE.In order to implement prompt therapies to lower the occurrence of PE, it would be extremely valuable to reliably predict PE by identifying early proteomic biomarkers of placental malfunction. To date, a number of placental dysfunction biochemical indicators have been employed to assess PE risk factors before the onset of clinical symptoms. Human chorionic gonadotropin (hCG), which has been implicated in PE in some studies, has been suggested as a serum maker for PE screening at 8–14 weeks of gestation [9,10]. The glycoprotein hormone -hCG, which is produced by trophoblast cells, is frequently utilised to identify pregnancies, ectopic pregnancies, and hydatidiform moles. The placenta's specialised cells known as trophoblasts serve a critical role in the exchange of gases and nutrients with the developing embryo. They are also essential for blastocyst attachment, placental implantation, and placental vascularization [11]. Between 10 and 12 weeks during a typical pregnancy, the level of -hCG rises and then steadily declines. Changes in serum -hCG levels may result from abnormal placental development or function [12]. Several investigations have suggested a connection between the first trimester decline in -hCG MoM levels and the emergence of PE [13]; however, some results are contradictory [14,15]. According to several research, individuals with severe PE only had elevated -hCG MoM levels, while those with mild PE experienced no appreciable change [14]. Although some researchers performed a meta-analysis of the predictive usefulness of serum -hCG MoM levels and found that the levels were considerably higher in pregnant women with PE compared to healthy pregnant women, the time of serum -hCG detection was not examined in that study [10] Numerous studies subsequently examined the relationship between blood -hCG MoM

levels and PE, and a number of articles found no statistically significant connection between the two [16,-19].

Maternal serum hCG reaches a peak at 8–10 weeks of pregnancy, drops to reach a plateau at 18–20 weeks, and then stays relatively constant until term. Although -hCG lacks hCG action, several lines of research suggest that it promotes growth. Transforming growth factor-, platelet-derived growth factor-B, and nerve growth factor are thought to limit growth when hCG is present [20]. Injected hCG has a biphasic half-life, with the faster phase's half-life being 5–6 h and the slower phase's half-life being 24-33 h. Injections of pure -hCG into humans have a half-life between 0.7 to 10 hours, which is less time than hCG. However, -hCG really fades more slowly than hCG does after a full-term pregnancy or an abortion. Consequently, the percentage of -hCG in the overall amount of hCG immunoreactivity rises from 0.8 percent at term to 27 percent after three weeks. Trisomy 21 trophoblasts exhibit a significant increase in -hCG mRNA and a less pronounced rise in -hCG mRNA, suggesting that the placenta's enhanced synthesis and release of hCG is one of the factors contributing to the elevated hCG levels in maternal serum [21]. The relative immaturity of the placenta, which continues to emit significant levels of hCG as in the first trimester [22], lends weight to these results.

Chemistry of hCG:

The two noncovalently coupled subunits, and, that make up human chorionic gonadotropin hormone are created by the placental syncytiotrophoblast cells. Three additional glycoprotein hormones, LH, FSH, and TSH, share a single -subunit with 145 amino acids connected by six disulfide bridges and a second -subunit with 92 amino acids linked by five disulfide bridges with hCG. Unique to hCG and setting it apart from other glycoprotein hormones is the -subunit (Fig. 6). It has two side chains that

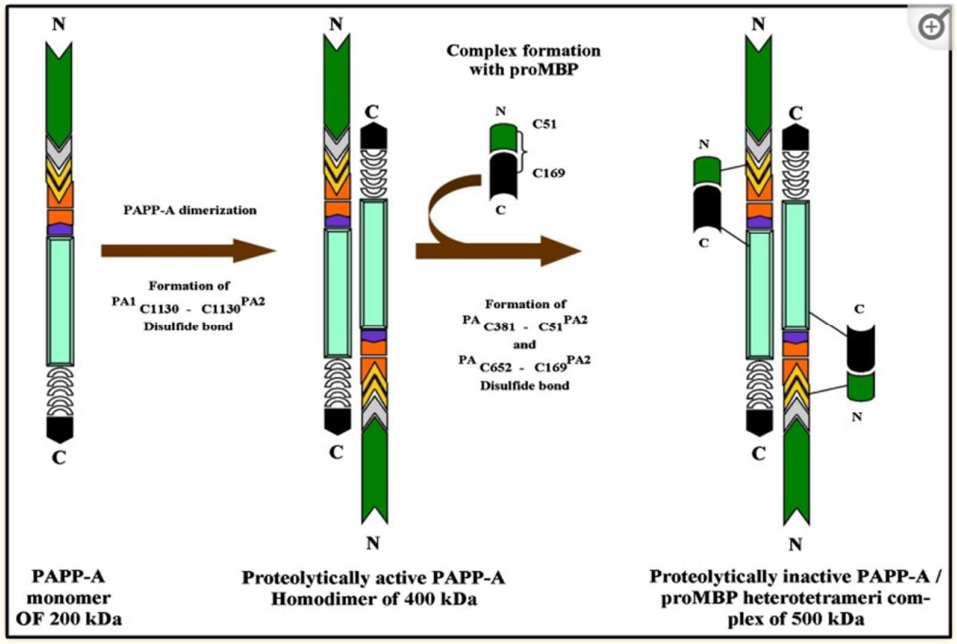
are N-linked oligosaccharides connected to residues 13 and 30 [23]. In the distinctive proline- and serine-rich C-terminal extension (residues 122-145), it also includes four O-linked oligosaccharide units. Two N-linked oligosaccharide side chains are connected to the subunit at amino acid residues 52 and 78 [23]. Maternal serum contains five hCG-related molecules: free -subunit, nicked free subunit, nonnicked hCG, which is the active hormone, and nicked free hCG [24]. The free -subunit can be produced by trophoblast cells directly, by hCG being split into free - and free -subunits, or by neutrophil or macrophage enzymes stealing the hCG molecule [25]. Only 0.3–4 percent of the total hCG is represented by the free -hCG that is present in maternal serum [25]. All four glycoprotein hormones are encoded by the same gene on chromosome 6, which is called the subunit (TSH, LH, FSH and CG). A set of genes on chromosome 19 are responsible for encoding the CG subunit [25]. From each, distinct messenger RNAs (mRNAs) are produced. The components in the maternal circulation are constantly released after combining spontaneously in the rough endoplasmic reticulum.

PAPP-A, was initially identified in the plasma of pregnant women in 1974 and was given that name [26]. Syncytial trophoblasts secrete PAPP-A, also known as pappalysin-1[27]By assisting in the breakdown of insulin-like growth hormone binding proteins (IGFBP), notably IGFBP-4 in plasma, it regulates insulin-like growth factor (IGF) homeostasis by raising the amount of accessible IGF in plasma and its mitogenic effects [28, 29]. Additionally, it affects immunomodulation, matrix mineralization, and angiogenesis [30]. In tests for detecting aneuploidies during the first trimester, PAPP-A is frequently utilised as a blood biomarker. Low levels of PAPP-A in the mother's plasma are also associated with a higher chance of aneuploidy, particularly with trisomy 21. Additionally, it is known that PAPP-A levels are lower in a number of harmful obstetric problems, including preeclampsia, low birth weight, gestational hypertension,

preterm labour, stillbirth, preterm premature rupture of membranes, and placental abruption [31]. In situations where placental growth factor measurements are not available, first trimester maternal plasma PAPP-A in conjunction with the uterine artery pulsatility index (UTPI) is also advised as a secondary screening technique for preeclampsia [32]. Recent research suggests that women with higher first trimester UTPI scores have lower PAPP-A levels [33, 34].

Chemistry of PAPP-A:

A glycoprotein called PAPP-A was first discovered in the plasma of pregnant women [35]. With a molecular weight of 400 kDa, the protein is released as a disulfide-bound homodimer (Fig. 4). Each component is produced from prepro PAPP-A, which has 1,627 residues of protein [36, 37, 38] and is processed into mature PAPP–A, which has 1,547 residues of amino acids and 14 probable N–glycosylation sites. Following intracellular cleavage of the PAPP-A polypeptide's C-terminal side, it is released as an active protease [36].



Source:[Shiefa et al.,2013]

PAPP-A in Pregnancy:

Both PAPP-A and proMBP are highly expressed in the human placenta during pregnancy, however they do so in various cell types. The placental syncytiotrophoblast is where the majority of PAPP-A is made, and extravillous cytotrophoblasts are where all proMBP is made, from which it is released without propeptide cleavage [39, 40]. PAPP-A/proMBP complex formation takes place extracellularly, most likely at the syncytiotrophoblast's surface. With gestational age, PAPP-A concentration in the maternal circulation rises in a healthy pregnancy. During the early trimesters, its concentration rises dramatically with a doubling time of 3–4 days, and it continues to climb up to delivery. The interpretation of a particular measurement is highly reliant on gestational age due to the fast rise in PAPP-A levels during the first trimester. As a result, the unit multiple of median (MoM) is frequently used as a gestational age-dependent expression of PAPP-A concentration. After a typical delivery, PAPP-A has an average half-life of 53 26 h (mean + SD) [41]. PAPP-A concentrations in foetal blood and amniotic fluid are 100- and 1,000-fold lower than those in maternal blood, respectively [42]. During pregnancy, a majority of PAPP-A is covalently linked to the proform of eosinophil major basic protein (proMBP) in a 2:2 complex. ProMBP serves as an endogenous inhibitor of PAPP-(a A's protease inhibitor in vivo) proteolytic activity, whose method of inhibition is currently unclear. Insulin-like growth factor binding proteins (IGFBPs) 4 and 5 are examples of PAPP-A substrates. IGFBPs 4 and 5 function to suppress the biological activities of insulin-like growth factors 1 and 2. PAPP-A functions as an IGFBP "protease," [43] assisting in the release of IGF from these binding proteins so that it may interact with its cell receptor in an autocrine or paracrine way (Fig. 5). The trophoblast invasion, which leads to the early development and vascularization of the placenta and placental bed, is considered to be significantly

influenced by IGF.Figure-5 PAPP-proteolytic A's activity in humans. PAPP-A, IGF, and IGFBP-4 have a relationship. PAPP-A is immobilised next to the IGF receptor by Heparin sulphate substituted receptors at the target cell. IGF is then released from IGFBP-4 by PAPP-A in close proximity to the IGF receptor. Free IGF then binds to the IGF receptor, causing cell growth, trophoblast invasion, and amino acid and glucose transfer into the placenta. ProMBP's b GAG chain attaches to the PAPP-A domain, causing PAPP-A to be released from the cell surface. PAPP-proteolytic A's activity is inhibited by proMBP.

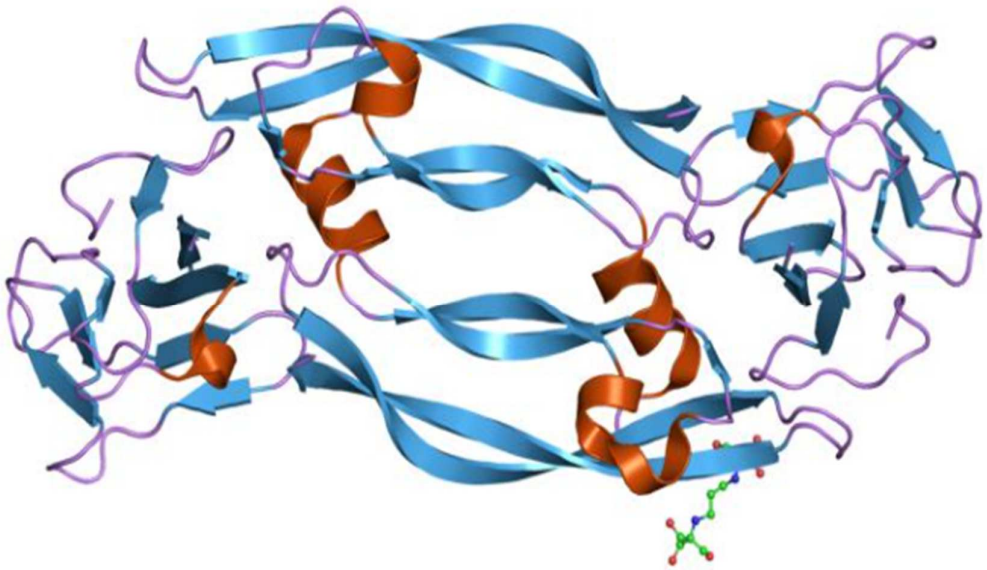
The first trimester screening for foetal Down syndrome is based on the finding that decreased PAPP-A levels are associated with impaired placental function [38, 40]. Non-Down syndrome foetal aneuploidies, as well as trisomy 21, trisomy 18, and trisomy 13, have low first trimester maternal serum levels. Additionally, PAPP-A and birth weight are thought to be positively correlated [44]. The risk of small-for-gestational-age newborns rises when PAPP-A levels drop. In ectopic gravidity, PAPP-A blood levels are reported to be decreased. Preterm birth, intrauterine growth restriction, gestational hypertension, and gestational hypertension with proteinuria are a few of the issues connected to an isolated low PAPP-A level that is not explained [45]. One of the potential reasons of spontaneous miscarriage in these women, according to studies, may be the downregulation of insulin-like growth factor-II availability brought on by a drop in PAPP-A blood levels [46]. Since PAPP-A mRNA expression is not noticeably reduced in Down's syndrome placentas, the drop in maternal serum PAPP-A is not related to any change in placental production of this protein. Additionally, in Down's pregnancies, the relationship between blood and tissue expression levels of PAPP-A is lost. These findings imply that the reduction in maternal serum PAPP-A is posttranslational and may result from a change in the mechanisms that release the

placenta or from a change in the stability of the released protein [47]. In twin pregnancies, PAPP-A levels are observed to be considerably greater. PAPP-A readings in twins are on average 1.86 times higher than those in singletons. Elevated PAPP-A in the first trimester has not been associated with any noteworthy obstetrical outcomes [45].

PLGF: Placental Growth Factor

The vascular endothelial growth factor family includes the dimeric glycoprotein known as placental growth factor (PlGF). It was initially discovered to be expressed mostly by trophoblast cells, placental villi, and human umbilical vein endothelial cells during pregnancy in 1991. [48] PlGF has powerful proangiogenic actions that lead to early placental vascular development, according to studies [49, 50, 51, and 52]. A protein called PlGF contributes to placental angiogenesis (the development of new blood vessels). PlGF levels might be excessively low in pre-eclampsia. When PlGF levels do not increase during pregnancy, there may be placental malfunction since PlGF levels normally rise and peak around 26 to 30 weeks of pregnancy [53]. The limit of detection for the test is 12 pg/mL, while a normal placental growth factor was defined as >100 pg/mL. The most recent advancement in prenatal diagnostics is the use of placenta growth factor (PLGF) testing to identify pre-eclampsia, a hypertension condition that affects 5 to 8% of pregnancies. Pre-eclampsia can be identified early thanks to PLGF testing, giving both the mother and the unborn child more choices for monitoring and treatment [53]. The PGF gene in humans encodes the protein known as placental growth factor [54]. The VEGF (vascular endothelial growth factor) subfamily includes placental growth factor (PGF), a crucial molecule in angiogenesis and vasculogenesis, particularly during development. During pregnancy, the placental trophoblast is the major source of PGF. The villous trophoblast is one of the numerous different tissues that express PGF [55]. A member of the vascular endothelial growth factor (VEGF)

family, the placental growth factor (PGF) gene codes for proteins. Only the placenta and human umbilical vein endothelial cells (HUVE) express the PGF gene. PGF eventually has a connection to angiogenesis. PGF specifically affects the development and differentiation of trophoblasts. The uterine wall and maternal spiral arteries are invaded by trophoblast cells, more especially extravillous trophoblast cells. For the growing foetus, the extravillous trophoblast cells create a bigger diameter blood artery that is not dependent on maternal vasoconstriction. For improved blood flow and decreased resistance, this is crucial [56]. Because the foetus needs more blood as the pregnancy progresses, proper placental blood vessel growth is essential. PGF is also minimally expressed in other organs such as the heart, lung, thyroid, and skeletal muscle under typical physiological circumstances.



Structure of PLGF

This protein comes in three different isoforms, PGF-1, PGF-2, and PGF-3. PGF-2 is only present in the early placenta up to the eighth week of development, whereas PGF-1 is only present in the colon and breast carcinomas. The only isoform that can bind to heparin is PGF-2. PGF-3 is mostly present in placental tissues [57, 58].

PLGF in Pregnancy:

The expression of placental growth factor in human atherosclerotic lesions is linked to plaque inflammation and neovascularization [59, 60]. Women with preeclampsia have changed levels of PGF and sFlt-1 (soluble fms-like tyrosine kinase-1, also known as soluble VEGF receptor-1). According to studies, women who present with preeclampsia had lower PGF levels and higher maternal blood levels of sFlt-1 in both early-onset and late-onset preeclampsia. In addition, when compared to women with straightforward pregnancies, preeclampsia patients' placental sFlt-1 levels were considerably higher and their PGF levels were lower. This implies that the maternal serum alterations are reflected in the sFlt-1 and PGF placental concentrations. This is in line with the idea that throughout pregnancy, the placenta serves as the primary source of sFlt-1 and PGF. PGF may serve as a biomarker for preeclampsia, a condition in which the placental blood vessels become too narrow and cause high blood pressure. Extravillous trophoblast cells enter maternal arteries, as was previously indicated. Improper differentiation may cause these arteries to hypo-invade and subsequently fail to expand adequately. Low levels of PGF have been observed in preeclampsia patients who were detected later in pregnancy, according to studies [61].

Insufficient blood flow to the placenta causes placental insufficiency, also known as uteroplacental vascular insufficiency. The PGF gene, as well as its GPCR and ERK signalling pathways, are altered in this condition .The expression of the PGF and PGF receptor mRNAs are altered, which prevents the placental vasculature from

developing normally [62] Another condition linked to the PGF gene is twin-to-twin transfusion syndrome. This unusual condition, in which blood from one sibling is transmitted to the other, typically affects identical twins. Usually, the twin whose blood is being transferred is smaller, anaemic, and at higher risk for heart failure than the other twin, who is born bigger, with too much blood. The TGF-Beta and AKT signalling pathways are the main PGF gene pathways that are impacted [63].

Serum analytes with adverse pregnancy outcomes:

Chromosomal anomalies Trisomies:

A significant risk factor for perinatal morbidity and mortality during pregnancy is incomplete foetal development. Early identification of foetuses at risk for growth limitation allows for better management of optimization, which has been demonstrated to lower the likelihood of negative foetal outcomes [64]. In many nations, prenatal care now includes prenatal screening for trisomy problems based on examination of biochemical markers in the mother's serum[65].The first trimester has become the preferred time to screen for chromosomal trisomies during pregnancy. Only maternal serum free hCG and pregnancy-associated plasma protein-A (PAPP-A) have been found to be useful among the biochemical indicators investigated. Currently, materials such as amniotic fluid, foetal blood, and chorionic villi are used to identify chromosomal abnormalities [66]. When there is a disturbance in the number or structure of the chromosomes, it is called a chromosomal abnormality. As a matter of fact, the chromosomal changes detected during prenatal testing included autosomal or sex chromosome aneuploidy, triploidy, balanced or unbalanced structural rearrangements, deletions and duplications, and mosaicism[66]. It is well known that these alterations can cause disturbances in the quantity or organisation of the genetic material present in the

cells, which can retard growth or affect the functioning of various bodily functions, including infertility, spontaneous abortions, stillbirths, congenital anomalies, mental retardation, and the pathogenesis of cancer. However, the majority of foetuses with chromosomal abnormalities, particularly numerical anomalies, do not often survive, while some may be born with these abnormalities [67]. According to studies, trisomies 21, 13, and 18 are all linked to older mothers, higher foetal nuchal translucency (NT), and lower PAPP-A levels. However, in trisomy 21, free hCG levels rise in the blood, but they fall in trisomies 18 and 13[65].

