SERUM CA125 LEVEL IN NORMOTENSIVE AND PRE ECLAMPTIC PREGNANCIES IN A TERTIARY CARE HOSPITAL

By

Dr. SAHITHYA S MBBS

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Under the Guidance of

DR. SHEELA S. R.

PROFESSOR

Department of Obstetrics and Gynaecology

And Co- Guidance of

DR. SHASHIDHAR K.N.

Professor Department of Biochemistry

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR 563101

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Dr. SHEELA SR

Professor

Department of OBG

Sri Devaraj Urs Medical College,

Tamaka, Kolar.

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Date:

Place: Kolar

SIGNATURE OF THE CO-GIUDE

Dr.SHASHIDHAR .K.N.

Professor and Head of department

Department of Biochemistry

Sri Devaraj Urs Medical College,

Tamaka, Kolar.

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Dr. RATHNAMMA P

Associate Professor & HOD

Sri Devaraj Urs Medical College

Tamaka, Kolar

Dr. SREERAMULU.P. N

Principal

Department Of Surgery

Sri Devaraj Urs Medical College ,

Tamaka, Kolar

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SERUM CA 125 LEVEL IN NORMOTENSIVE AND PRECLAMPTIC PREGNANCIES IN A TERTIARY CARE HOSPITAL ABSTRACT Background: Preeclampsia is one main reason for high-risk pregnancy. Among the disorders in hypertension, preeclampsia develops in antenatal period and it is defined by high blood pressure of more than 140/90 mmHg and arteriolar vasoconstriction, both of which lower uteroplacental perfusion and ultimately lead to placental hypoxia. Objectives: 1. To estimate CA 125 level in normotensive and pre eclamptic pregnancies 2. To predict severity of Pre eclampsia with CA 125 levels with cut off value of CA125 level as 23.7IU/ml Material and method: This two year cross sectional study was conducted on all antenatal mothers between 20 -40 weeks gestational age getting admitted RLJH and research centre Tamaka (Jan 2021- Dec 2022), for the period of 2 years who fulfilled inclusion and exclusion criteria. Detailed clinical history along with antenatal examination was done. For each study subject the blood pressure was recorded. Complete blood picture was done and CA 125 levels were done of the study subjects. Results: The comparison of distribution of subjects with preeclampsia according to severity of preeclampsia: Antepartum Eclampsia [1 (2.0%) Preeclampsia] followed by Imminent eclampsia [5 (10.0%) Preeclampsia], Postpartum eclampsia [1 (2.0%) Preeclampsia], Preeclampsia [24 (48.0%) Preeclampsia] and Severe preeclampsia [19 (38.0%) Preeclampsia]. Conclusion: In the current study, we found a statistical significance in gestational age between two groups. The mean CA-125 among pregnancies with normal study subjects was observed to be significantly low when compared with preeclamptics in this study. Introduction Preeclampsia and it's spectrum of disorders affect 7.7% of primigravida women and it's a worldwide leading cause of fetomaternal complications which can also cause death of mother and fetus.1 Preeclampsia is one main reason for high-risk pregnancy. Among the disorders in hypertension, preeclampsia develops in antenatal period and it is defined by high blood pressure of more than 140/90 mmHg and arteriolar vasoconstriction, both of which lower uteroplacental perfusion and ultimately lead to placental hypoxia. Fetal growth may be hampered by persistent placental hypoxia.2 According to the WHO, preeclampsia kills over 10,000 women worldwide and is more common in developing nations (2.8%) than in industrialized ones (0.4%). Hypertensive diseases are estimated to be the cause of 16% of maternal deaths.3 Preeclampsia is associated with race and ethnicity; it is most prevalent in African-American and Hispanic patients, where it causes nearly 26% mortality of mothers., compared to 9% in African continent countries and Asian continent countries. Despite the fact that high-income countries have lower rates of maternal mortality than developing nations do, hypertensive disorders account for 16% of maternal mortality.4 Pregnancy-related hypertensive disorders during pregnancy are all thought to occur at a rate of 5.9% in the USA. According to reports, 8–10% of pregnant women in India get preeclampsia. In India, researchers found that the frequency of disorders in hypertension during antenatal period was 7.8%, with preeclampsia occurring in 5.4% of the population.5 Preeclampsia's underlying etiology is poorly defined, however the clinical appearance, diagnostic standards, and treatment of preeclampsia are all well understood. The hypothesis of aberrant placentation leading to severe maternal physiological dysfunction is a commonly accepted cause of preeclampsia. Preeclampsia's most well- supported etiology has been

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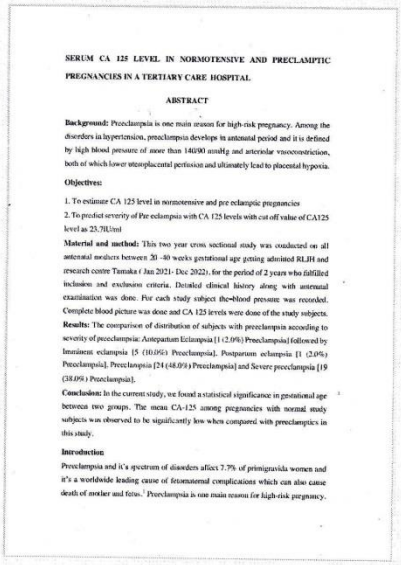

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Introduction

Preeclampsia and it's a spectrum of disorders affect 7.3% of primigravida women and it's a worldwide leading cause of fetomaternal complications which can also cause death of mother and fetus.[1] Preeclampsia is one main reason for high-risk pregnancy.

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DR. SAHITHYA S

ABBREViATIONS

CA125	– Cancer antigen 125
BP	– Blood Pressure
NK cells	– Natural Killer cells
MUC16	– Mucin 16, Cell Surface Associated Protein Coding Gene
SEA Domain	– Sperm protein, Enterokinase and Agrin Domain
LSCS	– Lower Segment Caesarean Section
NVD	– Normal Vaginal Delivery

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Preeclampsia and it's spectrum of disorders affect 7.7% of primigravida women and it's a worldwide leading cause of fetomaternal complications which can also cause death of mother and fetus.[1] Preeclampsia is one main reason for high-risk pregnancy. Among the disorders in hypertension, preeclampsia develops in antenatal period and it is defined by high blood pressure of more than 140/90 mmHg and arteriolar vasoconstriction, both of which lower uteroplacental perfusion and ultimately lead to placental hypoxia. Fetal growth may be hampered by persistent placental hypoxia.[2]

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Preeclampsia's underlying etiology is poorly defined, however the clinical appearance, diagnostic standards, and treatment of preeclampsia are all well understood. The hypothesis of aberrant placentation leading to severe maternal physiological dysfunction is a commonly accepted cause of preeclampsia. Preeclampsia's most well-supported etiology has been

linked to defective placentation, which causes placental ischemia, aberrant spiral artery remodelling, hypoxia, and oxidative stress.[6]

Risk factors for onset of hypertension and it's related complications during antenatal period include systemic lupus erythematosus, nulliparity, multiple pregnancies, history of increased blood pressure readings in prior pregnancy, history of increased blood glucose level during the antenatal period or prior to pregnancy, coagulation disorders, pre-pregnancy body mass index more than $30kg/m^2$, antiphospholipid antibody syndrome, older age of conception, deranged renal function, assisted reproductive technique's, and sleep-related breathing disorders.[7]

Preeclampsia can be diagnosed by (a) blood pressure measurements (i)systolic blood pressure of 140 mm Hg or more or (ii) diastolic blood pressure of 90 mm Hg in atleast two occasions of four-hour intervals after viability period with previous normal level of blood pressure. (Severe hypertension can be identified in a matter of minutes, enabling prompt antihypertensive treatment) and (b) proteinuria if the protein/creatinine ratio more than or equal to 0.3 mg/dL, or if the proteins measuring 300 mg or more in 24-hour urine collection. Dipstick reading of urine is 2+ or more (only used in the absence of better quantitative procedures).[8]

Preeclampsia in pregnancy almost every organ (liver, kidney, retina). Evidently, in preeclampsia, defective invasion of trophoblasts into maternal decidua results in vascular injury, which increases CA-125 expression.

CA-125, a biomarker frequently seen in ovarian malignancy of epithelial origin and among other pelvic diseases, pregnancy, and infections of upper genital tract. During first 14 weeks of antenatal period and after delivery there is an increase in its level. Elevated CA-125 level may be used as early indicator in pregnancy's outcome in cases of approaching loss and may represent the intensity of the inflammatory reaction in pre-eclampsia.

Studies have revealed that pre-eclampsia causes an increase in CA-125 levels. Ovarian tumors of epithelial origin and other healthy tissues of Mullerian origin express the glycoprotein antigen CA-125. The maximum CA-125 concentrations were found in ovarian malignancy patients, while other malignancies, benign diseases, and physiological circumstances such as pregnancies and women who are in their menstrual cycle may also be associated with high serum CA-125 levels. The fetal membrane, liquor amnii, and maternal uterine tissue involved in placenta formation are likely sources of the high levels of blood CA -125 during pregnancy. CA-125 can be used among other gynecological illnesses used in following up ovarian malignancy patients.[9]

Similar to that, some investigations found increased CA-125 in preeclampsia. According to reports, adenocarcinomas of the endometrium and endocervix as well as non-mutinous and mutinous ovarian carcinomas all include the CA-125 antigenic determinant. CA-125 is frequently expressed in benign ovarian tumors as well as endometriotic lesions in non-cancerous tissue. Invaginations and proliferations of the epithelium, as well as inclusion cysts, typically express CA-125 in healthy ovaries. It can be inferred that CA-125 expression is not unique only for ovarian malignancy. The presence of the CA-125 antigen has been found in benign and malignant tumor cystic fluids, benign and malignant pleural effusions, benign and malignant ascites, breast milk, seminal plasma, amniotic fluid, and cervical mucus. Many normal human epithelia likely secrete CA-125, and the antigen is lost from the cell surface, presumably by an active shedding mechanism. Both during menstruation and during first trimester of antenatal period, CA-125 levels can be remarkably high, exceeding 65 U/ml. A fast rise in levels above 300 U/ml has been seen during the start of menstruation, probably as a result of circulation of CA-125 during menstruation from the endometrial epithelial lining. Another explanation could be that the seeding of endometrial cells by retrograde menstruation in the abdominal cavity leads to localized inflammatory responses

and rise in CA-125. Utility of CA-125 test in differential diagnosis among different cancers appears to be minimal. CA-125 serum levels may function as prognostic indicators.[10] Serum CA-125 levels can be detected using one of two tests. The original test is a radioimmunoassay that uses OC125 monoclonal antibody to identify antigenic determinant factors on CA-125 glycoprotein. The OC125-like and M11 antibodies are utilized in the second-generation CA-125 test, which demonstrated increased precision and sensitivity but yielded few false positive results. Later studies contrasting two exams, meanwhile, did not demonstrate which testing technique was superior to the other.[11]

A healthy person's CA-125 level should be between 0 and 30 U/ml, and if it is more than 35 IU/ml, it raises ovarian malignancy suspicion as well as useful diagnostic tool for other gynecological illnesses.

In preeclampsia, CA125 concentration was significantly higher and it positively correlated with clinical parameters such as blood pressure and fetomaternal outcome. It is a biochemical diagnostic for the detection of preeclamptic pregnancies that has great specificity and sensitivity, with respective values of 93.7 and 88.0%.[12] Preeclampsia and CA-125 have been linked in a number of studies, but further research is needed to fully understand pathophysiology in preeclamptic women's increased serum CA-125 level.

In light of this, our goal is to look into serum CA 125 levels among normotensive and preeclamptic pregnancies at a tertiary care facility.

NEED FOR STUDY:

Preeclampsia is inflammatory syndrome involving multiple systems with less understood etiology. It affects 2-8% and a major cause of neonatal and maternal morbidity and mortality.[13]

In our health setup, many antenatal mothers are referred with late onset of preeclampsia. They remain undiagnosed and not investigated. Clinical studies related to use of CA125 level among hypertensive pregnant patients are limited.[14]

Hence I would like to do this study to determine CA 125 level as a biochemical marker in prediction and diagnosis of preeclampsia.[15] Because CA125 levels have a significant association with parameters: blood pressure level, uric acid cconcentration in blood and pre-eclampsia outcomes like oligohydramnios and intrauterine growth restriction, CA125 levels can be used to predict disease progression.[15]

Research question: Can CA125 Level help in prediction and diagnosis of preeclampsia?

Research hypothesis: To prove CA125 level as a marker of severity in preeclampsia

AIMS & OBJECTIVES

OBJECTIVES:

1. To estimate CA 125 level in normotensive and pre eclamptic pregnancies
2. To predict severity of Pre eclampsia with CA 125 levels with cut off value of CA125 level as 23.7IU/ml

REVIEW OF

LITERATURE

REVIEW OF LITERATURE:

Pregnancy-related hypertensive diseases are leading reasons for maternal complications and death along with neonatal complications and mortality. Preeclampsia is one important cause in high-risk pregnancies. Elevated blood pressure and constriction of arterioles are underlying problems of pre-eclampsia, which lower uteroplacental perfusion and eventually lead to placental hypoxia. Fetal growth can be hindered by prolonged placental hypoxia.[16]

The main cause leading to maternal and perinatal illness and death globally meant to be preeclampsia. When proteinuria and raised blood pressure appearing first time antenatally after viability period.[17] Along with elevated blood pressure and proteinuria when there are neurologic abnormalities, preeclampsia is considered severe. Thrombocytopenia, placental abruption, fetal growth restriction, hepatic dysfunction, renal impairment, and pulmonary edema are further criteria.