Additionally, PAPP-A and hCG levels are independent determinants in the trisomy 21 diagnosis; if these two markers are combined with NT ultrasonography, the conditions are ideal for prenatal trisomy 21 diagnosis[68]. According to some recent studies on prenatal screening, testing the double marker during first trimester screening can help identify 90% of people who are at risk for Down syndrome and 94% of people who are at risk for other chromosomal defects like Patau syndrome, Edward syndrome, triploidy, and Turner syndrome [65]. Maternal age, prior family history, biochemical analyses of the mother's blood, and foetal ultrasound indicators can all be used to determine the risk of foetal aneuploidy[69]. Women at high risk can get genetic counselling, genetic testing, and aftercare [70]. Despite the fact that chromosomal abnormalities have a substantial impact on foetal outcomes, the combined research of these chromosomal numerical and structural changes has not been carried out.

The median and mean values of free beta-hCG in pregnancies with Down syndrome were 2.56 and 2.01 MoM, respectively, and were significantly different from pregnancies without the condition in a different study by Hsu et al. to assess high levels of maternal serum free -hCG in pregnancies with the condition[71] .A substantial correlation between free -hCG concentrations equivalent to or above the cutoff of 1.5

MoM and chromosomal abnormalities was seen in a study by [68] A substantial correlation between NT readings and chromosomal anomalies was discovered in a study, another Polish study by that evaluated with a median of 1.03 and 2.67 mm, respectively [68-72]. Saw the completion of the clinical value of ultrasonography (NT) and biochemical indicators (-hCG, PAPP-A) in the first trimester of pregnancy for 251 pregnant women. Amniocentesis was done for trisomy 21 in high-risk pregnancies (risk more than 1: 300), and the results showed that 217 patients had normal chromosomal cultures and 34 patients had trisomy 21. Only 52.94% of those with trisomy 21 had 0.001 PAPP-A 0.5 and 85% had increased free hCG levels over 1.5 MoM. Additionally, this study has demonstrated that not all Down syndrome foetuses have increased NT levels [68] .In a separate study, [73], evaluated the genetic amniocentesis indices in 632 pregnant women in Poland. Mothers who underwent an amniocentesis on average were 34 years old; 52.1% of patients were over 35 and 47.9% were under 35. Amniocentesis was performed on moms under the age of 35 due to abnormal ultrasound results and first trimester screening. The findings showed that trisomy 13 or any other aberrant karyotype was seen in both age groups, along with 74 chromosomal abnormalities. Nine patients (1.42%) experienced complications from amniocentesis, including intrauterine death or abortion.

Fetal growth restriction:

Small for gestational age (SGA) and intrauterine growth restriction (IUGR) have been used interchangeably up until recently [74] due to inconsistent and unclear nomenclature. However, it is difficult to distinguish between foetuses that are little for pathological reasons and those that are naturally small but healthy when an estimated foetal weight is below the tenth percentile. The PORTO research [75] assessed tighter standards for the designation of IUGR in an effort to distinguish between pathologically

tiny and constitutionally small foetuses. When compared to pregnancies with normal umbilical artery (UA) Doppler and estimated foetal birth weight between the 3rd and 10th percentiles, the authors discovered that those pregnancies were more likely to have an unfavourable pregnancy outcome or NICU hospitalizations. Studies of serum screening indicators often define IUGR using birth weight rather than estimated foetal weight. Extreme analyte readings seem to be more frequently linked to more extreme low birth weight. [76] have compiled the research on PAPP-connection A's to IUGR,[77]assessed the efficiency of the serum markers in detecting IUGR, which was defined as being below the tenth percentile or below the fifth percentile for birth weight [77, 78], as a follow-up to the FASTER experiment. Table demonstrates that more pregnancies with birth weights below the fifth percentile than the tenth percentile are detected by PAPP-A, AFP, hCG, uE3, and inhibin. The difference between the two percentile cut-offs may not seem as large because the below the tenth percentile group includes all pregnancies below the fifth percentile. The detection rates of the serum markers are noticeably higher for the more extreme low birth weight group, as seen by a comparison of those pregnancies with birth weights below the fifth percentile with those with birth weights between the sixth and tenth percentiles

In another study the pattern shown with the other serum markers held true for second trimester free hCG as well.The connection between low second trimester free hCG (0.5 MoM) and birth weight below the third percentile was shown to be stronger, according to the authors (relative risk = 2.30), than it was for birth weight below the tenth percentile (relative risk of 1.98).[79]

Criteria for IUGR included estimated foetal weight below the tenth percentile.[80] The authors also divided the IUGR cases into groups based on umbilical artery (UA) Doppler. Pregnancies with IUGR and absent reverse end diastolic velocity

(AREDV) had serum marker levels that differed more significantly from those with IUGR and normal UA Doppler compared to pregnancies with normal growth. Additionally, 73% of the IUGR/AREDV patients were identified with a 5% false positive rate utilising a combination of serum markers. 91% of IUGR/AREDV cases were identified by incorporating maternal variables (history of chronic hypertension, lupus, pregestational diabetes, and thrombophilia) in addition to serum indicators.

Gestational Diabetes Mellitus:

The most prevalent metabolic complication of pregnancy is gestational diabetes mellitus (GDM), which is characterised by poor glucose tolerance with start or first detection during pregnancy and is linked to significant maternal and newborn morbidities [81,-83]. According to estimates, the prevalence of GDM ranges from 3–7% in the United States, with rates varied by racial/ethnic origin [84]. Increases in type 2 diabetes and obesity rates have been seen globally over the past ten years, and these trends appear to be correlated with increased GDM prevalence rates [85]. The greatest predictor of GDM among the several risk variables discovered is a history of GDM [86]. Glucose testing is typically done between 24-28 weeks of gestation to diagnose GDM, [86, 87] when a mother's insulin resistance rises in order to protect nutrition for the developing fetus's rapid growth [88]. However, there is evidence that suggests that women with GDM may show metabolic changes earlier in pregnancy given the association between elevated first trimester fasting glucose levels within the nondiabetic range and increased risk of GDM diagnosis later in pregnancy and adverse pregnancy outcomes [89, 90, 91]. An earlier diagnosis and treatment of GDM, a better knowledge of the pathophysiology of GDM, and more effective targeted intervention may all be made possible by measuring first trimester biomarkers indicative of these metabolic abnormalities [89, 91, 92]. When detected at abnormal levels, common prenatal

screening markers have been linked to a number of negative perinatal and delivery outcomes [93, 94, 95, and 96]. Reduced levels of first trimester pregnancy associated plasma protein-A (PAPP-A) and free human chorionic gonadotropin (free hCG) are risk factors for preterm delivery, preeclampsia, and spontaneous miscarriage in the absence of aneuploidy and anatomical defects. The degree of glycemic control within a person may be indicated by PAPP-A, according to the inverse association between haemoglobin A1c and PAPP-A (a marker used to quantify glucose maintenance over a three-month period) [97, 98]. PAPP-A and free hCG tests may be helpful for detecting GDM in addition to chromosomal abnormalities because of their putative roles in placental pathology and carbohydrate homeostasis [95]. Results from the several studies that have looked at the connection between first trimester PAPP-A, free hCG levels, and GDM development have been contradictory. If first trimester measurements of prenatal screening biomarkers differ in women with and without GDM, and whether these early patterns could help predict GDM, are still hotly contested issues.

Early-pregnancy selective screening [91, 99, and 100] was used in three studies to identify women at high risk for developing GDM (such as those with a family history of diabetes, a high BMI, or prior GDM) earlier in pregnancy in addition to universal screening later in pregnancy. These women could have had GDM identified based on the results of their glucose tests prior to the widespread adoption of regular testing at 24-28 weeks of gestation. We performed a post-hoc stratified analysis in which pooled MDs were calculated separately for studies reporting biomarker MoM measurements for women who were diagnosed with GDM early and later in pregnancy to ascertain whether the MDs for first trimester PAPP-A and free -hCG differed depending on timing of GDM diagnosis. For early and late GDM diagnostic groups, [99, 100] showed independent PAPP-A MoM findings. In these studies, the PAPP-A MoM measurements

for those who were diagnosed with GDM later in pregnancy were pooled with all other studies for each biomarker, and the PAPP-A MoM levels reported for those who were diagnosed with GDM early in pregnancy were computed using pooled MDs. In the other study, [91], only the combined GDM group (containing those identified early and late in pregnancy) and the early GDM diagnostic group were given different PAPP-A MoM levels. Consequently, this study was not included in the pooled estimate for late GDM diagnosis but was included in the pooled MD calculation for early GDM diagnosis. We were unable to conduct a stratified analysis to see if free hCG varied depending on when GDM was diagnosed because [99] 's study was the only one to report distinct free hCG MoM values for women who were diagnosed with GDM early and later in pregnancy.

Low birth weight:

Low birth weight (LBW), which is a strong predictor of perinatal illness and mortality, is a huge public health burden. By enhancing mother care during pregnancy and using interventions that target the population most at risk of foetal development abnormalities, nations could lower their neonatal and infant mortality rates. The efficacy of new approaches to LBW prevention hinges on early detection, though. As part of a panel of tests, biochemical markers are frequently employed in the first trimester of pregnancy to screen for foetal chromosomal disorders. Poor perinatal outcomes such preeclampsia, preterm birth, and foetal growth retardation (FGR) have been linked to abnormal analyte levels, such as lower pregnancy-associated placental protein-A (PAPP-A) levels [101, 102, 103]. PAPP-A, which functions as a protease on insulin-like growth factor binding proteins, is abundantly expressed in the syncytiotrophoblasts of the placenta and is thought to enhance the stimulatory effects of placental insulin-like growth factors [104].

Low PAPP-A levels (0.4 multiples of median [MoM]) in the first trimester are linked to a higher incidence of poor perinatal outcomes, according to research by the Genetics Committee of the Society of Obstetricians and Gynecologists of Canada [105]. Biochemical screening at the first trimester using multiple markers for predicting FGR and LBW newborns has been advocated in recent years. None of these markers, however, are reliable enough for use to be advised [106]. Placental growth factor (PLGF), soluble FMS-like tyrosine kinase-1, soluble endoglin, vascular endothelial growth factor, or angiopoietin-2 have all been mentioned in several studies as angiogenesis-related biomarkers. [107-109] Overall, these biochemical parameters had low predictive power.

Missed abortion:

Miscarriage, also known as spontaneous abortion, is a common pregnancy complication, but there are still no indicators that can be used to predict it in people who are asymptomatic before it happens. A missed abortion (MA) is a particular kind of miscarriage that occurs when the retained intrauterine products of conception are not spontaneously expelled after the embryonic or foetal death. Although it can go undetected in some women, MA affects 8 to 20% of clinically diagnosed pregnancies [110, 111]. Maternal morbidity brought on by the MA may include endometrial damage, coagulation issues, depression, and anxiety. Several etiologic factors have been identified for MA at this time, including parental chromosomal abnormalities, immunological factors, endocrine disorders, uterine abnormalities, hereditary thrombophilia, infections, and environmental factors; these conditions may exist in up to 50% of all women who experience miscarriages [112].

The ability of various biochemical indicators to predict the outcome of impending miscarriage (i.e., identify people at risk of eventual miscarriage) has been

investigated, but the results have been inconsistent. Serum hCG, progesterone, estradiol, cancer antigen 125 (CA 125), human placental lactogen (HPL), alpha feto-protein (AFP), inhibin A, follistatin, and activin A are a few of the biochemical markers that are frequently examined [113-118].

hCG, the earliest detectable marker, is still the cornerstone of contemporary pregnancy identification even though a number of pregnancy hormones have been suggested as viable diagnostic markers for early pregnancy. hCG can be found as soon as 8 to 11 days after ovulation, or right after implantation [119]. Blood levels of hCG rise quickly, reaching a peak of 50 000–100 000 IU/ml at around 8–10 weeks of pregnancy. Quantitative hCG measurements are an important tool in the clinical assessment of early pregnancy problems due to the consistency of this pattern [120]. A glycoprotein called hCG has a non-specific subunit that is comparable to LH and FSH and a subunit that is specific to it [121]. Therefore, some research [122, 123, 116, 124, 118] have employed the hCG subunit for early pregnancy prognosis and others have used whole hCG for this purpose [113,125, 126]. However, it has been established that during the first half of pregnancy, measuring the free hCG subunit has no therapeutic advantage over measuring the intact hCG [127]. The first study of PAPP-A in the prediction of pregnancy outcome in women presenting with a threatening miscarriage was conducted by another study [128]. They came to the conclusion that PAPP-A testing could help distinguish between pregnancies that will have a normal result and those that won't [128]. While the foetus was still living, the aberrant levels were frequently noticed weeks before the clinical course of spontaneous miscarriage [128,129] found that early vaginal bleeding in pregnancy was associated with significantly lower blood levels of PAPP-A compared to other pregnant women, but they were unable to distinguish between those who later miscarried and those who carried the pregnancy to term. Inability to distinguish

between normal and abnormal pregnancies at very early gestation (6-7 weeks) [130, 129]; Ethnic variation in serum concentrations are just a few of the limitations of PAPP-A as a biochemical marker for the prediction of early pregnancy outcomes [131,132].

Oligohydramnios:

Reduced amniotic fluid volume (AFV) for gestational age is referred to as oligohydramnios. The amount of amniotic fluid varies during the course of pregnancy, rising linearly up until 34 to 36 weeks, at which point it levels off (at about 400 mL) and stays stable until term [133]. After 40 weeks of gestation, the AFV starts to gradually decline, which results in post-term gestations with less volume. This pattern enables clinical evaluation of AFV utilising fundal height measures and ultrasound analysis during pregnancy [134]. 4.4% of term pregnancy complications are caused by oligohydramnios. In preterm pregnancies, oligohydramnios occurs less frequently than 1% of the time [135].

The findings of and from Australia and Italy, respectively, were at odds with those of the past investigation and showed significantly lower PAPP-A and -hCG levels in abortions.[136,137]

Placental abruption:

Placental abruption is the early detachment of the placenta from the uterine lining before the second stage of labour is fully completed. It is one of the reasons why women bleed in the second half of their pregnancies. A critical but relatively uncommon pregnancy condition called placental abruption puts the health of both mother and foetus in jeopardy. Abruptio placentae is another name for placental abruption [138,139].

A potentially fatal obstetric condition brought on by improper placental implantation is placenta accreta. With placenta previa and the number of prior caesarean deliveries, the risk of placenta accreta rises noticeably [140]. Although they have often only been used in high-risk pregnancies, ultrasonography and MRI are currently the best methods for diagnosing placenta accreta [141] Therefore, enhancing the ability to employ biomarkers to selectively identify foetuses at high risk for placenta accreta should aid in improving the effectiveness of these imaging methods [141-144]. According to Desai et al., PAPP-A is not linked to placenta previa or previous caesarean sections, but high levels of PAPP-A are linked to an increased risk of placenta accreta [145]. Likewise, demonstrated that PAPP-A was not connected to previa.[146] This suggests that PAPP-A may be used in conjunction with clinical placenta previa evaluation and caesarean section history to help identify patients who are at high risk for placenta accreta. [145] discovered using a continuous model that a PAPP-A of 2 MoM was linked to a 2-fold increase in risk and a PAPP-A of 3 MoM was linked to a 4-fold increase in risk. A PAPP-A of 0.5, on the other hand, was linked to a 5-fold reduction in risk. These risk changes correspond, respectively, to the risk change of one or two extra caesarean deliveries or two less caesarean deliveries.

Preeclampsia:

PAPP-A and free human chorionic gonadotropin (free hCG) from the first trimester have both been studied as potential indicators of preeclampsia [76, 146-150]. Preeclampsia was generally not associated with free hCG in these trials, but it was associated with low PAPP-A, which led to detection rates of 8%-15% at a 5% false positive rate. A systematic meta-analysis of cohort studies examining second trimester indicators and preeclampsia was carried out by [151]. The threshold utilised to identify people at high risk as well as the effectiveness of screening varied significantly between

research. The most effective thresholds were 2.0 multiples of the median (MoM) for alpha-fetoprotein (AFP), which produced a positive likelihood ratio (LR) of 2.36 and a negative likelihood ratio (LR) of 0.96; 2.0 MoM for hCG; 0.5 MoM for unconjugated estriol (uE3); and 2.79 MoM for inhibin (dimeric inhibin A), which produced a positive LR of 19.5 and a negative LR. In a similar manner, [152] discovered that inhibin and preeclampsia were significantly associated, whereas AFP and uE3 were not. The detection rate in a three marker technique using PAPP-A, inhibin, and hCG was 40% with a 5% false positive rate. Preeclampsia and inhibin were also linked in the FASTER experiment [153], with a detection rate of 17% and a false positive rate of 3%, however additional markers did not help with identification.

Even though these instances make up just around 10% of all preeclampsia cases, nearly 70% of perinatal deaths and 60% of severe neonatal morbidity cases in preeclampsia pregnancies happen in early onset (34 weeks) preeclampsia [154]. As a result, with successful screening programmes for the early-onset type of the disease, perinatal morbidity and mortality can be significantly reduced. [158] discovered that early onset preeclampsia (34 weeks) was more strongly associated with higher levels of inhibin, hCG, and AFP than was late onset preeclampsia. These markers could individually detect 22%–28% of preeclampsia at an approximate 5% false positive rate. PAPP-A may function more effectively as a marker for early-onset preeclampsia than for late-onset preeclampsia, according to other research [156, 157, 158].

According to Kang et al., [152], inhibin was more significantly linked to early-onset preeclampsia than late-onset preeclampsia. To detect 18% of early onset (32 weeks) preeclampsia, established a multiple marker method using first trimester PAPP-A and second trimester AFP, hCG, and uE3. [159] The likelihood of detection could increase greatly if inhibin and maternal factors (such as prior history or family history

of preeclampsia, parity, and chronic hypertension) were included in such a technique. Recent research has shown that over 90% of early-onset preeclampsia pregnancies can be detected in the first trimester using a direct screen that includes maternal characteristics, PAPP-A, placental growth factor (PlGF), uterine artery doppler pulsatility index, and mean arterial pressure [160-162]. Coincidentally, PlGF and AFP, when paired with PAPP-A and free hCG, have been shown to be successful in first trimester Down syndrome screening [163-165]. An enlarged Down syndrome screening protocol may therefore enable the early detection of preeclampsia.

Preterm delivery:

Preterm birth occurs when a baby is delivered too soon, before the full 37 weeks of pregnancy have passed. One in ten babies born in the US in 2021 suffered from preterm birth. In 2021, the preterm birth rate increased by 4%, from 10.1% to 10.5%. However, there are still racial and ethnic disparities in preterm birth rates. Preterm birth rates for African-American women (14.8%) in 2021 were almost 50% higher than those among white or Hispanic women (9.5% and 10.2%, respectively).