An unidentified etiology of preeclampsia syndrome is characterized by organ failure, proteinuria, and/or hypertension. The majority of the time, pathology shows signs of placental insufficiency along with anomalies including aberrant trophoblastic invasion of the endometrium and an inflammatory placental decidual vasculopathy. The most widely accepted theory for the pathophysiology of preeclampsia is that it is caused by defective trophoblastic invasion of placenta into maternal endometrium, which causes damage to the endothelium, decrease in the intravascular volume, persistent inflammation, and alteration in the vascular activity. An immunological reaction against maternal placenta and paternal origin antigens on fetus resulting to form hypoxic placenta and inflammatory mediators get secreted which affect endothelium.[18]

CA125 is one of these inflammatory mediators. CA125's sensitivity is good but less-specific tumor marker used to monitor treatment of ovarian cancer. CA125 antigenic determinant can

be recognized using OC125 murine monoclonal antibody and it is quantifiable via radioimmunoassay.[19] The CA125 significance in obstetrics is still not well known because the majority of clinical investigations that support its usage are very experimental and unrecognized. The fetal membrane, liquor amnii and maternal endometrium are major sources of serum CA125 during antenatal period and puerperium. Levels of CA125 raising during first fourteen weeks of antenatal period and returning to normal during second-trimister and third-trimester. CA125 from maternal endometrium and amniotic fluid enters maternal blood circulation when decidual cells are damaged during chorionic villus invasion in initial period of gestation, also when separation of placenta during third stage of labour. As result of underlying mechanism, CA125 levels rise in preeclamptic antenatal mothers is postulated to be an expansion of degradation of the decidua and separation of trophoblasts from degraded decidua.[20]

Preeclampsia is a multisystem disorder whose cause is not well known. Many patients with late-onset pre-eclampsia were sent to our healthcare system. They are still undiagnosed and not being looked into. There are few clinical trials on the use of CA125 levels in pregnant individuals with hypertension.

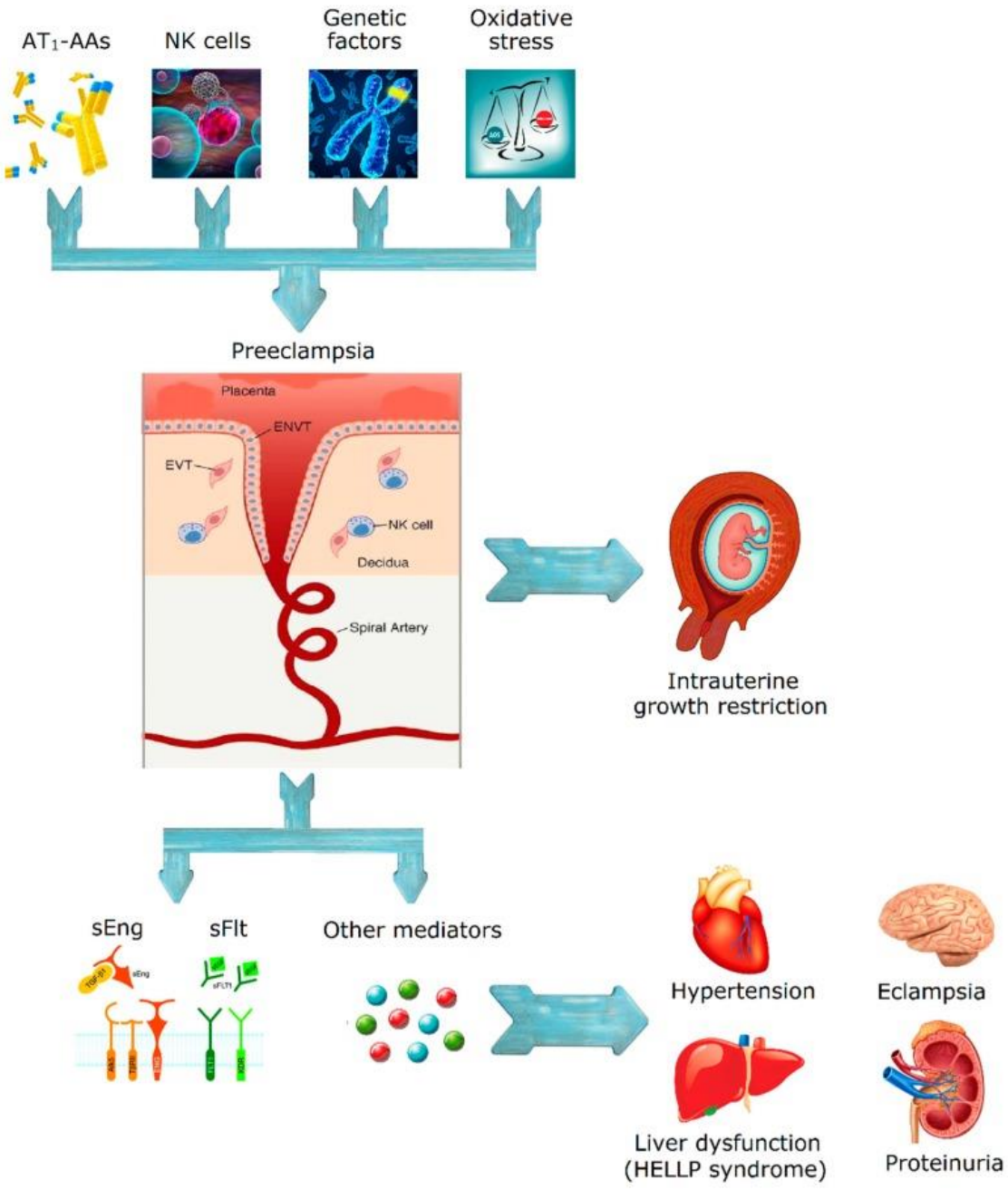


Figure 1: Proposed mechanism for pre-eclampsia and eclampsia.[21]

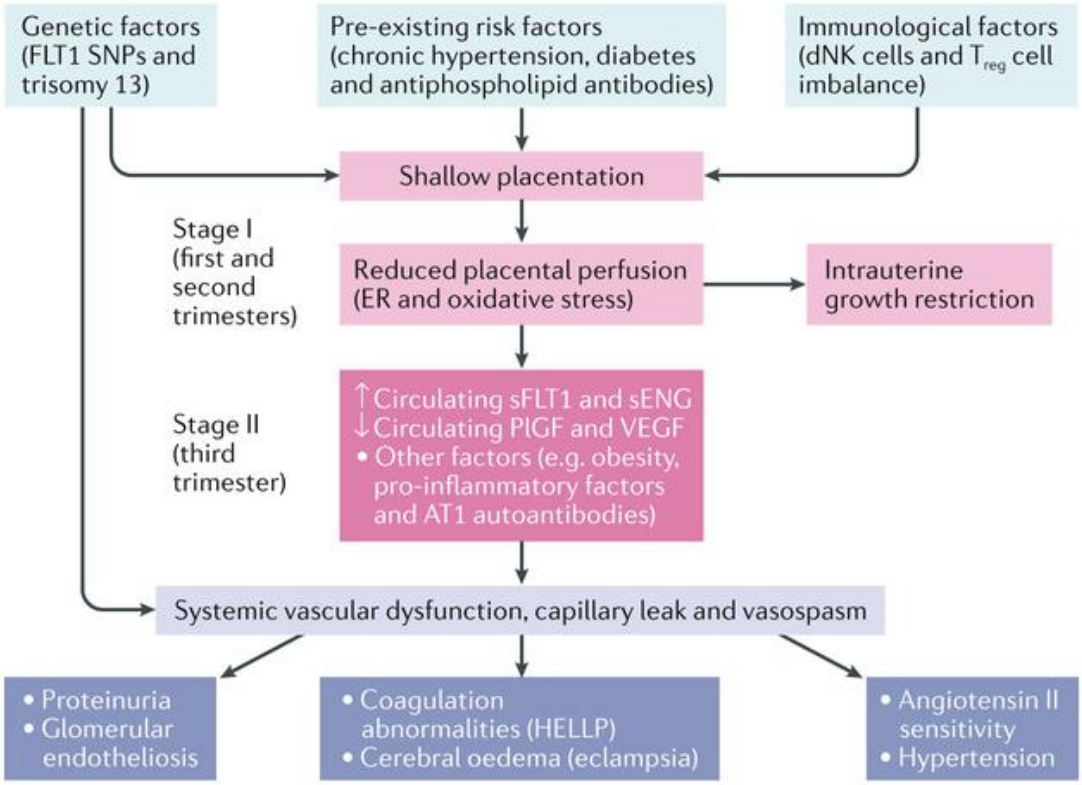


Figure 2:- The pathogenesis of pre-eclampsia.[6]

Therefore, our goal is to investigate CA 125 level as a biochemical marker in preeclampsia prediction and diagnosis.

Table 1:- Clinical features of preeclampsia.[21]

Systems	**Signs/Symptoms**
Neurological	Headache or light headedness Blurring of vision Convulsions
Renal	Loss of prteins in urine, reduced urine output, deranged renal function tests
Vascular	Elevated blood pressure
Cardiac and respiratory	Pain in chest breathlessness fall in oxygen level in blood

	Pulmonary edema
Hepatic	Deranged liver function tests icterus pain in epigastric region Nausea and vomiting
Hematologic	Haemorrhage Deranged coagulation profile or Consumptive coagulopathy Shock

Mild pre-eclampsia management.:[21]

The aim is to maintain blood pressure at less than 150/100 mmHg:

In the proposed expectant management, a preeclapmtic anetanatal mothers should maintain:

- Strict control of blood pressure
- Adequate rest
- inpatient management need should be assessed

Severe pre-eclampsia management.

Labetalol: First line drug

Initial dose- 20 mg IV over two minutes.

Repeat doses- 20–80 mg in ten minutes interval (total dose: 300 mg)

Maintenance infusion of 6 to 8 ml/hour (approximately from 2ml/hr to 12ml/hr depending on the patient's blood pressure range).

Nifedipine: Second line drug

- Dose starting from 10mg to 20 mg immediate-release forms (never consume sublingually)
- Hydralazine:

- 5 mg as IV bolus over 2 minutes
- Dose can be repeated in 20 minutes interval, until maximum of 20 mg
- Maintenance dose can be at the rate of 2 mg/hr

The CA 125 level can be utilized as predictor in assessing severity of preeclampsia because it positively correlates with clinical variables like blood pressure level and pre-eclampsia outcomes like oligohydramnios and fetal growth restriction.

Cancer antigen 125:

Antigenic membrane protein with large-molecular-weight glycoprotein known as CA 125. Cells from the coelomic epithelium express it in a few different tissues, including the peritoneum, pleura, and pericardium. The monoclonal antibody OC 125 was initially utilized by researchers to find CA 125, and numerous other antibodies were developed throughout the succeeding years. The CA 125 antigen is now recognized by three antibody subgroups that separately recognize non-overlapping epitopes. OC 125-like antibodies make up the initial category, which is followed by M-11- and Ov197-like antibodies..[9]

It is still unsure what the CA 125 membrane protein's fundamental role is. Recent research suggests that the oligosaccharides connected to CA 125 may contribute to cell-mediated immunity.[25] CA 125 may prevent the Natural Killer cells from cytotoxic reactions (NK cells).[26]

Under physiological circumstances, CA-125 gets expressed over the cell membrane, but CA125 does not have the ability to pass the junctional complexes of the cells and enter the circulation. The antigen is shed into the blood during pathological conditions linked to the rupture of this membrane barrier, which causes the levels of CA 125 to rise serologically.[27]

There are two procedures for measuring CA 125 concentrations.

(i) OC-125 monoclonal antibody- identifies antigenic determinants over cancer antigen 125 glycoprotein, is used in radioimmunoassay.

(ii)OC 125-like and M 11 are the two antibodies used in second-generation CA 125 test.[28]

STRUCTURE AND FUNCTION OF CA125:

CA125 Gene:

It was discovered CA 125 is glycoprotein of plasmalemma with several splice-site variants which share same transmembrane domains after two groups of researchers successfully cloned the gene encoding the CA125 protein.[29] Due to CA125's resemblance to mucin, the gene was given the moniker MUC16. This characteristic consists of C-terminal non-tandem repeated sequence with one probable membrane-spanning protein domain and site that can undergo tyrosine protein phosphorylation, as well as N-terminal section involving nine tandem repeats (156 amino acids each) with high serine, threonine, and proline contents. Evolution has preserved CA125.[30]

CA125 was discovered to be an O-linked cell membrane glycoprotein of mucin type, with a molecular weight estimated to range around five million Daltons influenced by natural conditions.[31] However, smaller subunits of proteins got reported.[32] The size and charge of CA125 are both diverse. The oligosaccharides associated with CA125 exhibit peculiar characteristics, including the production O-GalNAc Glycans and strong N-linked glycosylation.[25] There have been several descriptions of CA125 subspecies, however, it is unknown if any of them are connected to certain bodily states.