As many as 2.8% of singleton births in 2012 were early preterm (34 weeks), making up 9.9% of all preterm births (37 weeks) [166]. A third of preterm births can be prevented by identifying pregnant women at high risk for preterm birth based on short cervixes [167]. Recent randomised control trials have shown that cervical cerclage [168] or progesterone therapy [169, 170, 167] can considerably lower premature birth. The addition of biochemical and other biophysicial markers may result in a decrease in the frequency of preterm birth and, consequently, a decrease in perinatal morbidity and mortality because only one-third of early preterm births (births before 34 weeks) have short cervixes below 1.5 cm. The relationship between PAPP-A and preterm delivery has been examined in numerous studies. PAPP-A is more closely linked to early

preterm birth than to preterm birth, as shown in Table 2. Early preterm birth was detected in 9%-15% of instances with a 5% false positive rate compared to preterm delivery in 5%-9% of cases [147, 148, 150, 153, 171, 172]. For early preterm birth, the positive probability ratio of PAPP-A below the fifth percentile ranged from 2 to 3. In contrast to other research, [173] examined PAPP-A at a 10% false positive rate and found that the preterm birth group had higher detection (24%) than the early preterm birth group (20%). The detection rate, however, was the same in both groups (38%) when maternal factors (African American race, Body Mass Index, Prior Preterm Birth, History of Chronic Hypertension, History of Pre-Gestational Diabetes) were taken into account.

The relationship between second trimester indicators and early preterm delivery (32 weeks) was examined by [153]. For AFP, hCG, uE3, and inhibin, the detection (false positive rates) were 9% (5%), 11% (1.7%), 17% (6.0%), and 22% (3.1%), respectively. The sensitivity was 16% for any pair of abnormal analytes, with a false positive rate of 2.9%, a positive likelihood ratio of 5.5, and a negative likelihood ratio of 0.87 for either zero or one abnormal marker. The strongest correlation between early preterm delivery and high AFP and inhibin was observed (Odds ratio = 20.37). Additionally, likelihood ratios can be created using information on the prevalence of early preterm birth and short cervix. The chance ratio for birth before 34 weeks for cervix lengths of 1.5 cm, 1.6–2.5 cm, and >2.5 cm is 24.3, 2.5, and 0.9, respectively, according to the condensed data from [174]. In a different study, [175] calculated the chance ratio for birth before 32 weeks to be 51.52, 2.66, 0.71, 0.48, 0.24, and 0.01 for cervix lengths of 1 cm, 1-2 cm, 3-4 cm, 4-5 cm, and 5-6 cm, respectively . These outcomes substantially concur with [174] findings. Pregnancies with negative fibronectin, a long cervical length, and no history of preterm delivery have a 1% risk of preterm birth, while those with positive fibronectin, a short cervical length, and a history of preterm birth have a 64%

risk [176, 177]. The data from these studies can be updated by using early biochemical marker likelihood ratios, even though this is not currently common practise, to further narrow risks and improve early preterm birth detection.

Previous studies:

[Kagan et al.,2008][178] conducted a There were 96 803 pregnancies with normal chromosomes and 491 trisomy 21 instances. PAPP-A was 57 % higher in women of Afro-Caribbean origin, 3 % higher in South Asians, 9 % higher in East Asians, 2 % higher in nulliparous women, 17 % lower in smokers, and % lower in those conceiving through in-vitro fertilization compared to values in Caucasian women who were parous, non-smokers, and had spontaneous conception (IVF). Free hCG levels were 12% higher in Afro-Caribbean women, 9% lower in South Asian women, 8% higher in East Asian women, 2% higher in nulliparous women, 4% lower in smokers, and 9% higher in IVF recipients. The predicted detection rate for trisomy 21 by maternal age, serum free hCG, and PAPP-A was 65%, with a false-positive rate of 5%. It is crucial to account for maternal and pregnancy factors when adjusting the observed levels of free hCG and PAPP-A during first-trimester biochemical screening for trisomy 21. ISUOG has 2008 copyright. John Wiley & Sons, Ltd. is the publisher.

Similarly by **[Nicolaides et al.,2011][179],** between 12 weeks (when first-trimester screening is done) and term, the incidence of foetal mortality ranges from around 30% for trisomy 21 to 80% for trisomies 18 and 13. (Snijders et al., 1994, 1995, 1999; Morris et al., 1999; Hecht and Hook, 1994; Halliday et al., 1995; Contrarily, only 1 to 2 percent of euploid foetuses die during pregnancy, and as a result, the risk for trisomies diminishes with gestation. For a woman who is 20 years old and 12 weeks pregnant, the risks for foetal trisomies 21, 18, and 13 are approximately 1 in 1000, 1 in 2500, and 1 in 8000, respectively. The risks of this woman giving birth to an affected child at term

are approximately 1 in 1500, 1 in 18 000, and 1 in 42 000, respectively. For a woman 35 years old at 12 weeks of pregnancy, the odds for each aneuploidy are around 1 in 250, 1 in 600, and 1 in 1800, while the risks of delivering an afflicted baby at term are 1 in 350, 1 in 4000, and 1 in 10,000.

[Di Lorenzo et al.,2012][180] evaluated, 46 (2.17%) of the 2118 women acquired GH, and 25 (1.18%) were identified as having PE, including 12 (0.57%) with early-onset and 13 (0.61%) with late-onset PE. Serum PlGF, free hCG, and chronic hypertension, respectively, indicated 67 and 75% of women who experienced early-onset PE with a fixed FPR of 10 and 5%. The uterine artery Doppler pulsatility index (UtA PI) in conjunction with PlGF and chronic hypertension achieved a sensitivity of 60% for a 20% FPR in the model for the prediction of overall PE. First trimester maternal blood biomarkers (free -hCG and PlGF) were combined with maternal features to produce a potential early-onset PE screening tool. UtA PI showed proven to be statistically significant in the overall PE model, however it did not increase the detection rate.

Whereas **[Saffer et a.,2013][181],** 1366 evaluable samples were obtained from 247 patients (242, 238, 226, 223, 222, and 215 samples in each GA period, corresponding to 20–24–29–32–35–37–40 weeks). In each individual GA period, the 5th percentile of PlGF was 76.4, 141.1, 139.3, 65.5, 31.7, and 23.4pg/mL. The parameters of the PlGF distribution are roughly log normal and continually change as a function of GA. Maternal age, race/ethnicity, parity, and maximal systolic blood pressure all have a marginal impact on plGF distribution (taken between weeks 20 and 24). Statistically significant as they were, these variables did not alter PlGF levels by more than 15%.

In another study **[Shiefa et al., 2013][182],** said a noninvasive alternative for the early identification of aneuploidy pregnancies is the first trimester screening programme. Serum free human chorionic gonadotrophin (free-hCG) and pregnancy associated

plasma protein A (PAPP-A), maternal age, and foetal nuchal translucency (NT) thickness at 11 + 0-13 + 6 weeks of gestation are used in conjunction for this screening. Early diagnosis of trisomies 21, 18, and 13 is a benefit of screening. The relative frequency of trisomies 18 and 13 to trisomy 21 is determined to be one to three and one to seven, respectively, at 11 + 0-13 + 6 weeks. All three trisomies are linked to older mothers, higher foetal NT, and lower PAPP-A, however trisomy 21 has higher serum free hCG levels than trisomies 18 and 13, whereas trisomies 18 and 13 have lower serum free hCG levels.

[Yu et al., 2017][183], Concluded that, the mean PAPP-A and ADAM12 were lower (P 0.001, P 0.05) in pregnancies complicated by preeclampsia (n = 462) and FGR (n = 350) compared to gestational age-matched controls (n = 200). Preeclampsia and FGR groups had greater median uterine artery mean PIs (P 0.001). The median free -hCG and PP13, however, did not vary substantially from baseline (P > 0.05). Assuming a fixed false positive rate (FPR) of 10%, the detection rates for a combination of PAPP-A, ADAM12, and UAD in preeclampsia and FGR screening were 72% and 68%, respectively.

Similarly by **[Sung et al.,2017][184],** This prospective, observational study comprised 175 pregnant women, and of these, delivery data were obtained from the medical records of 155 women, including 4 twin pregnancies, due to participant withdrawal or loss to follow-up. The PlGF and PAPP-A levels at 11 to 13 gestational weeks were measured, along with the women's maternal histories. The systolic/diastolic ratio of the maternal uterine artery was assessed during the second trimester. PlGF and PAPP-A multiples of the median (MoM) were calculated, and the correlations between these values and the risk variables for SGA and PE were examined. To test if PlGF and PAPP-A are helpful indicators for foretelling SGA newborns, logistic regression analysis was

utilised. Mothers with advanced maternal age, multipara women, and women with gestational diabetes had considerably lower PAPP-A MoM levels than their peers. Women carrying twins had greater PlGF and PAPP-A MoM levels than did those carrying singletons. The uterine artery systolic/diastolic ratio in the second trimester was significantly correlated with the maternal serum PAPP-A MoM level in the first trimester. Low levels of PlGF and PAPP-A MoM were identified as predictors of SGA babies by the results of logistic regression analysis (odds ratio, 0.143; 95 % confidence interval, 0.025 to 0.806; odds ratio, 0.191; 95 %confidence interval, 0.051 to 0.718, respectively).PlGF and PAPP-A have the potential to be helpful first-trimester indicators for SGA babies and various obstetric hypertensive diseases.

In study including **[Pakniat et al.,2019][185],** 994 singleton pregnant women aged 18 to 35 were referred for first-trimester screening tests, such as PAPP-A and -hCG, at the ages of 6 days and 11 to 13 weeks, and were then monitored during the remainder of their pregnancies. Serum levels of PAPP-A, -hCG, and negative pregnancy outcomes were measured and examined. By determining the receiver operating characteristic curve's area under the curve, the test's sensitivity and specificity were evaluated (ROC). PAPP-A and hCG had mean serum concentrations of 1.10 0.69 and 1.09 0.8 MoM, respectively. Regardless of percentile, pregnancy-associated plasma protein A shown a strong correlation with the prevalence of preeclampsia, preterm delivery, and foetal low birth weight (p 0.001 for each). However, there was no statistically significant link between PAPP-A and abortion ($p > 0.05$). According to ROC, the findings showed a significant association between PAPP-A and the likelihood of preeclampsia, preterm delivery, and low birth weight foetuses (p 0.001). However, there was no correlation between high levels of -hCG and poor pregnancy outcomes. A lower level of PAPP-A and -hCG may be a predictor of preterm labour, according to the study's findings.

Additionally, according to this study, PAPP-A readings could be used as a screening test for pregnancy complications such preeclampsia, low birth weight, and premature labour.

METHODOLOGY

1. Study design

A prospective observational study, To determine the association of 1st trimester PAPP-A, BETA- hCG and PLGF with adverse pregnancy outcomes.

2. Study Setting:

The study was carried out at the teaching hospital of KAHER'S Dr. Prabhakar Kore Hospital and Medical Research Centre.

3. Study period:

The study was conducted from January2021 until December 2021 for a priod of one year.

4. Study population :

All antenatal women between 9 weeks and 13 weeks 6 days period of gestation attending the out patient department, were included in the study .All of these pregnancies were followed up at delivery and the results were noted.

5. SELECTION CRITERIA:

Inclusion criteria

Antenatal women between 9 weeks and 13 weeks 6 days period of gestation attending the Obstetric OPD were included in the study after taking adequate informed consent.

Exclusion criteria

Patients who were a k/c/o diabetes mellitus, chronic hypertension, cardiac disorders, renal disorders, multiple gestation were excluded.

Outcomes Measured

Pre-Eclampsia, fetal growth restriction , preterm delivery, oligohydramnios, low birth weight, placental abruption, gestational diabetes mellitus , chromosomal anomalies like trisomies and missed abortion.

Sample size: Sample size formula based on prevalence rate

$$n = \frac{z_\alpha{}^2 P(1-P)}{d^2}$$

P is the percentage of prevalence and 'd' is the percentage likely difference in the prevalence.

z_α is linked with the level of significance.

For 5% level of the significance $z\alpha = 1.96$.

Ref: Sung et al., 2017 [184]

With P = 43.08% and d = 10% the sample size is 95

To make the study more confirmative, the sample size was raised to 110

6. DATA COLLECTION AND SAMPLING TECHNIQUE

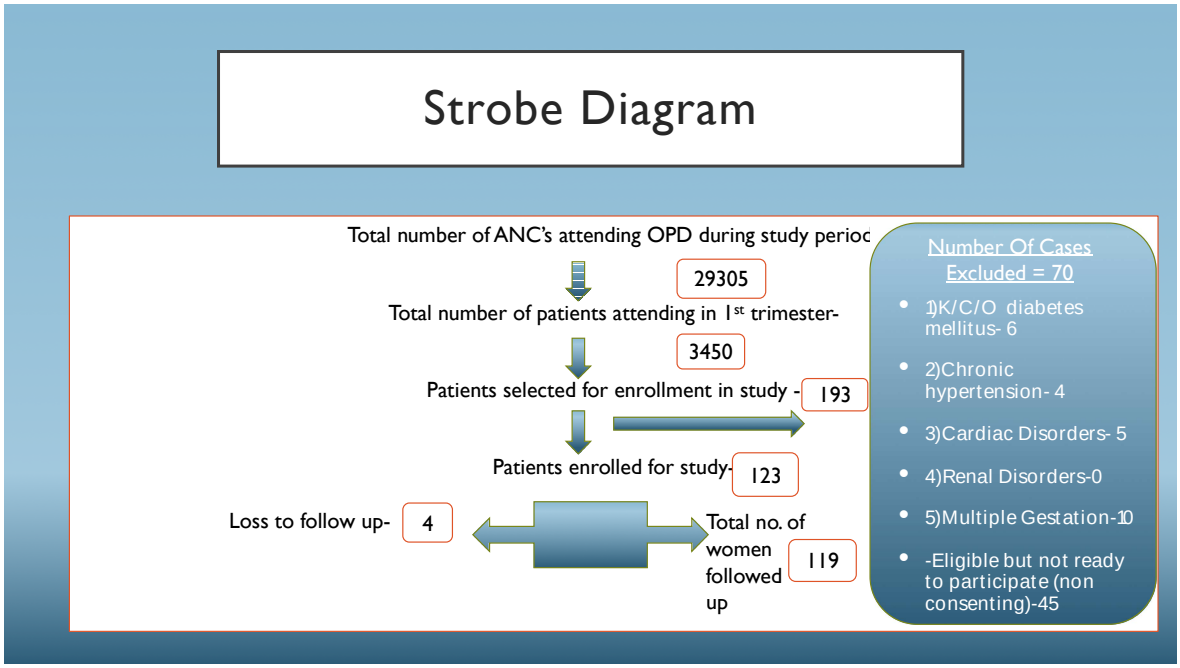
Detailed history of the patient, including their present history, past history, any significant medical history was noted and general physical examination was done. 3ml of venous blood was taken in a plain vacutainer, provided by the laboratory and transported within 4 days for analysis. The sample was processed by – Time Resolved Fluroimmunoassay on Auto-Delfia. The Software used for analysis-Lifecycle software from PerkinElmer Life and Analytical Sciences. The reports were dispatched within 5- 7 working days.

8) Data analysis

Data was analyzed using statistical Software R version 4.2.1,and Microsoft Excel. Categorical variables were represented by frequency and percentage. Continuous variables were given in Mean ± SD / Median (Min, Max) form. Normality of variable is checked by Shapiro Wilk test. Mann Whitney U test was used to compare the distributions of serum analytes over different Adverse Pregnancy Outcomes. P-value less than or equal to 0.05 indicates Statistical Significance.

RESULTS

Figure -01 Distribution of subjects according to their inclusion criteria



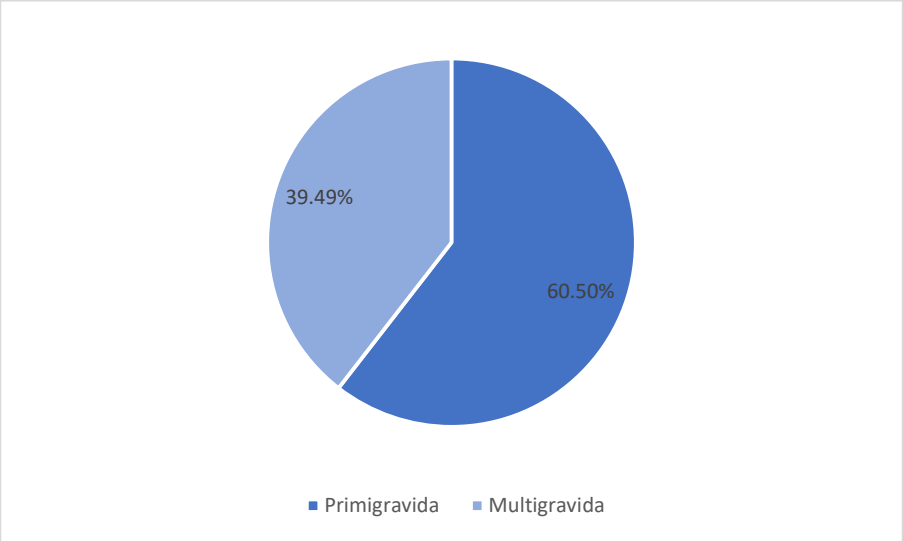
The above figure depicts the distribution of subjects according to their inclusion criteria. The total number of antenatal patients attending OPD during the study period were 29,305. Total number of patients attending in the 1st trimester of pregnancy were 3,450. Patients selected for enrollment in study were 193, among these 123 patients were enrolled in the study, as 70 patients were excluded as per the exclusion criteria. Loss to follow up were 04. Total number of women followed up were 119.

TABLE-1 Sociodemographic and Clinical Characters of Study Participants

VARIABLES	SUB CATEGORY	NUMBER OF SUBJECTS(%)
Age (yrs)	Mean ± SD	27.80 ± 4.55
	Median (Min, Max)	28 (19, 38)
Gravidity	Primigravida	72 (60.50%)
	Multigravida	47 (39.5%)
Conception	Spontaneous	116(97.47%)
	Infertility Treatment	3 (2.52%)
Consanguinity	Consanguineous	6 (5.04%)
	Non-consanguineous	113 (94.95%)
Gestational Age at Enrolment in weeks		12.89 ± 0.54
BMI	Mean ± SD	22.13 ± 3.70
	Median (Min, Max)	21 (15.60, 37.3)
Mean Arterial Pressure (mmHg)	Mean	83.4 ± 8.1

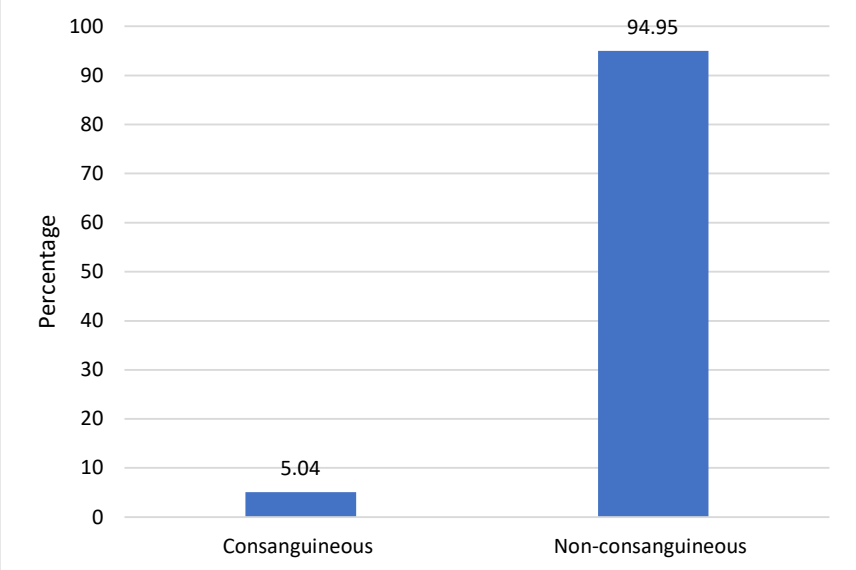
The above table shows the sociodemographic and clinical characters of study participants. The mean age of patients in this study was, 27.80±4.55 years. Age of the participants was found to be between 19 to 38 years. 72 (60.50%) participants were primigravida and 47 (39.49%) were multigravida. 116 (97.47%) study participants had spontaneous conception and 3 (2.52%) had conceived post infertility treatment. 6 (5.04%) of study participants had a consanguineous marriage and 113 (94.95%) had a non-consanguineous marriage. The gestational mean age at enrolment in weeks was found to be 12.89±0.54. The mean BMI was found to be 22.13±3.70. Finally the mean arterial pressure for the study participants was found to be 83.4±8.1.