The primary CA125 subunit still has the ability to bind M11 class and OC125 class antibodies. CA125 has denatured, purified subspecies that show evidence of autoproteolysis;

this is most likely because the molecule possesses an endogenous protease activity. The signal transduction pathway of epithelial growth factor receptor gets directly connected to the release of CA125. Prior to being released from cultured cells, the transmembrane domain of CA125 is phosphorylated at either/both serine and threonine, which causes the membrane surface to be cleaved by a potential extracellular protease.[29] The SEA domains in the glycoprotein mucin16 appear to have similarity with one another than to any other SEA domains, indicating that SEA domains get multiplied following the appearance of MUC16.[34]

In 2000, N Aslam et al. tested the maternal blood CA125 levels in 188 women who were carrying healthy babies from 11 to 14 weeks of pregnancy. On ultrasound inspection, it was noted that the ovaries of each woman were morphologically normal. With gestation, the median blood CA125 levels remained constant at 23.4 U/mL. They come to the conclusion that CA125 level rise during first trimester of antenatal period and that pregnant women cannot utilize cutoff values to analyze characteristics of ovarian masses in non-pregnant women.[35]

In a **2009 study by Fatma Bahar Cebesoy et al.**, included fifty-four preeclamptic/eclamptic women and fifty-six antenatal subjects with good health. Study group(preeclamptic/eclamptic women) had relatively high CA-125 level. Researchers also observed that significantly higher CA 125 in severe preeclampsia and eclampsia groups than in the moderate preeclampsia group. CA-125 causes an increase in preeclampsia.[14]

242 women had singleton pregnancies in 2011, according to **Mustafa Ozat et al**. Study participants divided as three groups: control group (hundred subjects), preeclampsia with moderate features group (seventy-eight subjects), and preeclampsia with severe features

group (sixty-four subjects). CA-125 serum concentrations had absolute association with blood pressure level, platelet concentration in blood, uric acid in serum and proteins in urine concentrations. They concluded CA-125 indicates severity of preeclampsia. Because it's easily accessible it helps in detection of preeclampsia. As a result, identified CA-125 cut-off value 50 IU/ml helped in screening for preeclampsia.[12]

Aruna Bhattacharya et al. reviewed 48 women who had only one pregnancy in total in **2014**. They were divided into three groups: controls (n = 40), subjects in group of preeclampsia with mild featured s(n = 38), and study subjects of preeclampsia with severe features (n = 10). In terms of age of antenatal study subject, period of gestation as well as body mass index, all three groups were statistically comparable. They proposed CA-125 (with cut-off value 50 IU/ml) as biochemical marker in assessing severity of inflammation in preeclampsia. There is a satisfying reason that preeclampsia may cause CA-125 release inside placenta due to decidual damage and defective trophoblastic invasion.[36]

In **2014, Erbil Karaman et al** investigated 91 ladies who had given birth to a singleton baby. Subjects are divided into severe group of pre-eclampsia and mild group pre-eclampsia and both had their CA-125 serum concentrations checked. Control group consisted antenatal study subjects in good health(n = 31). In comparison to the groups with moderate preeclampsia and controls, the group with severe preeclampsia CA-125 level was considerably greater. Blood pressure and proteinuria had favorable correlation with CA-125 levels. Contrarily, the birth weight and gestation at birth had negative correlation with CA-125 serum concentrations. In conclusion, severe group of pre-eclampsia study subjects associated with an elevated CA-125 level, which indicated aberrant trophoblastic invasion and ongoing inflammation. When CA-125 increased in those antenatal mothers who are

having increased blood pressure readings, it may indicate that the patient's condition is severe.[37]

Rattapon Amampai et al study .'s from **2018** comprised 136 women; of these, 87 instances had blood tests for estimation of CA-125 among different trimesters of antenatal study subjects. Median CA-125 reported as 16.44 and 16.76 in first trimester and second trimester, with a range of 5.94 to 77.54 IU/ml and 5.2 to 5.81 IU/ml. In first trimester, only 9.1% of study subjects displayed abnormality in CA-125 level, and in second trimester, just 1 case did the same. Few normal pregnancies, they found, displayed increasing CA-125. The adnexal lesion should be looked at if it is high in pregnant women for any reason.[38]

Preeclampsia was detected in 70 women in **2018**, according to **Gbemisola E. Osanyin et al**., and in 70 antenatal subjects with good health as controls who matched age, past obstetric history and antenatal gestation. Women with preeclampsia had mean serum CA125 levels that were considerably higher than those with normal pregnancies. Additionally, there was a favorable association between CA-125 level and following measurements: platelet count, blood pressure and urine protein levels. The three participant categories in the study had different CA125 levels: normotensive control, mild preeclampsia, and severe preeclampsia. They came to the conclusion that preeclampsia and its severity are related to elevated maternal blood CA 125 levels.[39]

Studies conducted by Geya Gottipati et al., in 2019 in south Indian costal region,165 subjects with a division as three study groups: pre-eclamptics subjects group, gestational hypertension subjects group, and antenatal subjects in good health group, with 55 subjects in each group documenting a higher mean value of CA125 of 56.7 IU/mL in

preeclampsia comparitively. Cancer antigen-125 had good association with many clinical parameters as well as blood parameters. Further, there was a strong association between increasing CA-125 and reduced amniotic fluid level, intrauterine growth restriction and onset of illness. But adverse association with platelet concentration and neonates' weight at the time of birth was observed. Study concluded cancer antigen 125 indicates severity of illness and can be used in screening of preeclampsia. Statement was restricted with a mention that rising trend in CA-125 levels also marks the progression of disease.[15]

Bijoya Mukherjee et al., in 2020 conducted a study in a tertiary care hospital in West Bengal, involving forty study subjects with no severity in pre-eclampsia, forty study subjects with severity in pre-eclampsia and forty antenatal subjects of good health. At recruitment, the study subjects were matched for the following: (i) age (ii)parity (iii)gestational age. The concentration of CA-125 in the three participant categories were: normotensive (15.76+/-2.95IU/ml) mild pre-eclampsia (26.98+/-2.28IU/ml), and severe pre-eclampsia (44.99±11.23IU/ml), p-value less than 0.001. The levels of CA125 adversely correlated with cconcentration of platelets and neonate's weight at the time of birth, favorably with systolic blood pressure. So cut-off CA-125 was recognized to be 35 IU/mL which was highly specific and sensitive with strong positive predictive value and strong negative predictive value.[40]

In **2020**, 97 antenatal subjects without preeclampsia were recruited to be as controls and 97 antenatal subjects with pre-eclampsia were recruited to be as cases by **Yetunde Bolatito Aremu-Kasumu et al**. The respondents' ages ranged from sixteen to forty-five. The control, severe preeclampsia, and control groups had respective mean ages of 28.6 ±5.9, 27.9 ±7.5, and 28.7 ± 7.2 years. Preeclampsia subjects mean CA125 was higher than control group (36.13± 23.02 vs. 24.53 ± 9.42). p= 0.001 indicates significant difference between mean

CA125 in severe and moderate preeclampsia (45.68± 23.38 vs. 21.94 ± 13.18). The mean arterial pressure was 112.82± 3.55 mmHg and 130.63 ± 12.87 mmHg in mild and severe preeclampsia, respectively. There was a very slight positive connection between the mean arterial pressure and CA125.[41]

METHODOLOGY

MATERIAL AND METHODS

SOURCE OF DATA:

Pregnant women between 20 -40 weeks gestational age admitted at RLJH and research center, Tamaka complying with inclusion criteria and exclusion criteria

STUDY DESIGN: CROSS-SECTIONAL STUDY

STUDY PERIOD- 2 YEARS (January 2021-December 2022)

Sample size: total n= 100, normotensive n=50 and preeclamptic pregnancy n=50

Sample size is calculated based on CA 125 levels as an indicator for preeclampsia with reference to the study conducted by Gottipati Geya, Kantharaju Supriya published in "Journal of South Asia Federation of Obstetrics and Gynaecology: A prospective analysis performed in a tertiary care hospital, Mangaluru"[15]

Considering alpha error of 1% with power of 90%, the estimated sample size was derived at n= 50 in normotensive group and preeclampsia group at n=50.

The sample size was calculated using nMaster 2.0 software.

The sample size calculation included allocation of subjects as per BP recording as high or normal.

INCLUSION CRITERIA

Study subjects were proposed at the start of study to be between 20 to 35 years with gestational age between 20 weeks – 40 weeks. However, the lowest was we could document was 18 years and the upper age limit was 37years

- Preeclampsia
- Singleton pregnancy

EXCLUSION CRITERIA :

Pregnant women with risk factors such as

- Chronic hypertension
- Renal disease
- Multiple pregnancy

METHODOLOGY :

After taking written informed consent from study participants after confirming about inclusion criteria and exclusion criteria. Patient information sheet to the study subjects of their understandable language was given.

Fifty normotensive and fifty pre-eclamptic subjects were recruited for the study. Detailed clinical history of the study subjects along with antenatal examination was done. For each study subject the blood pressure was recorded. Study subjects with first recorded increased BP reading were repeated one more reading of blood pressure after an interval of four hours and that BP reading was documented. Urine was examined for proteinuria. Complete blood picture was done to all study subjects white blood cell count, platelet count and CA 125 levels were done of the study subjects. It's not follow up study. No serial monitoring of

CA125 concentration was done. Only at admission time blood sample for CA125 was taken and estimated. The entire procedure for the CA125 has been done using electrochemiluminescence instrument no 5600which is a blended version of biochemistry with electrochemiluminescence and this methodology is comparable with the ELISA method and also accuracy of the method was compared with other methods. As per the kit inserted and methodology that has been supplied, relationship between methods determined using Passing-bablok regression. However, the chemiluminescence value was correlated well with the other methods. Hence it is feasible at our institution and kits are readily available and routinely we are doing, so the present study was carried out by electrochemiluminescence for CA125 estimation. The immunometric immunoassay technique used in the CA125 immunodiagnostic system includes the simultaneous interaction of OC125 defined antigen found in sample with biotinylated antibody known as " M11 mouse monoclonal anti-OC125 defined antigen" as well as a horse radish peroxidase labeled conjugated antibody known as "OC125 mouse monoclonal anti OC125 defined antigen". Streptavidin on the wells captured the antigen-antibody complex. The unbound particles were removed automatically through gentle washing. A luminescent reaction was used to determine the bounded horse radish peroxidase conjugate. The luminescent reagents such as luminal derivative and peracid salt and electron transfer agent were added to wells using an automated method. The luminal derivative gets oxidized by horse radish peroxidase in a bound conjugate producing light. Acetanilide, an electron transfer agent, increases the amount of light produced and lengthens its emission. The system read the light signals. The concentration of OC125 defined antigen in serum sample is directly linked to quantity of horse radish peroxidase conjugate bound. The methodology that has been used is immunometric immuno assay by using VITROS ECI 5600 with an incubation time of 29 minutes and the time of first result is around 37 minutes with a test temperature of 37 degrees Celsius by using the reaction sample volume of 25ml.

The limit of detection of CA125 level is 5.5 to 1000 IU/ml. An assessment of CA125 levels was done in normotensive study subjects and study subjects with pre-eclampsia. A correlation between CA125 levels and the severity of pre-eclampsia was also carried out. Efforts were made to prove CA125 levels are elevated in pre-eclampsia study subjects more than in normotensive study subjects. The proposed outcome of this study was to prove CA125 can also be used as a biochemical marker in pre-eclampsia to predict, diagnose and assess the severity.

STATISTICAL ANALYSIS:

Data entered in Microsoft excel and analyzed using SPSS-22 increased version software. Frequencies and proportions used to represent categorical data. To test the significance of qualitative variables, Chi-square test or Fischer's exact test used.

Mean +/- standard deviation used in showing continuous variables. **Independent t-test** used as statistical test to determine difference in mean among two quantitative variables.

Receiver operating characteristic (ROC)curve was constructed for CA 125 and preeclampsia. For the determination of (i)specificity (ii)sensitivity (iii)positive predictive value (iv)negative predictive value, receiver operating characteristic (ROC)curve with optimal cut-off values were chosen. The test was interpreted based on a prediction of overall result and area under ROC curve of value 0.5. A greater than 0.8 area under ROC curve indicated reasonable prediction.

Graphical representation of data: Data graphs were created using MS Excel and MS Word

p value of less than 0.05 considered statistical significance.

Statistical software: To analyze data, MS Excel and SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA) were used.

RESULTS

RESULTS

Table 2: Age-case frequency Distribution.

	Normal		Preeclampsia		P value
	N	%	N	%	
18-22yrs	13	26.0%	24	48.0%	0.022
23-27yrs	23	46.0%	13	26.0%	0.037
28-32yrs	12	24.0%	9	18.0%	0.461
33-37yrs	2	4.0%	4	8.0%	0.399

In age frequency distribution, with lower limit of age as 18 years and with upper limit as 37 years, the study subjects were distributed under fixed interval. p-value 0.067, no statistical significance between the two groups with respect to age. Twenty-four (48%) preeclamptic subjects were belonging to early age group of 18-22 years. This indicates that lower age group had higher risk in devolping preeclampsia whereas literature says advancing maternal age is aalo risk factor in preeclampsia.