Figure-02: Showing distribution of subjects according to gravidity



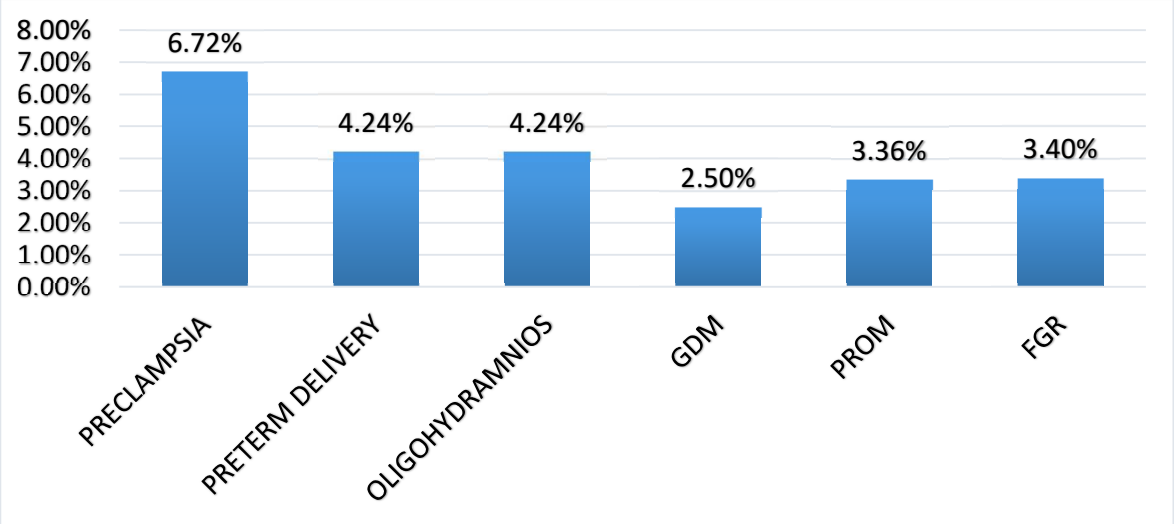
As depicted in the figure, 72 participants (60.50%) of the study participants were primigravida and 47 participants (39.5%) were multigravida.

Figure-03: Showing distribution of subjects according to consanguinity



The figure above shows the distribution of subjects according to consanguinity.(5.04%) 6 of the study participants had a consanguineous marriage and (94.95%) 113 participants had a non consanguineous marriage.

Figure-04: Distribution of Subjects According to Different Adverse Pregnancy Outcomes



As shown in figure-4 the study participants had various adverse pregnancy outcomes such as, 8 (6.72%) of the participants had preeclampsia, 5 (4.24%) had preterm delivery, 5 (4.24%) had oligohydramnios, 3 (2.50%) had Gestational diabetes mellitus ,4 (3.36%) had Premature rupture of membranes (PROM) and 4 (3.40%) showed fetal growth restriction (FGR).

TABLE-2: Association of PIH with serum analytes (Beta hCG, PAPP-A, PLGF)

Variables	Sub Category	No. of patients (n=119)	Mean Beta-hCG (mom)	Mean PAPP-A (mom)	Mean PLGF (mom)
PIH (n=18)	Gestational HTN	10(8.40%)	0.9 ±0.3 (0.9-1.4)	1.0 ± 0.6 (0.4-2.3)	1.2 ± 0.8 (0.3-3.0)
	p-value		0.75	0.97	0.56
	Preeclampsia	8 (6.72%)	1.26±0.61 1.26 (0.61,1.91)	1.59 ±0.75 1.4 (0.95,2.63)	0.78 ±0.13 0.77 (0.63,0.93)
p-value			0.5371^{MW}	0.0982^{MW}	0.1307^{MW}

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in the table-2, the association of pregnancy induced hypertension with serum analytes (Beta hCG, PAPP-A, PLGF) where 18 participants developed PIH. Among 18 participants, 10 (8.40%) of study population showed gestational hypertension. Mean value for the following serum analytes was as follows, Beta- hCG 0.9±0.3(0.9-1.4), PAPP-A 1.0±0.6 (0.4-2.3), PLGF 1.2±0.8 (0.3-3.0) and their p-values are 0.75, 0.97, 0.56, respectively.

Similarly 8 participants 6.72%, of study population developed preeclampsia. The mean value of serum analytes were, Beta- hCG-1.26±0.61, PAPP-1.59±0.75A, PLGF 0.78±0.13, and their p-values 0.5371^{MW},0.0982^{MW},0.1307^{MW}, respectively.

TABLE-3 Association of Oligohydramnios with Serum Analytes (Beta hCG, PAPP-A, PLGF)

Variables	No. of patients (n=119)	Mean Beta-hCG (mom)	Mean PAPP-A (mom)	Mean PLGF (mom)
Oligohydramnios	5 (4.24%)	1.55 ± 1.04 1.26 (0.67, 3.3)	0.94 ± 0.63 0.8 (0.21, 1.78)	0.85 ± 0.56 0.68 (0.24, 1.63)
p-value		0.2465^{MW}	0.644^{MW}	0.2187^{MW}

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in table - 3, the association of oligohydramnios with serum analytes. 5 (4.24%) of study participants, had oligohydramnios with serum analytes as follows, Beta- hCG 1.55±1.04, PAPP-A 0.94±0.63, PLGF 0.85±0.56 and their p-values were 0.2465^{MW},0.644^{MW},0.2187^{MW} respectively.

TABLE-4:**Association of GDM With SerumAnalytes**

(Beta hCG,PAPP-A ,PLGF)

Variables	No. of patients (n=119)	Beta-hCG (mom)	PAPP-A (mom)	PLGF (mom)
GDM	3 (2.52%)	1.33 ± 1.01 0.89 (0.61, 2.48)	1.3 ± 0.36 1.29 (0.95, 1.66)	1.25 ± 0.63 0.93 (0.84, 1.97)
p-value		0.799^{MW}	0.2408^{MW}	0.7572^{MW}

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in table – 4, the association of gestational diabetes mellitus with serum analytes. 3 (2.52%) study participants, showed association of GDM with serum analytes as follows, Beta- hCG 1.33±1.01, PAPP-A 1.3±0.36, PLGF 1.25±0.63 and their p-values were 0.799^{MW},0.2408^{MW},0.7572^{MW} respectively.

Table-5: Association of Preterm Labor with Serum Analytes

(Beta hCG, PAPP-A ,PLGF)

Variables	No. of patients	Mean Beta-HCG (mom)	Mean PAPP-A (mom)	Mean PLGF (mom)
Preterm Labor	5 (4.24%)	1.34 ± 0.78 1.14 (0.41, 2.48)	0.94 ± 0.46 1.21 (0.33, 1.31)	1.22 ± 0.6 1.07 (0.52, 1.97)
p-value		0.3857^{MW}	0.8422^{MW}	0.7383^{MW}

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in table 5, the association of preterm labor with serum analytes. 5 **(**4.24%) of study population had preterm labour with serum analytes as follows, mean Beta-hCG was 1.34±0.78,and that of PAPP-A was 0.94±0.46, followed by PLGF 1.22±0.60. Their p-values were 0.3857^{MW},0.8422^{MW},0.7383^{MW} respectively.

Table-6: Association of PROM With Serum Analytes

(Beta hCG, PAPP-A , PLGF)

Variables	No. of patients (n=119)	Mean Beta-HCG (mom	Mean PAPP-A (mom)	Mean PLGF (mom)
PROM	4 (3.36%)	0.81±0.53 0.67 (0.37, 1.4)	1.21±0.14 1.21 (1.07,1.3)	1.97±0.42 1.84 (1.63,2.4)
p-value		0.4183^{MW}	0.3128^{MW}	**0.0194^{MW*}**

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in table – 6, the association of PROM with serum analytes. Among the study participants n=4 ,3.36% showed association of (PROM) Prelabor rupture of the membranes with serum analytes as follows, Beta- hCG was 0.81±0.53,and that of PAPP-A 1.21±0.14,followed by PLGF 1.97±0.42. Their p-values were 0.4183^{MW},0.3128^{MW},0.0194^{MW}. .PLGF value was found to be statistically significant.

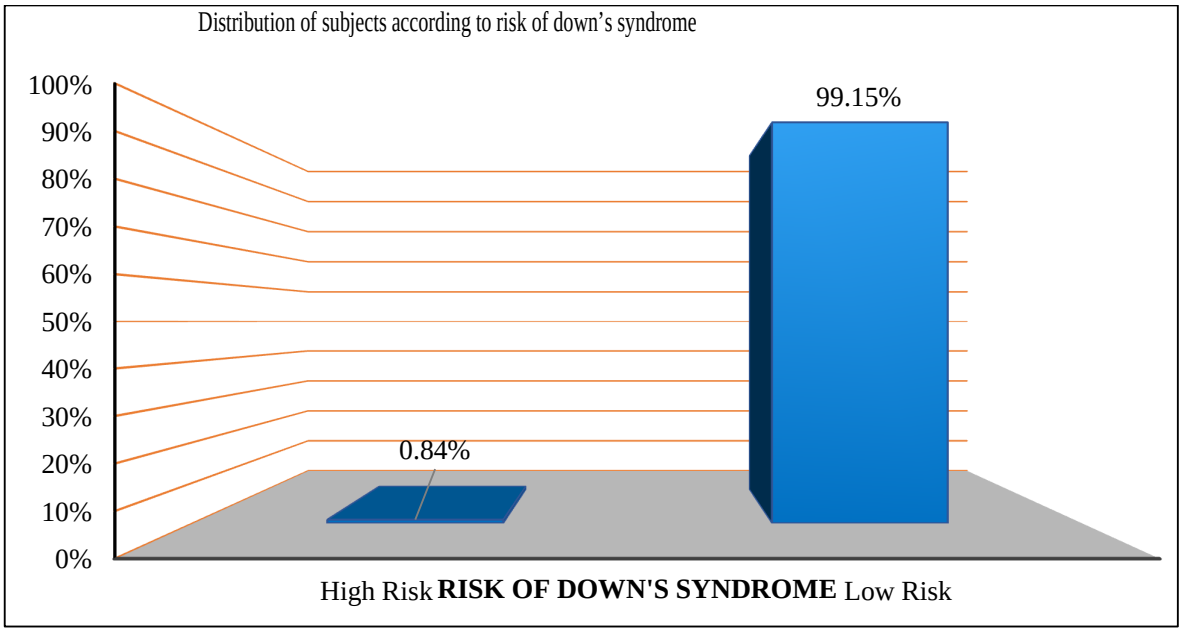
Table-7: Risk of Trisomies Observed Based On Serum Analytes Evaluation Among The Study Participants

Variables	Sub Category	Number of Subjects (%) (n=119)
Risk of Down's Syndrome Cut-off 1:250	Increased risk	1 (0.84%)
	Low risk	118 (99.15%)
Risk of Edward's Syndrome Cut-off 1:100	Low risk	119 (100%)
Risk of Patau's Syndrome Cut-off 1:100	Low risk	119 (100%)

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in the table-7 ,the risk of trisomies observed based on serum analytes was 0.84%, 1 participant , showed increased risk for Down's syndrome, and the remaining 118 participants had low risk for Down's, Edward's and Patau's Syndrome.

Figure-05: Distribution of Women According to Risk for Down's syndrome



As shown in the figure-5, 1 participant, 0.84% of study population showed increased risk for Down's syndrome and 118 (99.15%) were at low risk.

Table-8: Distribution of Women Based on Risk of PE at Different Period of Gestation

Risk of PE	Sub Category	Number of subjects (%) (n=123)
< 32 Cut off- 1:100	Increased risk	1 (0.84%)
	Low risk	118 (99.15%)
32-34 Cut off- 1:100	Increased risk	3 (2.43%)
	Low risk	116 (97.47%)
34-37 Cut off-1:100	Increased risk	17 (14.28%)
	Low risk	102 (85.71%)

As shown in the table-8, risk for pre eclampsia was divided based on the period of gestation, as follows, 1 participant (0.84%) had increased risk for PE at <32 weeks. Similarly 3 participants (2.43%) had increased risk for PE at 32-34 weeks ,and lastly 17 participants (14.28%) had increased risk for PE at 34-37 weeks.

The total number of participants screened high risk for PE irrespective of the gestational age were 17 (14.28%).

Table-9: Results of Multivariate Analysis for The Association Of Serum Analytes with Pre eclampsia

Variable	Odds ratio	95% confidence interval	P-value
BETA-hCG	0.98	0.9530 to 1.005	0.01*
PAAP-A	1.0	1.000 to 1.000	
PLGF	1.01	1.002 to 1.031	

*Abbreviation: MW – Mann Whitney U test, * indicates statistical significance.*

As shown in table 9, the results of multivariate analysis for the association of serum analytes with preeclampsia predicts that for Beta-hCG , odds ratio is 0.98 for CI ,0.9530 to 1.005, for PAAP-A odds ratio is 1.0 for CI 1.000 to 1.000 which is equivocal and that for PLGF, odds ratio is 1.01 for CI 1.002 to1.031 and their p-value was 0.01, which was found to be statistically significant.

Table-10: Results of Multivariate Analysis for Predicting Gestational Hypertension

Variables	Odds ratio	95% confidence interval	P-value
BETA-hCG	0.99	0.9637 to 1.008	0.08
PAAP-A	0.99	0.9997 to 1.000	
PLGF	1.012	1.001 to 1.033	

As shown in the table 10, results of multivariate analysis for predicting gestational hypertension predicts that for BETA-hCG odds ratio 0.99 for CI was 0.9637 to 1.008, PAAP-A odds ratio was 0.99 for CI 0.9997 to 1.000 and PLGF was Odds ratio 1.001 for CI 1.001 to1.033 and their p-value was found to be 0.08

Table-11: Neonatal Outcomes

Variables	Number Of Subjects (n=116)	Percentage (%)
FGR	4	3.44%
Prematurity	2	1.69%

As shown in the table-11 , neonatal outcomes were observed, the mean for birth weight was 2.67±0.32, Fetal growth restriction was seen in 4 subjects (3.44%) and 2 subjects (1.69%) had prematurity.

Table-12: Birth Weight Characteristics among Babies Born to Study Participants

Birth Weight (Kg)	Number of subjects (%) (n=116)
<1.0 Kg (ELBW)	0
1 - 1.5Kg (VLBW)	4 (3.44%)
1.5 – 2.5Kg (LBW)	27 (23.27%)
>2.5 Kg	85 (71.55%)

As shown in the figure-12 birth weight characteristics among babies born to study participants were observed, 3.44% of the study instances gave birth between 1-1.5 kg (VLBW), 23.27% instances gave birth between 1.5-2.5 kg and 71.55% gave birth between >2.5Kg.

DISCUSSION

This prospective observational study aimed to study the, "Association between maternal first trimester serum analytes (PAPP-A, BETA-hCG, PLGF) and adverse pregnancy outcomes".

In our study the mean age of the participants was found to be between 27.80±4.55 yrs. However a similar study done by **Pakniat** et al in Iran also had a mean age of 27.73±6.12 years, which is comparable to our study. As per the ACOG guidelines, dual markers and first trimester genetic screening is adviced for all pregnant women irrespective of their risk factor. However only a few women comply for the test in low income countries considering the cost factor. The elderly group of patients >25 years of age are more compliant to follow the advice because of better compliance followed by this set of population.[185]

The instances in our study were of two types, primigravida, 60.50% and multigravida, 39.49%. 8 participants (6.72%) developed PE, out of which 5 participants (62.5%) were primigravida 3 participants (37.5%) were multigravida. 1 participant was screened to have increased risk for Down's Syndrome which was a primigravida. However in a similar study conducted at Harold Wood Hospital, screening for chromosomal abnormalities by a combination of maternal serum free beta-hCG and PAPP- A in a One Stop Clinic for assessment of risks, free beta-hCG appeared to be a significant positive association with increasing gravidity or parity. However PAPP-A also appeared to have a positive association with increasing parity and to a lesser extent with gravidity. Although these trends showed some association with changing gravidity or parity, when the individual $\log_{10}$ MoMs were regressed against gravidity (or parity) the correlation was not significant. [186-188]

In the present study, spontaneous conception was seen in 97.47%, and 2.52% had conceived with infertility treatment. As per a study conducted in Australia , on prenatal screening and diagnosis where data was collected from three private ultrasound clinics, which included: PAPP-A and free beta hCG MoM, the biochemical platform utilized (Brahms Kryptor or Immulite 2000), adjusted risk of Down syndrome, method of conception, and the maternal characteristics. PAPP-A was significantly lower in IVF pregnancies as compared to spontaneously conceived pregnancies.[189]

All antenatal women between 9 weeks and 13 weeks 6 days period of gestation were enrolled in our study and the mean gestational age was between 12.89 ± 0.54 weeks. However a similar prospective study of women undergoing first-trimester screening was conducted at the Gupte Hospital and Research Center and the Birthright Genetic Clinic, Pune, India, where blood samples for first-trimester screening were collected between 11 weeks and 13 weeks and 6 days period of gestation.[186]

In our study, the mean BMI was 22.13±3.70, with a range of 18.5 to 24.9kg/m^2 which was comparable with studies conducted by Francois Audibert et al, Bernat Serra et al, Poon L C et al and Francesca Crovetto et al. In our study women had the normal range of BMI.

In our present study the primary outcomes were pre eclampsia equalling 6.72% ,preterm delivery and oligohydramnios were 4.24% each ,GDM was found to be 2.50%, PROM were 3.36% and lastly FGR was found to be 3.40%.

In a similar study, First And Second Trimester Evaluation of Risk (FASTER) trial, which was a multicenteric study, to compare the diagnostic performance of several first and second trimester screening markers. The first-trimester markers that were evaluated were PAPP-A level, free beta hCG. In this study, women with PAPP-A of ≤5th percentile were significantly more likely to experience spontaneous fetal loss at

≤24 weeks of gestation, low birth weight, preeclampsia, gestational hypertension, preterm birth, stillbirth, preterm premature rupture of membranes, and placental abruption . The free beta hCG at ≤1st percentile was associated with an increased risk of spontaneous loss at ≤24 weeks of gestation.

Our study has shown a positive association with PLGF ,PAPP-A and beta-hCG with pre-eclampsia. Precisely, PLGF value of <0.9 mom, PAPP-A value of <0.5mom and beta-hCG of >2.5 mom. Other studies also have shown a positive association of PLGF and PAPP-A with pregnancy induced hypertension.

A study conducted at **University Viale del Policlinico, Rome**, has highlighted a significant relationship between low maternal serum PAPP-A and more precisely values ≤0.8 MoM at 10 ± 13 weeks 6 days gestation are positively associated with later development of PIH.[190]

Another nested prospective cohort study conducted in two public hospitals in Accra, Ghana, where pregnant women attending antenatal clinics between 8 and 13 weeks, provided a blood sample. PAPP-A and PlGF concentrations were measured by the AutoDELFIA immunoassay method.