Figure 3:- Graph representation Age-case frequency Distribution

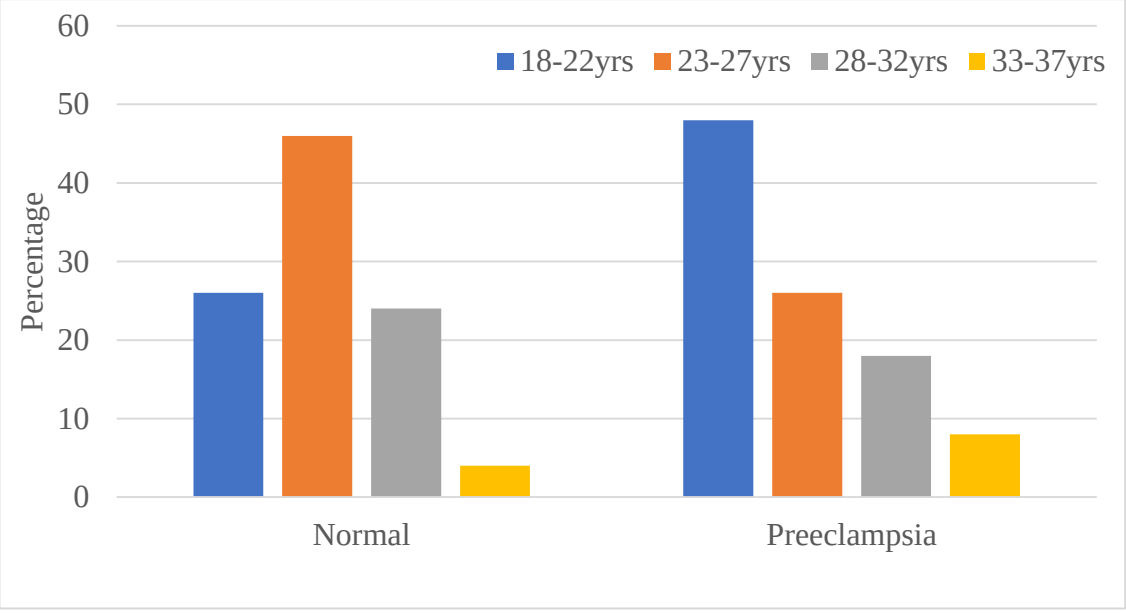


Table 3:- Parity case frequency distribution.

	Normal	Preeclampsia	Total	p value
Primi gravida	20	30	50	0.131
	40.0%	60.0%	50.0%	
Gravida 2	17	12	29	
	34.0%	24.0%	29.0%	
Gravida 3	6	6	12	
	12.0%	12.0%	12.0%	
Gravida 4	7	2	9	
	14.0%	4.0%	9.0%	

Thirty preeclamptic subjects were primigravida constituting the maximum of the study population about 60%. p-value of 0.131 indicates no statistical significance between two groups in aspect of parity.

Figure 4:- Graph showing Distribution of subjects according to parity between two groups.

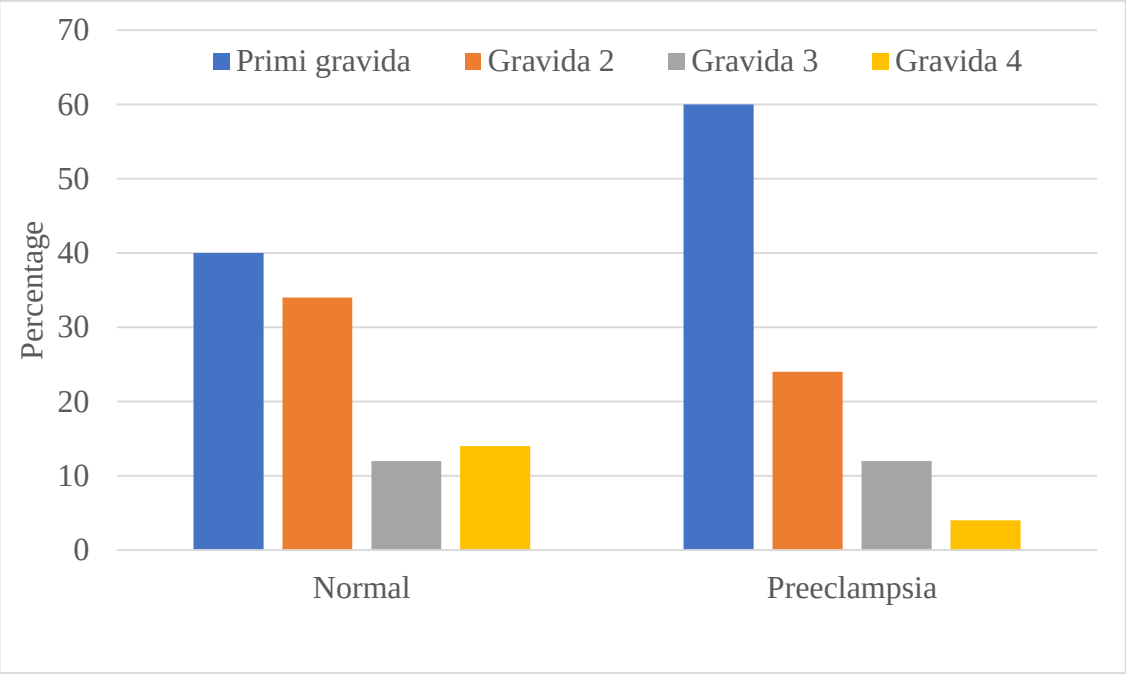


Table 4:- Gestational age-case frequency Distribution.

	Normal		Preeclampsia		P value
	N	%	N	%	
29-32weeks	4	8.0%	4	8.0%	1.00
33-36weeks	4	8.0%	15	30.0%	0.005
37-40weeks	40	80.0%	31	62.0%	0.047
41-44weeks	2	4.0%	0	.0%	0.468

In preeclampsia, the maximum number of subjects (31 cases) belonged to term gestation of 37-40 weeks of about 62%. p-value of 0.023 indicates that there was statistical significance found between two groups in aspect of gestational age

Figure 5:- Graph showing Gestational age-case frequency Distribution.