This study concluded that, the addition of PlGF and PAPP-A together to the model markedly improved its predictive ability, with an increase in AUC from 0.75 to 0.82 for multiparous women and 0.89 to 0.95 for primigravid women, whereas adding either one of the two had only a marginal effect.[191]

Though our study sample size is small we got a positive association with pre eclampsia. Therefore PLGF and PAPP-A are the potential biomarkers of pre eclampsia in a small cohort.

Addition of PLGF to the 1st trimester screening has not given any extra benefit of a positive association with pre eclampsia. In low resource settings, PAPP-A has an equal potential to identify the high risk population who likely to develop pre eclampsia.

Other adverse pregnancy outcomes of our study such as , fetal growth restriction , preterm delivery, oligohydramnios, low birth weight, placental abruption, gestational diabetes mellitus , chromosomal anomalies like trisomies and missed abortion have not shown any positive association in our study.

An observational study conducted at District general hospital between January 2011 and December 2013 at the Heatherwood and Wexham Park Hospitals Foundation Trust, have demonstrated that low maternal circulating concentration of PAPP-A at 11–14 weeks of gestation, significantly predicts adverse perinatal outcomes for SGA and preterm birth.[192]

Another prospective analytical study performed on singleton pregnant mothers at the first obstetrical visit before 14 weeks of gestational age, at the health care centers of Qazvin province, Central region of Iran, during years 2016–2017, investigated the relationship between PAPP-A and beta-hCG with adverse pregnancy outcomes in the Iranian population. The result of this study revealed that lower level of PAPP-A and beta-hCG could be a predictive factor in preterm labor. Also, this study indicated that PAPP-A measurements could be a screening test for adverse pregnancy outcomes, such as preeclampsia, low birth weight and preterm labor. [193]

In our study we could not find any association which can be explained by our small sample size. Therefore we recommend large scale studies to study the association in low resource settings.

In our study beta hCG values were not associated with adverse pregnancy outcomes.

A cohort study performed on the association of beta hCG with adverse pregnancy outcomes by the Literature searches in PubMed, EMBASE, Medline, Central, China National Knowledge Infrastructure (CNKI), Wanfang, and China Science Digital Library (CSDL) databases. This study concluded that high levels of beta-hCG is a risk factor for IUGR, PIH, preterm delivery , and miscarriage in singleton pregnancy. However the relationship between high levels of *beta* -hCG and GDM still needs further research to confirm.[194]

Another retrospective cohort study conducted at Baoding Maternal and Child Health hospital from June 2018 to June 2020, to investigate the prediction performance of serum PLGF , free beta-hCG and PAPP-A levels in early pregnancy for pregnancy outcomes concluded that pregnant women with an abnormal pregnancy had significantly higher beta-hCG and PLGF, and lower PAPP-A than those with normal pregnancy.[195]

In the present study women with pregnancy induced hypertension, were 18, of which 10 (8.40%) individuals had gestational hypertension, and the mean value for the subsequent blood analytes were as follows: beta hCG was 0.9±0.3mom(0.9-1.4), PAPP-A 1.0± 0.6(0.4–2.3), and PLGF 1.2 ± 0.8 (0.3-3.0). However 8 participants , 6.72% of the study population were diagnosed with preeclampsia and their mean value of serum analytes were, beta-hCG was 1.26±0.61, and PAPP-A 1.59±0.75 PLGF 0.78±0.13, and their p-values, were 0.5371MW, 0.982MW, 0.1307MW respectively.

In a similar prospective cohort study of pregnant women, by the Prenatal Diagnosis and Gynecologic Unit of the Institute for Maternal and Child Health – IRCCS "Burlo Garofolo" , all women were recruited and were followed up from first trimester screening to delivery , 46 women were affected by gestational hypertension (2.2%), 25

women developed pre eclampsia (1.2%), including 12 early-onset PE (0.6%) and 13 late-onset PE (0.6%).

For a fixed FPR of 10 and 5%, serum PlGF, free β-hCG and chronic hypertension identified respectively 67 and 75% of women who developed early-onset PE. The combination of the uterine artery Doppler pulsatility index (UtA PI) with PlGF and chronic hypertension reached a sensitivity of 60%.[196]

The research population who had preterm labour were around 5 (4.24%) with the following serum analytes: the mean of Beta-hCG was 1.34±0.78; that of PAPP-A was 0.94±0.46; and that of PLGF was 1.22±0.60. They were determined to have a p-value of 0.3857MW, 0.8422MW, 0.7383MW, respectively, which was not statistically significant.

Four recent studies have investigated the relationship between low PAPP-A and preterm delivery. Of these, 2 retrospective cohort studies found a statistically significant association between low PAPP-A level (below the 10th percentile in one study and below the 5th percentile in another) and preterm delivery. However the study did not find a strong enough association to endorse the use of PAPP-A level to screen for preterm delivery. The other 2 recent studies included a retrospective case-control study of 663 women that did not find an association between PAPP-A level below the 10th percentile and preterm delivery,

A study conducted in 2011, which was a retrospective cohort study of 28 566 women that concluded a PAPP-A level below the fifth percentile was not predictive of preterm labour. The current evidence for an association between low PAPP-A levels and preterm labour remains mixed, and no evidence exists to support the measurement of low PAPP-A level as a test for preterm delivery. [197]

Of the total study population,1 participant (0.84%) had a risk Down's syndrome , while no participants showed risk for Edward's and Patau's syndrome.

In a prospective validation trial, done by Santorum et al.,2017, [198] the first-trimester combination test detected > 95% of cases of monosomy X and triploidies, 90%, 97%, and 92% of trisomies 21, 18, and 13, respectively, as well as > 50% of other chromosomal abnormalities, with an FPR of 4%.

Similarly study done by **Wapner** et al., 2003 ,8514 individuals with singleton pregnancies underwent screening. With a false positive rate of 9.4 percent, this screening method correctly detected 85.2% of the 61 instances with Down's syndrome (95 percent confidence interval, 73.8 to 93.0). (95 percent confidence interval, 8.8 to 10.1). The detection rate was 78.7% with a false positive rate of 5%. (95 percent confidence interval, 66.3 to 88.1). With a false positive rate of 2%, screening detected 90.9 percent of the 11 instances of trisomy 18 (95 percent confidence interval, 58.7 to 99.8). With a false positive rate of 15.2 percent, screening found 100% of foetuses with trisomy 18 and 89.8 percent of foetuses with trisomy 21 in women 35 years of age or older.[199]

Shiefa et al.,2013 in their study non invasive alternative for the early identification of aneuploidy pregnancies is the first trimester screening programme. Serum free human chorionic gonadotrophin (free-hCG) and pregnancy associated plasma protein A (PAPP-A), maternal age, and foetal nuchal translucency (NT) thickness at 11 + 0-13 + 6 weeks of gestation are used in conjunction for this screening. .[199] Early diagnosis of trisomies 21, 18, and 13 is a benefit of screening. All three trisomies are linked to older mothers, higher foetal NT, and lower PAPP-A, however trisomy 21 has higher serum free hCG levels than trisomies 18 and 13, whereas trisomies 18 and 13 have lower serum free hCG levels. [201-202]

As we did not interfere with the physicians choice for aspirin therapy (non intervention study), majority of our study population 70 participants (58.82%) received aspirin therapy for other factors related to their previous obstetric history, physicians decision and patients choice, irrespective of the risk categorization. Out of 70 participants, 7 participants developed PE.This could be a confounding factor for our study results.

In our study 17 participants were screened as high risk for PE, out of these participants aspirin therapy was taken by 13 participants and 5 participants developed PE inspite of the aspirin therapy.

As per a multinational study conducted to check the efficacy of intake of low-dose aspirin during pregnancy to reduce the risk of preeclampsia at 13 maternity hospitals. In this double-blinded study, placebo-controlled trial, aspirin at a dose of 150 mg per day was compared with a placebo that was administered from 11 to 14 weeks of gestation until 36 weeks of gestation in women with singleton pregnancies who were at high risk for preterm pre-eclampsia. This study concluded that treatment with low-dose aspirin in women at high risk resulted in a lower incidence of preterm preeclampsia than placebo.

As aspirin is known to decrease the incidence of pre eclampsia and other adverse outcomes like FGR, preterm delivery , we could observe that our adverse pregnancy outcome results are affected this factor and we could not get a positive association with other adverse outcomes like preterm delivery and FGR. But we could get the association of pre-eclampsia, it shows that PLGF and PAPP-A screening has the potential to detect high risk individuals who could develop PE, and such subjects can be detected early and preventive measures can be implemented for better outcomes.

CONCLUSION

- First Trimester serum analytes PAPP-A and PLGF are equivocal as per the multivariate analysis for the association with pre eclampsia.
- Addition of PLGF to the Dual markers (PAPP-A and beta hCG) in the 1st trimester, helps to increase the prediction of pre eclampsia.
- Routinely Dual markers (PAPP-A and beta hCG) is being advised with NT scan in the 1st trimester genetic screening program.
- We can detect women at risk of pre eclampsia early in the first trimester so that such women can be subjected to preventive strategies like aspirin therapy.

SUMMARY

This was a prospective observational study, to determine the association of 1st trimester PAPP-A, BETA- hCG and PLGF with adverse pregnancy outcomes. It was carried out at the teaching hospital of KAHER'S Dr. Prabhakar Kore Hospital and Medical Research Centre, from January 2021 until December 2021 for a priod of one year. All antenatal women between 9 weeks and 13 weeks 6 days period of gestation attending the out patient department, were included in the study. 3ml of venous blood was taken in a plain vacutainer, and the sample was processed by – Time Resolved Fluroimmunoassay on Auto-Delfia. The Software used for analysis-Lifecycle software from PerkinElmer Life and Analytical Sciences. The reports were dispatched within 5-7 working days. All of these pregnancies were followed up at delivery and the results were noted. The outcomes measured were pre-eclampsia, fetal growth restriction , preterm delivery, oligohydramnios, low birth weight, placental abruption, gestational diabetes mellitus , chromosomal anomalies like trisomies and missed abortion. The minimum sample size with P = 43.08% and d = 10% was 95.

123 participants were enrolled in the study and 70 participants were excluded as per the exclusion criteria. Loss to follow up were 4 participants thus total number of women followed up were 119. The mean age of the study participants was , 27.80±4.55 years. Among the outcomes measured, 6.72% of the participants had preeclampsia, 4.24% had preterm delivery, 4.24% had oligohydramnios, 2.50% had gestational diabetes mellitus ,3.36% had premature rupture of membranes (PROM) and 3.40% showed fetal growth restriction (FGR).

Pregnancy induced hypertension was developed among 18 participants, among which 10 (8.40%) of study population showed gestational hypertension. Mean value

for the serum analytes was as follows, Beta- hCG 0.9±0.3, PAPP-A 1.0±0.6, PLGF 1.2±0.8.

8 participants 6.72%, developed pre eclampsia and the mean value of serum analytes was , Beta- hCG-1.26±0.61, PAPP-1.59±0.75A, PLGF 0.78±0.13, however their p-values were not significant.

Oligohydramnios was seen in 18 participants (4.24%), with mean, Beta- hCG 1.55±1.04, PAPP-A 0.94±0.63, PLGF 0.85±0.56. GDM was seen in 3 study participants (2.52%), with mean Beta-hCG 1.33±1.01, PAPP-A 1.3±0.36, PLGF 1.25±0.63. Preterm labour was seen in 5 participants with mean Beta- hCG 1.34±0.78, and that of PAPP-A was 0.94±0.46, followed by PLGF 1.22±0.60. Their p-values were not significant. (PROM) Premature rupture of the membranes was seen in 4 study participants 3.36% with serum analytes, Beta- hCG 0.81±0.53, PAPP-A 1.21±0.14 and PLGF 1.97±0.42. However the p-value for PLGF value was found to be statistically significant.

Increased risk for Down's syndrome, was seen in 1 participant , 0.84% and the remaining participants were screened as low risk for Down's, Edward's and Patau's Syndrome.

The total number of participants screened as high risk for PE irrespective of the gestational age were 17 (13.82%). Among them, 13 (10.92%) women received aspirin. On the contrary 102 (58.82%) women were screened as low risk for PE. Among them 57 (45.89%) women received aspirin medication, and showed a statistically significant p value of 0.04.

BETA- hCG mom, PAPP-A mom, and PLGF mom levels were statistically significant for predicting preeclampsia, according to the findings of multivariate

analysis. The optimum cut-off point for predicting preeclampsia, according to the ROC curve, was 0.74 mom.

Neonatal outcomes observed were, the mean birth weight was 2.67±0.32kg, fetal growth restriction was found to be 3.44%, and prematurity was 1.69%. However 5.08% of population underwent NICU admission.

It was concluded that the first trimester serum analytes PLGF and PAPP-A are equivocal as per the multivariate analysis for the association with pre eclampsia. However ,addition of PLGF to the Dual markers helps to increase the prediction of pre eclampsia in the 1st trimester, and we can detect women at risk of pre eclampsia early in the first trimester so that such women can be subjected to preventive strategies like aspirin therapy. Routinely Dual markers (PAPP-A and beta Hcg) is being advised with NT scan in the 1st trimester genetic screening program. However, the results of this can be validated by large scale studies.

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ANNEXURE - I- INFORMED CONSENT

This ICF is for women attending Teaching hospital attached to KAHER, Belagavi, and who we are inviting to participate in research on Association between maternal serum analytes PAPP-A, BETA HCG, PLGF and adveres pregnancy outcome. Levels of pregnancy associated plasma protein A (PAPP-A) and placental growth factor (PLGF) around 9 to 13 weeks of gestational age are associated with obstetric complications such as preeclampsia, small for gestational age(SGA), intra-uterine growth restriction (IUGR), preterm delivery, oligohydraminos, low birth weight, placental abruption, intrauterine death and chromosomal anomalies like trisomies. PAPP-A together with human chorionic gonadotropin and ultrasound obtained fatal nuchal translucency thickness, is used to predict the risk for fatal aneuploidies including Downs syndeome.

Placenta associated disorders in pregnancy are among the major causes of global maternal and neonatal morbidity and mortality, especially in low resource settings. Risk prediction in early pregnancy in theses settings will allow for efficient resource allocation and targeted prevention strategies including aspirin and calcium supplementation. In addition neonatal morbidity and mortality such as IUGR, SGA and stillbirth can be addressed concomitantly.

Therefor we will be looking into productivity of these markers with overall adverse outcomes in pregnancy **The title of my research is**

“Association between maternal serum analytes PAPP-A, BETA HCG, PLGF and adveres pregnancy outcomes one year observational study at KAHER'S Dr. Prabhakar Kore hospital and medical research centre.

Principal Investigator:

Dr. _____

Associate Professor

Department Of Obstetrics & Gynaecology

J.N. Medical College, Belagavi

Co-investigator:

REG. NO. BJ0120004

Post Graduate

Department Of Obstetrics & Gynaecology

J.N. Medical College, Belagavi

This Informed Consent Form has two parts:

1. **Information sheet (To share the information about my study)**
2. **Certificate of Consent**

You will be given a copy of the full Informed Consent Form

Purpose of the study

I have been informed by REG. NO. BJ0120004, Post Graduate in M.S. Obstetrics and Gynecology under the guidance of Dr. _____, Department of Obstetrics and Gynaecology, J.N. Medical College, KAHER University, Belagavi is conducting a study to find out the association between maternal serum analyses PAPP-A, BETA HCG, PLGF and adverse pregnancy outcomes.

Study procedure:

Once I have signed the informed consent form, the personal details like name, age, place, address, my education, my health, reproductive history and other information will be noted down.

A) All antenatal women between 9 weeks to 13 weeks pop and meeting the inclusion and exclusion criteria presenting to the OPD at KLE'S Prabhakar Kore Hospital, Belagavi will be identified.

B)Patients will be given an informed consent form and a patient information sheet in their own vernacular language about the risk of fatal aneuploidies.

The informed consent will be directed to her spouse is she is illiterate or fails to conceive the concept of risk.

C)Patients exact age, weight, gestational age by LMP/1ST trimester CRL, presence of diabetes mellitus, hypertension or cardiovascular diseases and history of any child with Downs Syndrome or anyother genetic disease will be determined.

D) all of these pregnancies will be followed up till delivery and results willl be obtained. The gestational age at delivery, neonatal birth weight, APGAR score and malformations will be assessed at the delivery.

Potential Risks

There are no observable risks associated with the study.

Alternatives

If I decide not to participate in the study, my health care provider will provide the usual standard care during my pregnancy, delivery and up to through 6 weeks after delivery**.**

Privacy

To protect my privacy, all the collected information will be given a number rather than using my name. Any information collected during the study will remain confidential.

My medical files will be reviewed only at the hospital (or study doctor's office) to check the information and verify the result without breaking my confidentiality. Only de-identified information on my pregnancy will be shared so as to learn the results of the study.

Authorisation to publish results

The information about me will be analysed together with other study participants.

Results of this study will be published and presented to scientific groups for scientific purposes, but I will never be individually identified in the presentation of the study results.

Institutional Policy

In case I have any questions related to the study, in future or in case of study related injury or illness, I can contact REG. NO. BJ0120004, Department of Obstetrics and Gynaecology, KAHER University's J.N Medical College. Dr._____ , Dept. Of Obstetrics and Gynaecology, KAHER University's J.N Medical College, Belagavi.

Voluntary Participation

My participation in the study is voluntary. In case I need any further information regarding my rights as study participant, I may contact Dr. Roopa M Bellad, Professor of Paediatrics, 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, Belagavi. My doctor will take care of me during this pregnancy or in the future. I am free to stop participation in this study at any time and for any reason.

Certification Of Consent

I have read the whole information, or it has been read to me. I have asked all the questions about it and those have been answered to my satisfaction. I consent voluntarily to participate in this research.

I also agree to be contacted for follow-up.

Print Name of Participant_____

Signature of Participant_____

Date_____ (dd/mm/yyyy)

If illiterate,

A literate witness must sign (if possible, this person should be selected by the participant and should have no relation to the research team).

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given the consent freely.

Print name of witness_____

Signature of witness_____

Date_____ (dd/mm/yyyy)

Thumb Print of Participant

Statement by the Researcher

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the following will be done:

1.

2.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered to the best of my ability. I confirm that the individual has not been coerced into giving consent and it has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Print name of Researcher_____

Signature of Researcher_____

Date_____ (dd/mm/yyyy)

ANNEXURE -II- PERFORMA

TITLE : "Association between maternal serum analytes PAPP-A, BETA HCG, PLGF and adveres pregnancy outcomes one year observational study at KAHER'S Dr. Prabhakar Kore hospital and medical research centre.

NAME:

AGE: IP NO: DOA: DOD:

OCCUPATION: ADDRESS:

SOCIO-ECONOMICS

LOW:

MIDDLE:

HIGH:

EDUCATION: DURATION OF HOSPITAL STAY

OBSTETRIC HISTORY:

MARRIED LIFE : CONSANGUINEOUS/ NON CONSANGUINEOUS

PREVIOUS PREGNANCY DETAILS

PRESENT PREGNANCY DETAILS :
TIME OF DIAGNOSIS
INFERTILITY TREATMENT
MODE OF CONCEPTION
NUMBER AND LENGTH OF HOSPITALISATION
PRENATAL CARE ULITIZATION :ADEQUATE /INADEQUATE

OBSTETRICS SCORE: **G** **P** **L** **A**

LMP (DD/MM/YY):

EDD:
C. EDD:

PERIOD OF GESTATION(WEEKS+DAYS)

HISTORY OF HYPERTENSION

HISTORY OF DIABETICS MELLITUS

HISTORY OF PRE-EXISTING RENAL /CARDIAC DISORDERS

HISTORY OF THYROID ABNORMALITY

HISTORY OF ALOCHOL CONSUMPTION

HISTORY OF ABRUPTIO PLACENTA

GENERAL PHYSICAL EXAMINATION

BULIT:
GENERAL CONDITION:
HEIGTH:
WEIGHT:
NOURISHMENT:
PULSE:
BLOOD PRESURE:
TEMPERATURE:

RESPIRATORY RATE:

PALLOR

ICTERUS

CLUBBING

CYANOSIS

LYMPHADENOPATY

EDEMA

BREAST
THYROID
SPINE

SYSTEMIC EXAMINATION:

RESPIRATORY SYSTEM:

CARDIOVASCULAR EXAMINATION:

PER ABDOMEN:

DETAILS OF DELIVERY:

INDICATION FOR CESAREAN SECTION

FETAL DISTRESS

CEPHALOPELVIC DISPROPORTION

BREECH:

PLACENTA PREVIA

FAILED PROGRESS

SEVERE PIH

OBSTRUCTED LABOR

OLIGOHYDRAMINOS

IUGR

ANTEPARTUM ECLAMPSIA

PROM

ABRUPTIO PLACENTA

UTEROPLACENTAL INSUFFICENCY

PRECIOUS PREGNANCY

DEEP TRANVERSE ARREST

TRANVERSE LIE

BROW PRESENTATION

CORD PROLAPSE

FACE PRESENTATION

IMPENDING ECLAMPSIA

MULTIPLE GESTATION

VASA PREVIA

IMPENDING RUPTURE

MEDICAL CONDITION:
ANY OTHER,SPECIFY:
OUT COME OF PREGNANCY

LIVE BIRTH

FRESH STILL BIRTH

MACERATED STILL BIRTH

BABY WEIGTH AT BIRTH:

BABY GENDER :MALE/FEMALE

DID THE BABY HAVE ANY CONGENTIAL ANOMALY :
IF YES SPECIFY

DID THE BABY HAVE BIRTH INJURY:

IF YES SPECIFY

WAS THE BABY ADMIITTED TO NICU FOR COMPLICATION:
IF YES CAUSE OF ADMISSION

INFECTION/SEPSIS:

BREATHING DIFFICULITIES:

ASPHYSIA:

RESPIRATORY DISTRESS:

JAUNDICE :

CONVULSION:

CONDITION OF BABY AT DISCHARGE:

IF BABY DIED ,CAUSE OF DEATH:

PREMATURITY:

LOW BIRTH WEIGHT:

SEPSIS:

BIRTH ASPHYXIA

APGAR SCORE

SIGNATURE AND NAME OF INVESTIGATOR

SrNo	AGE	IP NO	POG DURING TEST	CONCEPTION (1-spontaneous, 2-others)	CONSANGUINITY (1-consanguinous, 2-non consanguinous)	OBSTETRIC SCORE	PAST OBSTETRIC HISTORY: ADDICTION (1-yes/0-no)	THY DIS (1-yes/0-no)	SIG HIST (1-yes/0-no)	BMI (kg/m2)	DT NT SCAN	NT (mm)	NT mom	CRL	NASAL BONE (1-PRESENT, 2-ABSENT)	UTPi	MAP	UTPi mom	HCG mom	BETA HCG	PAPP-A mom	PAAP-A	PLGF mom	PLGF	POG @ DEL	RISK OF DOWN'S SYNDROME	RISK OF EDWARD'S SYNDROME	RISK OF PATAU'S SYNDROME	RISK OF PE <32	32-34	34-37
1	32	1089996	13 wks 2 days	1	2	G2P1L1	0	0	0	20	20-07-2021	1.5mm	1.1mom	72mm	1-	1.22pi	88.33mmhg	0.82mom	0.84mom	90.2	1.28mom	2998	0.91mom	35.5	38+2	1;100000	1;100000	1;100000	1;1070	1;1044	1;100000
2	30		13 wks 3 days	1	2	G2P1L1	0	0	0	21	12-07-2021	1.2mm	1.2mom	71mm	1-	1.34pi	88.33mmhg	0.80mo	2.34mom	56.4	1.22mom	2699	0.36mom	72.1	38+1	1;100001	1;100001	1;100000	1;100000	1;1010	1;100000
3	24		12 wks 6 days	1	2	PRIMI	0	0	0	20	12-07-2021	1.5mm	1.1mom	62mm	1-	1.15pi	89mmhg	0.56mom	2.35mom	57.2	1.07mom	3180	0.32mom	61.1	38+6	1;100002	1;100002	1;100000	1;1070	1;100000	1;100000
4	26	1063842	13 wks 1 day	1	2	PRIMI	0	0	0	21.1	12-07-2021	1mm	0.72mom	65mm	1	1.27pi	83.33mmhg	0.76mom	1.26mom	49.68	0.21mom	1070	0.24mom	13.9	17+6	1;221 INCREASED RISK	1;3533	1;6659	1;245	1;91	1;28
5	19	1088023	12wks 4 days	1	1	G2A1	0	0	1	27.4	28-06-2021	1.5mm	1.14mom	60mm	1-	1.27pi	83.33mmhg	0.75mom	0.37mom	13.59	1.21mom	3340	1.84mom	81.3	39+2	1;100000	1;100000	1;100000	1;00000	1;17613	1;1301
6	30	1078136	12 wks 5 days	1	2	G2A1	0	1	1	22	15-06-2021	1.5mm	1.11mom	63mm	1-	1.41pi	78.33mmhg	0.85mom	0.89mom	34.4	0.95mom	3300	0.93mom	45.5	34+5	1;78370	1;100000	1;100000	1;29446	1;5686	1;672
7	32	1058908	13 wks 4 days	1	2	PRIMI	0	1	1	28.1	02-06-2021	1.6mm	1.13mom	68mm	1-	1.06pi	83.33mmhg	0.67mom	0.9mom	26.2	1.78mom	7140	1.2mom	73.5	17+2	1;83962	1;100000	1;100000	1;48300	1;7777	1;702
8	28	1082052	13 wks 6 days	1	2	G2P1L1	0	0	1	19.5	02-06-2021	1.5mm	1.17mom	58mm	1-	1.2pi	83.33mmhg	0.69mom	1.4mom	142.5	1.07mom	5740	2.44mom	128	38+1	1;2963	1:100000	1;100000	1;85365	1;12623	1;1004
9	22	1082809	12 wks 2 days	1	2	G2A1	0	1	0	20.6	17-05-2021	1.5mm	1.17mom	58mm	1-	1.2pi	87.5mmhg	0.69mom	1.4mom	62.05	1.07mom	3440	2.44mom	108	40+1	1;100000	1:100000	1;100000	1;00000	1;100000	1;100000
10	33	1078635	13 wks 1 day	1	2	G2P1L1	0	0	0	22.8	17-05-2021	1.5mm	1.09mom	64mm	1-	1.59pi	83.33mmhg	0.96mom	0.52mom	18.43	0.93mom	3880	0.82mom	46.3	36+6	1;93000	1;100000	1;100000	1;5457	1;100000	1;100000
11	29	1076348	12wks 3 days	1	2	G2P1L1	0	0	1	19.8	15-04-2021	1.5mm	1.16mom	59mm	1-	1.45pi	82.5mmhg	0.83mom	3.17mom	149.7	1.23mom	4860	1.58mom	75.4	38+3	1;35976	1;100000	1;100000	1;72948	1;100000	1;100000
12	31	1088297	13 wks 6 days	1	2	G4A3	0	0	0	20	23-04-2021	1.48mm	1.07mom	63.4mm	1-	0.85pi	85mmhg	0.53mom	0.83mom	21	0.88mom	3380	1.35mom	87.5	38	1;88105	1;100000	1;100000	1;98871	1;100000	1;100000
13																															
14	20	1090258	13 wks 1 day	1	1	PRIMI	0	0	0	25.2	21-12-2021	1.15mm	0.82mom	67.05mm	1-	0.88pi	81.67mmhg	0.6mom	0.92mom	30.31	2.8mom	10100	0.99mom	51.1	37+6	1;100000	1;100000	1;100000	1;78156	1;12046	1;1019
15	29	1087575	12wks 3 days	1	2	G3A2	0	0	0	20.6	17-12-2021	1.22mm	0.93mom	60.21mm	1-	1.77pi	83.33mmhg	1.15mom	0.34mom	14.78	0.46mom	1570	0.71mom	33.5	38+1	1;100000	1;24806	1;42177	1;3277	1;903	1;180
16	36	1065288	12 wks 4 days	1	2	G4P2L2A1	0	0	0	26.5	08-07-2021	1.53mm	1.2mom	58mm	1-	1.1pi	78.33mmhg	0.67mom	1.0mom	53.42	1.38mom	3160	1.14mom	53	38	1;14219	1;100000	1;100000	1;00000	1;21015	1;1664
17																															
18																															
19	27		12 wks 4 days	1	2	PRIMI	0	0	0	20	02-06-2021	1.09mm	0.81mom	62mm	1-	1.25pi	84.4mmhg	0.74mom	1.06mom	40.77	0.68mom	2360	1.62mom	79.5	38+3	1;100000	1;100000	1;100000	1;100000	1;66618	1;4208
20	34	1062280	12 WKS	1	2	PRIMI	0	0	1	31.2	28-04-2021	1.63mm	1.36mom	53.8mm	1-	0.98pi	75mmhg	0.58mom	2.48mom	92.24	1.29mom	2280	1.97mom	79.3	36	1;18191	1;100000	1;100000	1;100000	1;100000	1;100000
21	31	1055017	12wks 3 days	1	1	G2P1D1	0	0	0	19.1	25-03-2021	1.35mm	1.04mom	59.12mm	1-	1.92pi	71.67mmhg	1.12mom	3.43mom	152.7	0.83mom	2990	0.74mom	35.5	38	1;1628	1;100000	1;100000	1;18751	1;100000	1;100000
22	26	1048882	12 wks 5 days	1	2	G2P1L1	0	0	0	15.6	30-03-2021	1.48mm	1.08mom	64.19mm	1-	0.93pi	66.67mmhg	0.53mom	0.84mom	45.76	0.85mom	4970	0.96mom	51	37+3	1;38902	1:100000	1;100000	1;100000	1;100000	1;100000
23	26	1061857	11 wks 4 days	1	2	G2A1	0	0	0	17.4	21-05-2021	1.05mm	0.8mom	60mm	1-	0.77pi	66.67mmhg	0.42mom	0.71mom	32.78	0.94mom	5400	0.71mom	40.1	37+6	1;100000	1:100000	1;100000	1;17288	1;4462	1;763
24	25	1073794	13 wks 1 day	1	2	G2P1L1	0	0	0	21.2	15-04-2021	1.9mm	1.33mom	69mm	1-	1.36pi	87.5mmhg	0.83mom	1.83mom	68.72	1.67mom	7750	1.45mom	78.9	38	1;42484	1:100000	1;100000	1;34008	1;10732	1;1019
25	27	1072232	13 wks 2days	1	2	PRIMI	0	0	0	24	10-04-2021	1.6mm	1.11mom	71mm	1-	1.35pi	84.17mmhg	0.84mom	0.67mom	24.01	1.36mom	6470	1.49mom	85.5	37+6	1;10000	1:100000	1;100000	1;34080	1;1044	1;100000
26	30		12 wks 4 days	1	2	PRIMI	0	0	0	22	23-07-2021	1.1mm	0.83mom	61mm	1-	2.05pi	83.34mmhg	1.23mom	1.03mom	39.62	0.52mom	1610	0.69mom	32.8	38	1;11946	1;100000	1;100000	1;521	1;173	5 increased
27	27	1061443	13 wks 2 days	1	2	G3P1A1	0	0	1	27.4	09-08-2021	1.4mm	1.04mom	62.5mm	1-	0.82pi	85mmhg	0.49mom	1.64mom	57.44	0.57mom	2600	0.52mom	30.1	36	1;1551	1:100000	1:00000	1;4496	1;979	1;139
28																															
29	28	1023905	13 wks 1 day	1	2	G5P1L1A3	0	0	0	29.3	24-08-2021	1.71mm	1.21mom	67.82mm	1-	0.6pi	98.5mmhg	0.38mom	0.89mom	25.84	0.79mom	2170	1.18mom	61.2	19+2	1;39870	1;00000	1;00000	1;65551	1;8806	1;607
30	28	1088231	12 wks 3 days	1	2	PRIMI	0	0	0	27.6	26-08-2021	1.34mm	1.03mom	58.99mm	1-	1.15pi	94.17mmhg	0.7mom	0.82mom	28.8	1.4mom	3160	0.93mom	40.3	38+6	1;100000	1:100000	1;100000	1;8816	1;1793	1;229
31																															
32	29	1081275	12 wks 5 days	1	2	PRIMI	0	0	0	21	24-08-2021	1.51mm	1.05mom	76mm	1-	1.01pi	89mmhg	0.8mom	1.3mom	42.28	1.05mom	3320	1.04mom	27.8	38+6	1;7990	1:100000	1;100000	1;640	1;186	0 increased
33	28	1087509	12 WKS	1	2	G2A1	0	0	0	22	18-06-2021	1.4mm	1.04mom	54mm	1-	1.53pi	88mmhg	0.54mom	0.72mom	25.14	0.8mom	2290	1.62mom	26.4	38+2	1;77066	1:100000	1;100000	1;100000	1;18021	1;1734
34																															
35	26	1089342	12 wks 4 days	1	2	G2P1L1	0	0	0	17.9	01-07-2021	1.37mm	1.03mom	61.33mm	1-	1.16pi	71.67mmhg	0.68mom	3.3mom	147	0.8mom	3220	0.68mom	33.1	39+2	1;1559	1;100000	1;100000	1;84601	1;14873	1;1529
36						G5L2L1A2																									
37	28		13 wks	1	2	PRIMI	0	1	0	20	15-12-2021	1.8mm	1.27mom	68mm	1-	1.01pi	86.67mmhg	0.67mom	2.34mom	98.9	1.5mom	7590	1.64mom	91.1	38	1;30013	1;100000	1;100000	1;89919	1;13026	1;1005
38	30		13 wks 2 days	1	2	G2P1L1	0	1	0	23.6	15-12-2021	1.6mm	1.11mom	71mm	1-	1.4pi	82.83mmhg	0.97mom	0.42mom	15.18	0.72mom	3510	1.45mom	85.7	37+6	1;100000	1;100000	1;100000	1;18699	1;3613	1;427
39	32		13wks 5 days	1	2	G2P1L1	0	0	0	26	30-12-2021	1mm	0.67mom	78mm	1-	1.86pi	84.83mmhg	1.35mom	1.62mom	45.65	1.14mom	5830	0.71mom	46.6	37	1;4564	1;100000	1;100000	1;562	1;188	NCREASED
40	21		12 wks 1 day	1	2	PRIMI	0	0	0	19	30-12-2021	1.1mm	0.89mom	56mm	1-	1.64pi	91.5mmhg	0.99mom	0.69mom	37.24	1.69mom	7520	2.08mom	93.6	38+3	1;100000	1;100000	1;100000	1;19552	1;3537	1;379
41	30		13 wks 3 days	1	2	PRIMI	0	0	0	20.2	03-01-2021	2mm	1.37mom	73mm	1-	1.98pi	81.67mmhg	1.39mom	0.41mom	13.19	1.21mom	6230	0.83mom	50.8	36	1;100000	1;100000	1;100000	1;2598	1;746	1;158
42	23		13 wks	1	2	PRIMI	0	0	0	37.3	20-01-2022	1.3mm	0.92mom	67mm	1-	1.45pi	83.17mmhg	0.99mom	1.91mom	59.82	2.63mom	8970	0.63mom	31.6	37+3	1;21711	1;100000	1;100000	1;767	1;230	NCREASED
43	19		12 wks 5 days	1	2	G2A1	0	0	0	30.2	20-01-2022	1.4mm	1.02mom	64mm	1-	1.84pi	85.33mmhg	1.17mom	0.82mom	36.48	1mom	4960	0.96mom	48.3	37	1;73514	1;100000	1;100000	1;806	1;237	NCREASED
44	30		13 wks 6 days	1	2	PRIMI	0	0	0	28.8	29-01-2022	1.55mm	1.04mom	77.9mm	1-	1.56pi	81.67mmhg	1.14mom	0.36mom	9.03	0.41mom	1870	0.79mom	52.1	37+2	1;82405	1;18411	1;38801	1;1602	1;457	NCREASED
45	24		12 wks 5 days	1	2	G2P1L1	0	0	0	20.9	11-08-2021	1.2mm	0.9mom	61mm	1-	0.88pi	86.67mmhg	0.5mom	1.47mom	73.55	0.83mom	4320	0.99mom	51.1	38+2	1;19533	1;100000	1;100000	1;26718	1;4384	1;407
46	26		13 wks	1	2	G3P2L2	0	0	0	31.6	09-08-2021	1.3mm	0.92mom	68mm	1-	0.92pi	83.33mmhg	0.57mom	0.5mom	17.14	1.1mom	3850	1.1mom	56.9	38+6	1;100000	1;100000	1;100000	1;33353	1;5378	1;486
47	35		12 wks 5 days	1	1	PRIMI	0	0	0	24	19-08-2021	1.6mm	1.18mom	63mm	1-	2.25pi	83.33mmhg	1.37mom	1.14mom	42.75	0.8mom	2640	1.36mom	68.6	38	1;17040	1;100000	1;100000	1;7108	1;1688	1;271
48	29		13 wks 6 days	1	1	PRIMI	0	0	0	21.3	03-06-2021	1.17mm	0.81mom	70mm	1-	0.92pi	83.33mmhg	0.56mom	4.62mom	166.6	0.67mom	4880	0.99mom	70.6	) FOL	1;745	1;100000	1;100000	1;27733	1;4700	1;458
49	26		12wks 4 days	1	2	PRIMI	0	1	0	19.6	11-12-2021	1.05mm	1.31mom	57.13mm	1-	1.18pi	90.17mmhg	0.73mom	1.17mom	60.48	0.69mom	8450	1mom	50.3	38+3	1;66565	1;100000	1;100000	1;7544	1;1565	1;205
50	29		12wks 3 days	1	2	PRIMI	0	1	0	20.3	31-01-2022	1.1mm	0.86mom	58mm	1-	1.8pi	85mmhg	1.14mom	0.56mom	26.55	0.63mom	2630	1.11mom	54	38	1;100000	1;100000	1;100000	1;4243	1;1044	1;176
51	26		12 wks 1 day	1	2	PRIMI	0	0	0	22.1	22-12-2021	1mm	0.8mom	56mm	1-	2.09pi	83.67mmhg	1.32mom	0.26mom	11.9	0.43mom	1340	0.4mom	17.3	37+3	1;100000	1;10404	1;28831	1;148	NREASED	NREASED
52	31		12 wks 6 days	1	2	G2P1L1	0	0	0	19.9	22-12-2021	1.5mm	1.08mom	65mm	1-	2.15pi	83.67mmhg	1.42mom	0.49mom	22.23	1.15mom	5860	0.87mom	47.7	38	1;100000	1;100000	1;100000	1;1290	1,393	NREASED
53	24		11 wks 5 days	1	2	G3P2L2	0	0	0	23.3	15-12-2021	1.2mm	1.07mom	50mm	1-	1.58pi	84.33mmhg	0.95mom	0.65mom	33.55	0.56mom	1530	0.57mom	22.5	37+6	1;28788	1;100000	1;100000	1;905	1;275	NREASED
54	30		13 wks 1 day	1	2	PRIMI	0	0	0	18.3	15-12-2021	1.6mm	1.12mom	69mm	1-	1.22pi	84mmhg	0.8mom	1.39mom	68.56	0.78mom	5370	o.8mom	48.2	36	1;8131	1;100000	1;100000	1;4551	1;1066	1;167
55	22		13 wks 3 days	1	1	PRIMI	0	0	0	20.4	18-11-2021	1.3mm	0.92mom	67mm	1-	1.81pi	84.33mmhg	1.19mom	2.39mom	95.54	0.97mom	6140	1.07mom	65.3	38	1;19609	1;100000	1;100000	1;3312	1;847	1;151
56	24		13 wks	1	2	PRIMI	0	0	0	21.6	18-11-2021	1.1mm	0.83mom	61mm	1-	1.76pi	84.17mmhg	1.13mom	1.12mom	45.83	0.52mom	2510	1.89mom	47.8	38+2	1;35241	1;100000	1;100000	1;2283	1;619	1;121
57	27		13 wks 2 days	1	2	PRIMI	0	0	0	17.1	22-11-2021	1.2mm	0.84mom	70mm	1-	1.7pi	87.17mmhg	1.13mom	0.47mom	22.39	1.6mom	11600	0.92mom	57.3	38+1	1;100000	1;100000	1;100000	1;2344	1;627	1;120
58	20		12wks 4 days	1	2	PRIMI	0	0	0	17.8	19-10-2021	1.41mm	1.05mom	62.2mm	1-	1.83pi	93.33mmhg	1.15mom	0.91mom	47.3	0.99mom	4960	0.83mom	40.6	38+1	1;87074	1;100000	1;100000	1;838	1;255	NREASED RISK)
59	22		13 wks 1 day	1	2	PRIMI	0	0	0	26.2	04-10-2021	1.4mm	0.98mom	69mm	1-	1.04pi	88.33mmhg	0.66mom	3.26mom	102.5	1.44mom	4730	1.88mom	96.9	38	1;68475	1;100000	1;100000	1;00000	1;20440	1;1375
60	30		13 wks 4 days	1	2	PRIMI	0	1	0	23.4	04-10-2021	1.5mm	1.02mom	76mm	1-	1.88pi	93.33mmhg	1.22mom	1.15mom	34.19	0.82mom	3440	0.83mom	50.9	37+6	1;9382	1;100000	1;100000	1;999	1;303	1;69
61	27		13 wks 4 days	1	2	G2P1L1	0	1	0	24	16-09-2021	1.1mm	0.87mom	57mm	1-	1.32pi	88.33mmhg	0.77mom	0.31mom	9.58	0.64mom	2870	1.99mom	122	37	1;100000	1;85072	1;100000	1;76166	1;11327	1;909
62	28		13 wks 4 days	1	2	G2P1L1	0	0	0	28.9	28-08-2021	1.8mm	1.24mom	72mm	1-	0.89pi	85mmhg	0.57mom	0.85mom	24.69	1.13mom	4530	2.39mom	144	37	1;100000	1;100000	1;100000	1;00000	1;44646	1;2257
63	20		12wks 4 days	1	2	G3P2L2	0	0	0	20	25-03-2021	2.1mm	1.56mom	62mm	1-	2.4pi	86.67mmhg	1.36mom	1.76mom	87.09	1.23mom	5760	0.91mom	44.1	) FOL	1;2095	1;100000	1;100000	1;1070		

SrNo	ANTENATAL COMPLICATIONS (0-NO, 1-YES): ABORTION (1-THREATENED, 2-COMPLETE, 3-MISSED, 4-INDUCED)	PRE ECLAM	PRE TER DEL	OLIGO	ABRUPT	PREVIA	GDM	JAUND	PROM	PPROM	PPH	FD	IUD	MODE OF DELIVERY	HTN DISORDER(1-YES, 2-NO)	TYPE	MEDICATION DURING DELIVERY	ECOSPRIN 75 TAKEN?(1-yes, 2-no)	INDICATION	SEX OF BABY	BIRTH WEIGHT (KG)	APGAR AT 5	CONGENITAL MALFORMATION (1-YES,0-NO)	NICU ADMISSION (1-YES, 0-NO)	SG A	FG R	NEONATAL COMPLICATIONS: STILL BRT	PRE MAT
1	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LASCS NOT W/F VBAC	M	2.8	8/10	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F VBAC	F	2.7	8/10	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.5	9/10	0	0	0	0	0	0
4	4	0	0	1	0	0	0	0	0	0	0	0	0	PV	2			2		M	0.1							
5	0	0	0	0	0	0	0	0	1	0	0	0	0	TV	2			1		F	3.3	8/10	0	0	0	0	0	0
6	0	1	0	0	0	0	1	0	0	0	0	0	0	PL	1	PRE ECLAMPSIA	TAB LABETALOL 200MG 1-1-1, TAB METFORMIN	1	UNCONTROLLED HTN , GDM	F	2.2	7/10	0	1	0	0	0	1
7	3	0	0	1	0	0	0	0	0	0	0	0	0		2			2	MISSED ABORTION									
8	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F VBAC	F	3.1	8/10	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	1	0	0	0	0	TV	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	1		F	2.7	6/10	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	PL	2			1	PREV LSCS NOT W/F VBAC	M	3.1	8/10	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	PREV LSCS IN LABOR	F	2.6	7/10	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PRECIOUS PREGNANCY	F	2.6	8/10	0	0	0	0	0	0
13																												
14	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.8	8/10	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.7	8/10	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F/ VBAC	F	2.6	7/10	0	0	0	0	0	0
17																												
18																												
19	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	1	PRE ECLAMPSIA	TAB LABETALOL 200MG 1-1-1	2		M	2.8	9/10	0	0	0	0	0	0
20	0	0	1	0	0	0	1	0	0	0	0	0	0	PL	2		TAB METFORMIN	1	GDM WITH MACRO	M	3.5	8/10	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.7	7/10	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F VBAC	F	2.8	8/10	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.6	7/10	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F VBAC	F	2.8	7/10	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CDMR	M	2.5	7/10	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	1		M	2.8	8/10	0	0	0	0	0	0
27	0	0	1	1	0	0	0	0	0	1	0	0	0	PL	2			1	ANAMNIOS	F	2.3	7/10	0	1	0	0	0	1
28																												
29	3														2				MISSED ABORTION									
30	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.9	9/10	0	0	0	0	0	0
31																												
32	0	0	0	0	0	0	0	0	0	0	0	0	0	TV				1		F	2.6	8/10	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	GEST HTN	TAB LABETALOL 100MG 1-0-0	2	SUSPICIOUS TRACE	F	2.8	9/10	0	0	0	0	0	0
34																												
35	0	0	0	1	0	0	0	0	0	0	0	1	0	TL	2			2	OLIGO WITH FD	M	2.5	8/10	0	0	0	0	0	0
36																												
37	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.8	9/10	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F VBAC	F	2.6	8/10	0	0	0	0	0	0
39	0	1	0	0	0	0	0	0	0	0	0	0	0	TL	1	PRE ECLAMPSIA	TAB LABETALOL 100MG 1-0-1	1	PREV LSCS WITH UNCONTROLLED	M	2.7	8/10	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.7	8/10	0	0	0	0	0	0
41	0	0	1	0	0	0	0	0	0	0	0	0	0	PV	2			2		M	2.2	7/10	0	1	0	0	0	0
42	0	1	0	0	0	0	0	0	0	0	0	0	0	TL	1	PRE ECLAMPSIA	TAB LABETALOL 200MG 1-1-1	1	SEVER PE	M	2.8	8/10	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.6	8/10	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	PRE ECLAMPSIA	TAB LABETALOL 100MG 1-0-1	1	CDMR	M	2.7	9/10	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NOT W/F VBAC	M	2.9	8/10	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			1		F	2.6	8/10	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	3.2	8/10	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0	0	LOSS TO FOLLOW UP									0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			1		F	2.7	8/10	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	1	CDMR	F	2.7	7/10	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.8	8/10	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	PRE ECLAMPSIA	TAB LABETALOL 100MG 1-0-1	1	PREV LSCS NOT W/F VBAC	M	2.6	9/10	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.8	8/10	0	0		0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0	0	PV	2			1		F	2.2	7/10	0	1	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.8	8/10	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.9	8/10	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.5	7/10	0	0	0	0	0	0
58														TL	2			1	CDMR	F	2.6	7/10	0	0	0	0	0	0
59	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.7	7/10	0	0	0	0	0	0
60														TV	2			2		M	2.5	8/`0	0	0	0	0	0	0
61	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.6	9/10	0	0	0	0	0	0
62	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.6	9/10	0	0	0	0	0	0
63		0	0	0	0	0	0	0	0	0	0	0	0							F			0	0	0	0	0	0

64	21		12 wks 2 days	1	2	PRIMI	0	0	0	21.2	08-04-2021	1.3mm	1.06mom	55mm	1-	2.26pi	81.67mmhg	1.28mom	2.35mom	102.6	0.93mom	2900	1.33mom	57.8	D FOL	1;44940	1;100000	1;100000	1;13670				0	0	0	0	0	0	0	0	0	0	0	0							F			0	0	0	0	0	0
65	26		12wks 3 days	1	2	G2A1	0	0	0	22	30-09-2021	1.37mm	1.09mom	56.78mm	1-	0.73pi	88.33mmhg	0.42mom	0.58mom	24.57	0.49mom	1620	0.65mom	30	38+2	1;42449	1;92900	1;90474	1;21789	1;3772	1;379	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.8	8/10	0	0	0	0	0	0
66	31		12wks 3 days	1	2	PRIMI	0	0	0	19.1	28-09-2021	1.16mm	0.9mom	58.92mm	1-	1.9pi	71.67mmhg	1.1mom	0.9mom	41.34	1.2mom	4590	0.73mom	35.4	37+3	1;62097	1;100000	1;100000	1;17434	1;4020	1;617	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.6	8/10	0	0	0	0	0	0
67	34		12 wks 6 days	1	2	PRIMI	0	0	0	28.2	17-09-2021	1.36mm	0.99mom	64.16mm	1-	1.66pi	86.67mmhg	1.04mom	0.96mom	30.28	1.49mom	3900	0.56mom	27.8	38+2	1;12006	1:100000	1;100000	1;1172	1;354	NREASED RISK)														TL	2			1	CDMR	F	2.7	8/10						
68	31		13 wks	1	2	PRIMI	0	0	0	16.4	03-09-2021	1.5mm	1.08mom	66mm	1-	0.64pi	75mmhg	0.37mom	0.84mom	41.62	0.59mom	3700	0.99mom	57.6	37+6	1;31753	1;100000	1;100000	1;100000	1;62392	1;3354	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	NPL	F	2.6	8/10	0	0	0	0	0	0
69	34		13 wks 4 days	1	2	PRMI	0	0	0	20.3	25-08-2021	1.6mm	1.09mom	73.33mm	1-	0.78pi	78.33mmhg	0.51mom	0.65mom	19.34	0.89mom	3750	0.82mom	51.4	38+2	1;31310	1:100000	1;100000	1;100000	1;32410	1;2400	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.8	8/10	0	0	0	0	0	0
70	37	1071891	12wks 3 days	1	2	G2P1L1	0	1	0	22.2	23-08-2021	1.2mm	0.97mom	56mm	1-	2.08pi	83.33mmhg	1.17mom	1.5mom	66.74	2.77mom	9990	1.61mom	79.5	38	1;100000	1;100000	1;100000	1;17573	1;3494	1;431	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.7	8/10	0	0	0	0	0	0
71	27		12wks 5 days	1	2	PRIMI	0	0	0	26.4	28-09-2021	1.24mm	0.92mom	62.11mm	1-	1.82pi	93.33mmhg	1.09mom	0.48mom	17.55	0.56mom	1810	1.43mom	69.2	37	1;100000	1;100000	1;100000	1;3972	1;928	1;145	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.6	7/10	0	0	0	0	0	0
72	37		12 wks 6 days	1	2	G3P1L1A1	0	0	0	27.3	27-09-2021	1.6mm	1.19mom	62mm	1-	1.6pi	78.33mmhg	0.98mom	0.58mom	20.44	0.42mom	1370	1.85mom	96.9	38	1;16238	1;7364	1;7209	1;51210	1;8549	1;814	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.8	8/10	0	0	0	0	0	0
73	31		13 wks 6 days	1	2	PRIMI	0	0	0	20.8	25-09-2021	1.5mm	1.05mom	69.72mm	1-	1.44pi	71.67mmhg	0.9mom	1.41mom	40.39	1.65mom	8220	0.92mom	62.3	38+6	1;19829	1;100000	1;100000	1;100000	1;18053	1;1861	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	NPL	M	2.7	9/10	0	0	0	0	0	0
74	24		13 wks 2 days	1	2	PRIMI	0	0	0	19.6	01-10-2021	1.61mm	1.12mom	70.74mm	1-	1.22pi	83.5mmhg	0.75mom	1.64mom	64.01	1.41mom	7730	1.44mom	84.1	37	1;74382	1;100000	1;100000	1;72627	1;11388	1;988	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.6	9/10	0	0	0	0	0	0
75	33		13 wks 4 days	1	2	G2P1L1	0	0	0	26.2	28-09-2021	1.15mm	0.85mom	63mm	1-	1.66pi	71.67mmhg	1.03mom	0.39mom	10.97	0.58mom	2180	0.88mom	53.8	37+3	1;100000	1;43263	1;63480	1;27235	1;5675	1;750	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	1	PREV LSCS WITH GEST HTN	F	2.6	9/10	0	0	0	0	0	0
76	29		12 wks 3 days	1	2	G2P1L1	0	0	0	26.8	05-10-2021	1.07mm	0.85mom	56.5mm	1-	1.53pi	88.33mmhg	0.9mom	0.97mom	35.47	0.7mom	1730	1.28mom	56.8	37+2	1;100000	1;100000	1;100000	1;13472	1;2688	1;333	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS	M	2.5	8/10	0	0	0	0	0	0
77	31		13 wks 6 days	1	2	PRIMI	0	0	0	18.4	09-10-2021	1.41mm	0.95mom	79.08mm	1-	1.73pi	76mmhg	1.23mom	0.34mom	12.22	0.52mom	3770	0.92mom	66.3	37+6	1;100000	1;42191	1;90144	1;6951	1;1741	1;301	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.6	8/10	0	0	0	0	0	0
78	26		13 wks 3 days	1	2	G2P1L1	0	0	0	26	16-10-2021	1.2mm	0.83mom	71.07mm	1-	1.29pi	76.67mmhg	0.92mom	0.37mom	10.8	1.11mom	38880	1.4mom	78.8	38+2	1;100000	1;100000	1;100000	1;99603	1;16167	1;1476	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.5	8/10	0	0	0	0	0	0
79	34		12wks 5 days	1	2	G2A1	0	0	0	28.8	16-10-2021	1.13mm	0.83mom	63.61mm	1-	0.99pi	85mmhg	0.64mom	1.78mom	84.06	1.11mom	5360	1.34mom	72	38+6	1;31960	1;100000	1;100000	1;16850	1;2918	1;293	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			1		F	2.7	9/10	0	0	0	0	0	0
80	32		12wks 5 days	1	2	PRIMI	0	0	0	23.8	19-10-2021	1.37mm	1.03mom	61,42mm	1-	2.19pi	80mmhg	1.44mom	1.05mom	42.15	1.33mom	4960	0.63mom	32.1	38+1	1;18446	1;100000	1;100000	1;789	1;265	NREASED RISK)														TV	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	2		M								
81	25		12 wks 3 days	1	2	PRIMI	0	0	0	27.2	23-10-2021	1.04mm	0.79mom	60.32mm	1-	1.74pi	80mmhg	1.15mom	3.04mom	110.5	2.36mom	5740	1.32mom	57.3	37	1;100000	1;100000	1;100000	1;24879	1;4943	1;609	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2		M			0	0	0	0	0	0
82	32		12wks 5 days	1	2	PRIMI	0	1	0	31.6	27-10-2021	1.53mm	1.12mom	63.27mm	1-	0.61pi	91.67mmhg	0.42mom	1.01mom	33.1	1.31mom	3250	1.69mom	79.9	36	1;100000	1;100000	1;100000	1;100000	1;24332	1;1305	0	0	1	0	0	0	0	0	0	0	0	0	0	PV	2			2		F	2.23	8/10	0	1	0	0	0	0
83	34	1108279	13 wks 2 days	1	2	G4P1L1A2	0	0	0	27.1	28-10-2021	1.52mm	1.14mom	61mm	1-	1.95pi	88.33mmhg	1.31mom	0.61mom	19.4	1.66mom	6360	0.84mom	48.6	37+1	1;83129	1;100000	1;100000	1;965	1;295	NREASED I	0	1	0	0	0	0	1	0	0	0	0		0	TL	1	PRE ECLAMPSIA	TAB LABETALOL 100MG 1-0-1	1	PREVIOUS LSCS WITH PE	F	3.49	9/10	0	0	0		0	0
84	26		13 wks 2 days	1	2	PRIMI	0	0	0	29.7	07-11-2021	1.28mm	0.9mom	68.94mm	1-	0.78pi	75.8mmhg	0.56mom	0.45mom	12.47	1.08mom	3090	1.2mom	63.2	38	1;100000	1;100000	1;100000	1;100000	1;29196	1;1966	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.6	8/10	0	0	0	0	0	0
85	34		13 wks 1 day	1	2	G2A1	0	0	0	19.3	09-11-2021	1.7mm	1.19mom	68.84mm	1-	0.88pi	73.33mmhg	0.6mom	0.81mom	31.91	0.51mom	2560	1.6mom	94.2	38+2	1;19438	1;48521	1;38289	1;100000	1;86238	1;4772	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.6	8/10	0	0	0	0	0	0
86	24		12 wks 3 days	1	2	G2P1L1	0	0	0	16	07-12-2021	1mm	0.89mom	54.81mm	1-	1.7pi	68.33mmhg	1.02mom	0.75mom	43.2	1.05mom	5420	1.13mom	55.4	38	1;100000	1;100000	1;100000	1;100000	1;17915	1;1851	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.5	8/10	0	0	0	0	0	0
87	26	1054081	13 wks 1 day	1	2	PRIMI	0	0	0	24.7	07-07-2021	1.5mm	1.05mom	69.77mm	1-	0.9pi	91.67mmhg	0.56mom	1.1mom	36.45	1.49mom	6900	0.61mom	36.2	37+3	1;23922	1;100000	1;100000	1;4616	1;1010	1;143	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	1	CDMR	M	2.65	8/10	0	0	0	0	0	0
88	34		12 wks 4 days	1	2	PRIMI	0	0	0	17.3	03-08-2021	1.42mm	1.06mom	61.55mm	1-	1.59pi	71.67mmhg	0.93mom	1.39mom	66.8	0.63mom	2820	0.36mom	18.8	37+6	1;314	1;100000	1;100000	11;3286	1;965	1;211	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CDMR	F	2.6	8/10	0	0	0	0	0	0
89	22	1065823	13 wks 3 days	1	2	PRIMI	0	0	0	22	21-07-2021	1.71mm	1.18mom	71.82mm	1-	1.17pi	73.33mmhg	0.74mom	0.93mom	22.2	0.98mom	30	1.46mom	559	37+3	1;35331	1:100000	1;100000	1;100000	1;36793	1;2611	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CPD	M	2.9	8/10	0	0	0	0	0	0
90	26	1089010	12 wks 6 days	1	2	PRIMI	0	1	0	21	22-07-2021	1.15mm	0.84mom	63.6mm	1-	0.54pi	85mmhg	0.33mom	0.67mom	21.56	1.35mom	3660	1.63mom	75.5	39+5	1;100000	1;100000	1;100000	1;100000	1;62850	1;2741	0	0	0	1	0	0	0	0	1	0	0	0	0	TL	2			2	PREV LSCS	F	3.08	8/10	0	0	0	0	0	0
91			12wks 5 days	1	2	prIMI	0	0	0	22	24-08-2021	1.3mm	0.96mom	62.47mm	1-	1.16pi	96.83mmhg	0.69mom	1.04mom	42.28	0.87mom	3320	0.54mom	27.8	38	1;7990	1;100000	1;100000	1;640	NREASED I	NREASED I	0	0	0	0	0	0	0		0	0	0	0	0	TL	2			1	CDMR	M	2.8	8/10	0	0	0	0	0	0
92	26	1069987	12 wks 1 day	1	2	G5P2L1A2	0	0	0	21	10-07-2021	1.06mm	0.86mom	55.22mm	1-	1.72pi	78.33mmhg	0.98mom	1.14mom	49.01	0.33mom	912	1.07mom	45.5	35+2	1;15542	1;45619	1;53431	1;12662	1;2709	1;372	0	0	1	0	0	0	0	0	0	0	0	0	0	PV	2			1		F	2.4	8/10	0	1	0	0	0	0
93	24	1093694	12 WKS	1	2	primi	0	0	0	22	18-01-2022	1.36mm	1.12mom	54.77mm	1-	1.02pi	65mmhg	o.64mom	0.57mom	25.14	0.78mom	2290	0.63mom	26.4	38+1	1;77066	1:100000	1;100000	1;00000	1;18021	1;1734	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.6	7/10	0	0	0	0	0	0
94	38	1125189	13 wks 3 days	1	2	PRIMI	0	0	0	20	20-07-2021	1.21mm	0.83mom	73mm	1-	1.12pi	78.33mmhg	0.72mom	0.48mom	15.57	0.75mom	3320	0.96mom	59.8	37+3	1;60238	1;50895	1;57886	1;40127	1;7134	1;746	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	PRE ECLAMPSIA	TAB LABETALOL 200MG 1-1-1	1	PE WITH UNCONTROLLED	F	2.8	8/10	0	0	0	0	0	0
95	27		13 wks 2 days	1	2	PRIMI	0	0	0	21	16/08/201	1.62mm	1.13mom	69.57mm	1-	0.77pi	78.33mmhg	0.47mom	0.61mom	22.49	0.97mom	4900	0.63mom	37.1	38	1;63267	1;100000	1;100000	1;74694	1;11958	1;1070	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.6	8/10	0	0	0	0	0	0
96	25	1093513	13 wks 1 day	1	2	G2P1L1	0	0	0	20	11-08-2021	1.35mm	0.94mom	70.33mm	1-	1.4pi	73.333mmhg	0.86mom	0.96mom	34.24	1.6mom	8460	1.04mom	62.6	37	1;100000	1;100000	1;100000	1;52602	1;9356	1;979	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NO W/F VBAC	M	2.6.	8/10	0	0	0	0	0	0
97	19	1069662	13 wks 2 days	1	2	pRIMI	0	0	0	19	19-03-2021	1.5mm	0.95mom	71.55mm	1-	1.2pi	74mmhg	0.4mom	2mom	77.77	1.75mom	10274	0.43mom	72.3	37	1;28909	1;100000	1;100000	1;100000	1;11327	1;1019	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			1		M	2.7	8/10	0	0	0	0	0	0
98	29	1118530	13 wks 5 days	1	2	PRIMI	0	1	0	20	22-12-2021	1.42mm	0.96mom	77mm	1-	1.02pi	82.33mmhg	0.75mom	0.31mom	8.85	0.71mom	3050	0.64mom	40.5	38+3	1;100000	1;100000	1;100000	1;6017	1;1390	1;214	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.8	8/10	0	0	0	0	0	0
99	29	1120273	12 wks 3 days	1	2	PRIMI	0	0	0	20	17-12-2021	1.22mm	0.93mom	60.21mm	1-	1.77pi	83mmhg	1.15mom	0.34mom	14.78	0.46mom	1570	0.71mom	33.5	38+1	1;100000	1;24806	1;42177	1;3277	1;903	1;180	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.8	8/10	0	0	0	0	0	0
100	19	1119189	13 wks	1	2	G2A1	0	0	0	20	21-12-2021	1.15mm	0.82mom	67.05mm	1-	0.88pi	81.67mmhg	0.6mom	0.92mom	30.31	2.8mom	10100	0.99mom	51.1	37	1;100000	1;100000	1;100000	1;78156	1;12046	1;1019	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CDMR	M	2.7	7/10	0	0	0	0	0	0
101	23	1115936	12 wks 6 days	1	2	PRIMI	0	0	0	21	04-12-2021	1.45mm	1.04mom	65.49mm	1-	1.12pi	101.67mmhg	0.73mom	3.03mom	32.4	0.69mom	3310	1.68mom	87.5	37+6	1;14100	1;100000	1;100000	1;12659	1;2306	1;250	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CDMR	F	2.67	9/10	0	0	0	0	0	0
102	23	109259	12 wks 2 days	1	2	PRIMI	0	0	0	19	08-12-2021	1.06mm	0.83mom	58.13mm	1-	1.76pi	83.33mmhg	1.1mom	0.33mom	16.12	0.84mom	3200	1.5mom	67.9	38+3	1;100000	1;100000	1;100000	1;21057	1;4174	1;512																			HYTEROTOMY DONE									
103	26	1122612	13 wks	1	2	G2A1	0	1	0	22	04-02-2022	1.14mm	0.81mom	67.05mm	1-	2.71pi	100mmhg	1.88mom	0.98mom	31.57	0.49mom	1590	0.32mom	16.5	38+1	1;2540	1;100000	1;100000	REASED	NREASED R	NREASED R	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	1	GEST HTN	TAB LABETALOL 100MG 1-0-0	1	CDMR	F	2.6	8/10	0	0	0	0	0	0
104	27		12 wks 3 days	1	2	PRIMI	0	0	0	20	11-01-2021	1.7mm	1.3mom	59.6mm	1-	1.96pi	75mmhg	1.25mom	1.08mom	47.11	0.93mom	3670	0.56mom	26.6	37+3	1;5599	1;100000	1;100000	1;2996	1;889	1;197	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.7	9/10	0	0	0	0	0	0
105	22		13 wks 3 days	1	2	PRIMI	0	0	0	18	31-01-2022	1.4mm	0.96mom	73.7mm	1-	1.47pi	80mmhg	1.02mom	1.12mom	34.78	3.01mom	14300	1.99mom	116	38	1;100000	1;100000	1;100000	1;100000	1;19300	1;1601	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.5	9/10	0	0	0	0	0	0
106	33		13 wks 2days	1	2	G2P1L1	0	0	0	21	19-02-2022	1.22mm	0.84mom	71.66mm	1-	0.77pi	81.67mmhg	0.54mom	0.59mom	18.73	0.52mom	2100	0.41mom	23.7	37+6	1;6959	1;54521	1;62442	1;3420	1;828	1;136	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NO W/F VBAC	F	2.6	8/10	0	0	0	0	0	0
107	24		13	1	2	PRIMI	0	0	0	20	11-12-2021	1.4mm	1mom	67.06mm	1-	1.48pi	75.83mmhg	0.99mom	1.34mom	54.8	2.36mom	11300	3mom	162	38	1;100000	1;100000	1;100000	1;100000	1;95778	1;5322	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	1	GEST HTN	TAB LABETALOL 100MG 0-1-0	2		M	2.8	8/10	0	0	0	0	0	0
108	37		12wks 4 days	1	2	G2P1L1	0	0	0	22	27-09-2021	1.6mm	1.19mom	62mm	1-	1.6pi	83.17mmhg	0.98mom	0.58mom	20.44	0.42mom	1370	1.85mom	96.9	37	1;16238	1;7364	1;7209	1;51210	1;8549	1;814	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	PREV LSCS NO W/F VBAC	M	2.9	9/10	0	0	0	0	0	0
109	28		12 wks 3 days	1	2	PRIMI	0	0	0	20	1/1021	1.41mm	1.09mom	59.1	1-	1.74pi	81.67mmhg	1.02mom	1.57mom	62.11	0.84mom	2730	1.36mom	64.9	38+1	1;43154	1;100000	1;100000	1;100000	1;46308	1;3841	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CDMR	M	2.5	9/10	0	0	0	0	0	0
110	34		13wks 1 day	1	2	PRIMI	0	0	0	20	09-11-2021	1.7mm	1.19mom	68.84mm	1-	0.88pi	87.17mmhg	0.6mom	0.81mom	31.91	0.51mom	2560	1.6mom	94.2	38+2	1;19438	1;48521	1;38289	1;100000	1;86238	1;4772	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.7	9/10	0	0	0	0	0	0
111	23		12 wks 6 days	1	2	G2A1	0	0	0	20	11-07-2022	1.6mm	1.15mom	66mm	1-	1.36pi	82.67mmhg	0.88mom	0.89mom	41.39	0.86mom	4550	1.89mom	106	CY CO	1;100000	1;100000	1;100000	1;68031	1;10732	1;940																												
112	31		13 wks	1	2	PRMI	0	0	0	21	11-07-2022	1.4MM	1.24MOM	67.82mm	1-	1.56PI	86.5mmhg	0.88MOM	0.89mom	46.56	0.88mom	4567	1.87mom	78	CY CO	1;100000	1;100000	1;100000	1;100000	1;100000	1;100000																												
113	31		12wks 6 days	1	2	primI	0	0	0	19	09-07-2022	1.9mm	1.36mom	66mm	1-	1.94pi	84.67mmhg	1.37mom	0.78mom	23.74	1.23mom	3370	1.55mom	83.3	CY CO	1;72594	1;100000	1;100000	1;11096	1;2442	1;350																												
114	29		13 wks 3 days	1	2	primi	0	0	0	18.5	16-06-2022	1.57mm	1.07mom	73.27mm	1-	1.01pi	89mmhg	0.71mom	0.56mom	20.24	1.46mom	8770	2.21mom	140	CY CO	1;100000	1;100000	1;100000	1;83111	1;11705	1;866																												
115	24		14wks	1	2	primi	0	0	0	20	18-06-2022	1.85mm	1.09mom	72.34mm	1-	1.03pi	87.5mmhg	0.76mom	0.54mom	18.76	1.56mom	8765	2.23mom	34.8	CY CO	1;100000	1;100000	1;100000	1;100000	1;100000	1;100000																												
116	32		13wks 1 day	1	2	primi	0	0	0	22	16-06-2022	1.33mm	0.93mom	69.54mm	1-	1.27pi	81.83mmhg	0.9mom	0.82mom	26.07	1.21mom	4560	1.13mom	62.8	CY CO	1;100000	1;100000	1;100000	1;36642	1;6794	1;756																												
117	30		12 wks 5 days	1	2	G2P1L1	0	0	0	22	16-11-2021	1.67mm	1.23mom	62.97mm	1-	0.92pi	83.17mmhg	0.62mom	0.84mom	30.22	1.12mom	3800	1.17mom	59.6	38	1;76716	1;100000	1;100000	1;100000	1;28647	1;2084	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NO W/F VBAC	M	2.6	8/10	0	0	0	0	0	0
118	23		12 wks 3 days	1	2	PRIMI	0	0	0	21	05-08-2021	1.05mm	0.81mom	59.12mm	1-	0.86pi	88.33mmhg	0.48mom	0.84mom	43.6	0.87mom	3980	0.32mom	15.5	37+6	1;12364	1;100000	1;100000	1;29250	1;5877	1;736	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.7	8/10	0	0	0	0	0	0
119	28		13wks 6 days	1	2	G2P1L1	0	1	0	20	03-08-2021	1.62mm	1.09mom	79.48mm	1-	2.04pi	89mmhg	1.38mom	1.04mom	25.8	1.4mom	5140	0.16mom	10	37+1	1;1827	1;100000	1;100000	1;117	1;53	1;21				0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LSCS NO W/F VBAC	F	2.7	9/10	0	0	0	0	0	0
120	31		12 wks	1	2	PRIMI	0	0	0	20	01-09-2021	1.15mm	0.95mom	54.15mm	1-	1.52pi	87.5mmhg	0.89mom	0.78mom	31.03	2.52mom	5210	0.75mom	30.4	38	1;100000	1;100000	1;100000	1;10760	1;2384	1;345	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		M	2.6	9/10	0	0	0	0	0	0
121	27		12wks	1	2	PRIMI	0	0	0	29	08-09-2021	1.18mm	0.97mom	54.43mm	1-	1.23pi	89mmhg	0.67mom	0.87mom	39.97	0.91mom	5220	1.61mom	90.9	38+2	1;100000	1;100000	1;100000	1;100000	1;33009	1;2236	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.5	9/10	0	0	0	0	0	0
122	26		13weeks	1	2	G2A1	0	0	0	22	16-09-2021	1.4mm	0.99mom	68.2mm	1-	1.06pi	88mmhg	0.64mom	1.04mom	41.05	0.43mom	1950	0.62mom	33.4	38+1	1;6557	1;100000	1;100000	1;23702	1;4681	1;571	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			2	CDMR	M	2.8	8/10	0	0	0	0	0	0
123	34		12wks 6 days	1	2	PRIMI	0	0	0	21	16-09-2021	1.6mm	1.16mom	65mm	1-	2.42pi	88.33mmhg	1.52mom	1.8mom	57.17	1.27mom	3790	1.37mom	71.3	38	1;18234	1;100000	1;100000	1;12185	1;2799	1;427	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.9	8/10	0	0	0	0	0	0
124	30		12wks 4 days	1	2	G2P1L1	0	0	0	22	17-09-2021	1.05mm	0.78mom	62.3mm	1-	1.3pi	98.5mmhg	0.76mom	0.84mom	35.75	1.58mom	6570	0.72mom	36.8	37+6	1;100000	1;100000	1;100000	1;8258	1;1834	1;266	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	1	GEST HTN	TAB LABETALOL 100MG 1-0-0	1	PREV LSCS NO W/F VBAC	F	2.6	9/10	0	0	0	0	0	0
125	26		12wks 6 days	1	2	G2A1	0	0	0	20	22-09-2021	1.51mm	1.1mom	64.68mm	1-	1.3pi	87.17mmhg	0.79mom	0.44mom	16.54	0.46mom	1710	1.01mom	51.5	38+1	1;100000	1;44887	1;54242	1;8522	1;1789	1;239	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.7	8/10	0	0	0	0	0	0
126	35		13 wks 5 days	1	2	PRIMI	0	0	0	23	21-04-2022	1.35mm	0.91mom	77.41mm	1-	1.76pi	88.33mmhg	1.29mom	1.48mom	49.32	1.56mom	7270	1.38mom	86.1	CY CO	1;24969	1;100000	1;100000	1;1071	1;299	1;61																												
127	21		13wks	1	2	G2A1	0	0	0	19	19-02-2022	1.3mm	0.92mom	68mm	1-	1.41pi	87.17mmhg	0.94mom	1.87mom	68.17	0.4mom	1860	0.48mom	25.9	38	1;488	1;100000	1;100000	1;1362	1;412		0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.7	8/10	0	0	0	0	0	0
128	26		11wks 2 days	1	2	PRIMI	0	0	0	20	18-03-2021	0.9mm	0.83mom	45mm	1-		76.67mmhg		3.58mom	144.8	1.24mom	3551.3	LOSS TO FOLI			1;22792	1;100000	1;100000				LOSS TO FOLLOW UP																											
129	32		12wks 2 days	1	2	PRIMI	0	0	0	22	11-06-2021	1mm	0.79mom	57mm	1-	1.54pi	87.5mmhg	0.91mom	0.64mom	24.69	0.6mom	1630	0.66mom	30.3	38+1	1;38713	1;100000	1;100000	1;9149	1;2156	1;341	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.6	9/10	0	0	0	0	0	0
130	26		12 wks 5 days	1	2	PRIMI	0	0	0	23	15-06-2021	1.5mm	1.11mom	63mm	1-	1.41pi	76mmhg	0.84mom	0.89mom	34.4	0.95mom	3300	0.93mom	45.5	37+6	1;78370	1;100000	1;100000	1;29446	1;5686	1;672	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.8	9/10	0	0	0	0	0	0
131	28		13wks 5 days	1	2	PRIMI	0	0	0	21	26-05-2021	1.45mm	0.98mom	77mm	1-	1.16pi	98.5mmhg	0.72mom	0.97mom	39.26	2.3mom	21200	1.62mom	124	37	1;100000	1;100000	1;100000	1;100000	1;91217	1;5309	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.8	9/10	0	0	0	0	0	0
132	20		12 wks 1 day	1	2	PRIMI	0	0	0	20	22-07-2022	1mm	0.8mom	56mm	1-	2.3pi	88.33mmhg	1.26mom	1.4mom	75.57	0.57mom	2220	0.99mom	43.2	CY CO	1;100000	1;100000	1;100000	1;100000	1;100000	1;100000																												
133	29		12 wks 6 days	1	2	G2P1L1	0	0	0	20	04-04-2022	1.5MM	1.08mom	66mm	1-	1.06pi	88.33mmhg	0.7mom	2.79mom	120.2	1.15mom	5480	1.4mom	75.2	37	1;20039	1;100000	1;100000	1;88073	1;13334	1;1098	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	M	2.6	9/10	0	0	0	0	0	0
134	21		13 wks 1 day	1	2	PRIMI	O	0	0	21	27-07-2022	1.7mm	1.19mom	68.89mm	1-	0.98pi	89mmhg	0.64mom	0.27mom	12.91	0.22mom	1450	0.68mom	41.4	y CON	1;100000	1;527	1;1818	1;5597	1;1250	1;183																												
135	31		12 wks 1 day	1	2	G2P1L1	0	0	0	20	01-04-2022	1.3MM	1.06mom	55mm	1-	2.2pi	88.33mmhg	1.44mom	1.11mom	48.94	0.36mom	804	1.03mom	40.9	CY CO	1;2564	1;33850	1;32445	1;1744	1;510	1;111																												
136	21		12 wks 2 days	1	2	PRIMI	0	0	0	21	19-02-2022	1mm	0.82mom	55mm	1-	1.16pi	88.33mmhg	0.73mom	4.78mom	213	2.56mom	8680	3.87mom	170	38	1;100000	1;100000	1;100000	1;100000	1;100000	1;5174	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	CDMR	F	2.8	9/10	0	0	0	0	0	0
137	20		12 wks 4 days	1	2	PRIMI	0	0	0	19	19-02-2022	1.5mm	1.14mom	60mm	1-	2.24pi	96.83mmhg	1.39mom	1.03mom	52.98	0.57mom	2930	2.11mom	104	38+2	1;73898	1;100000	1;100000	1;15224	1;3132	1;406	0	0	0	0	0	0	0	0	0	0	0	0	0	TV	2			2		F	2.6	9/10	0	0	0	0	0	0
139	30		13 wks 1 day	1	2	G2P1L1	0	0	0	20	20-02-2022	1.4mm	0.99mom	68mm	1-	1.23pi	97mmhg	0.85mom	2.47mom	81.36	1.16mom	4470	1.59mom	86.9	37	1;32728	1;100000	1;100000	1;39669	1;6679	1;644	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV LASCS NOT W/F VBAC	M	2.7	9/10	0	0	0	0	0	0
140	37		13 wks 2 days	1	2	G3P2L2	0	0	0	21	14-06-2021	0.6mm	0.46mom	59mm	1-	1.25pi	87.17mmhg	0.73mom	4.13mom	167.3	2.53mom	14700	2.13mom	134	38+3	1;12936	1;100000	1;100000	1;100000	1;16487	1;1144	0	0	0	0	0	0	0	0	0	0	0	0	0	TL	2			1	PREV2 LSCS	M	2.6	8/10	0	0	0	0	0	0

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