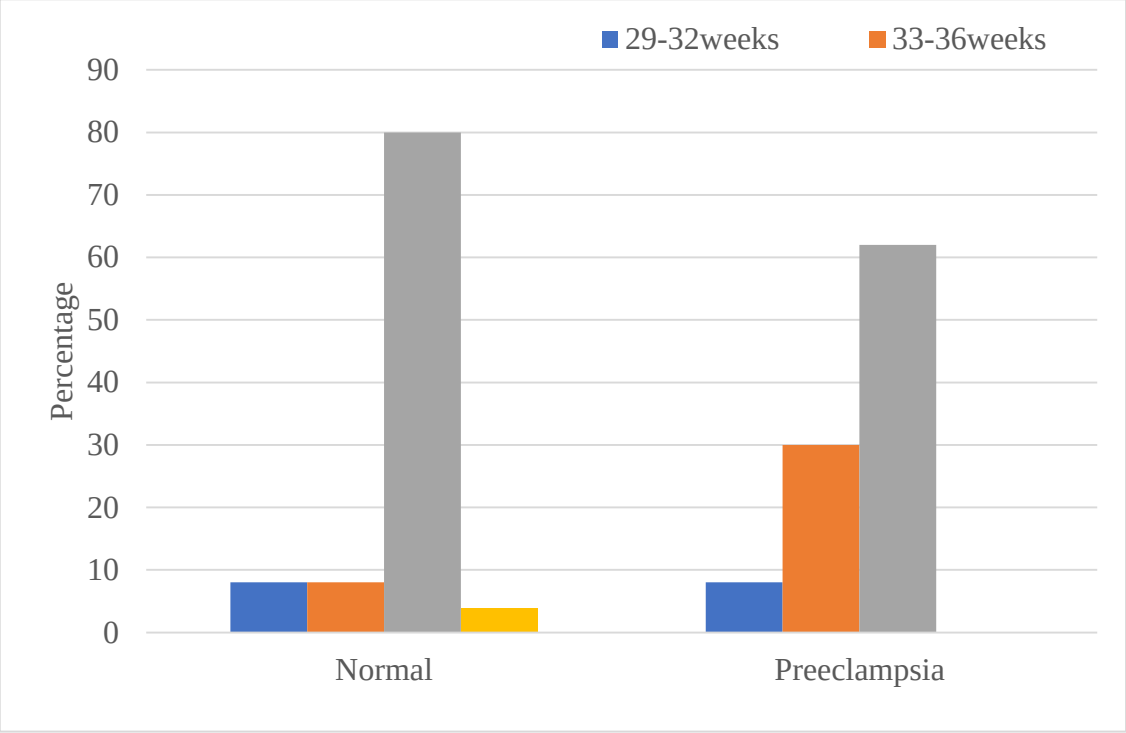


Table 5:- Mode of delivery- case frequency Distribution.

	Normal	Preeclampsia	Total	p value
Lower segmen caesarean section	38	29	67	0.088
	76.0%	58.0%	67.0%	
Vaginal delivery	12	21	33	
	24.0%	42.0%	33.0%	

p-value 0.088, indicates that no significant difference seen statistically among two groups in aspect of mode of delivery

Figure 6:- Graph showing Mode of delivery- case frequency Distribution.

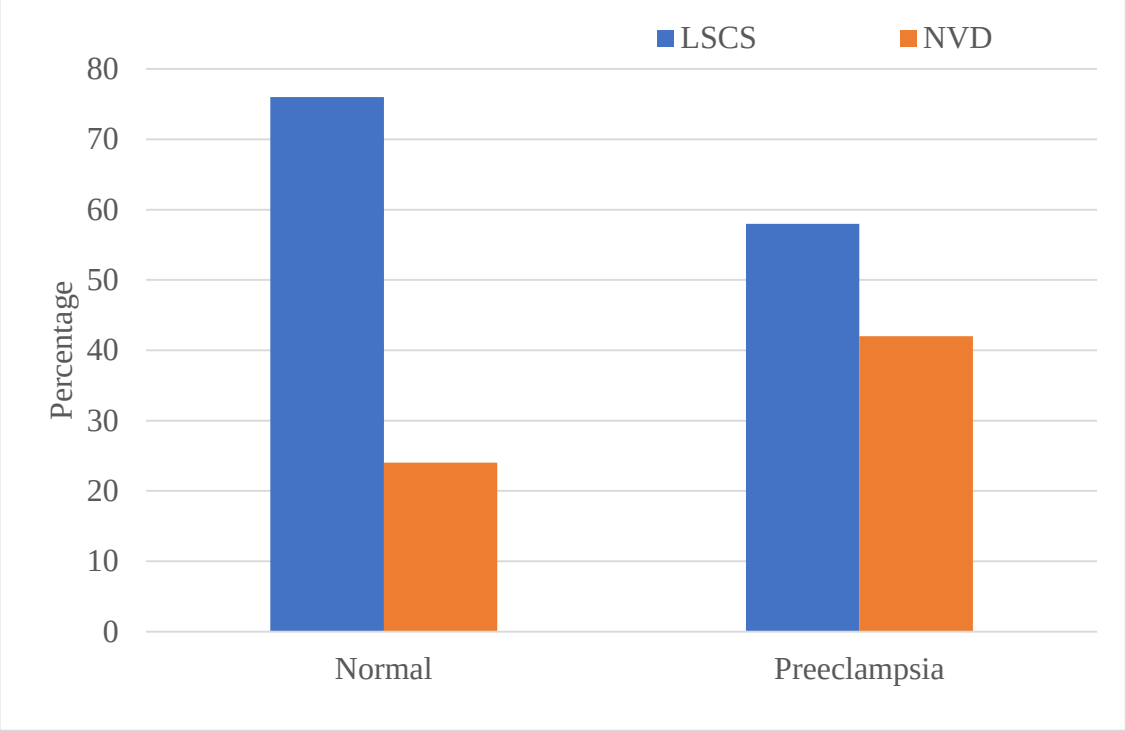


Table 6:- Indications for LSCS between two groups.

	Normal		Preeclampsia	
	N	%	N	%
Anhydroaminios	1	3.0%	0	.0%
Breech	1	3.0%	1	3.4%
Caesarean Delivery Under Maternal Request	2	6.1%	3	10.3%
Contracted Pelvis	1	3.0%	2	6.9%
Cephalopelvic disproportion	1	3.0%	1	3.4%
Transverse Lie	1	3.0%	0	.0%
Epilepsy	1	3.0%	0	.0%
Fetal Distress	11	33.3%	15	51.7%
Failed Induction	0	.0%	2	6.9%
Gestational diabetes	1	3.0%	0	.0%
Hydrops Fetalis	1	3.0%	0	.0%
Non Progression	1	3.0%	1	3.4%
Placenta Accreta	1	3.0%	0	.0%
Previous LSCS	10	30.3%	4	13.8%

In both preeclamptic and normotensive study groups, fetal distress was one frequent indication for LSCS.

Figure 7:- Comparison of indications for LSCS between two groups.

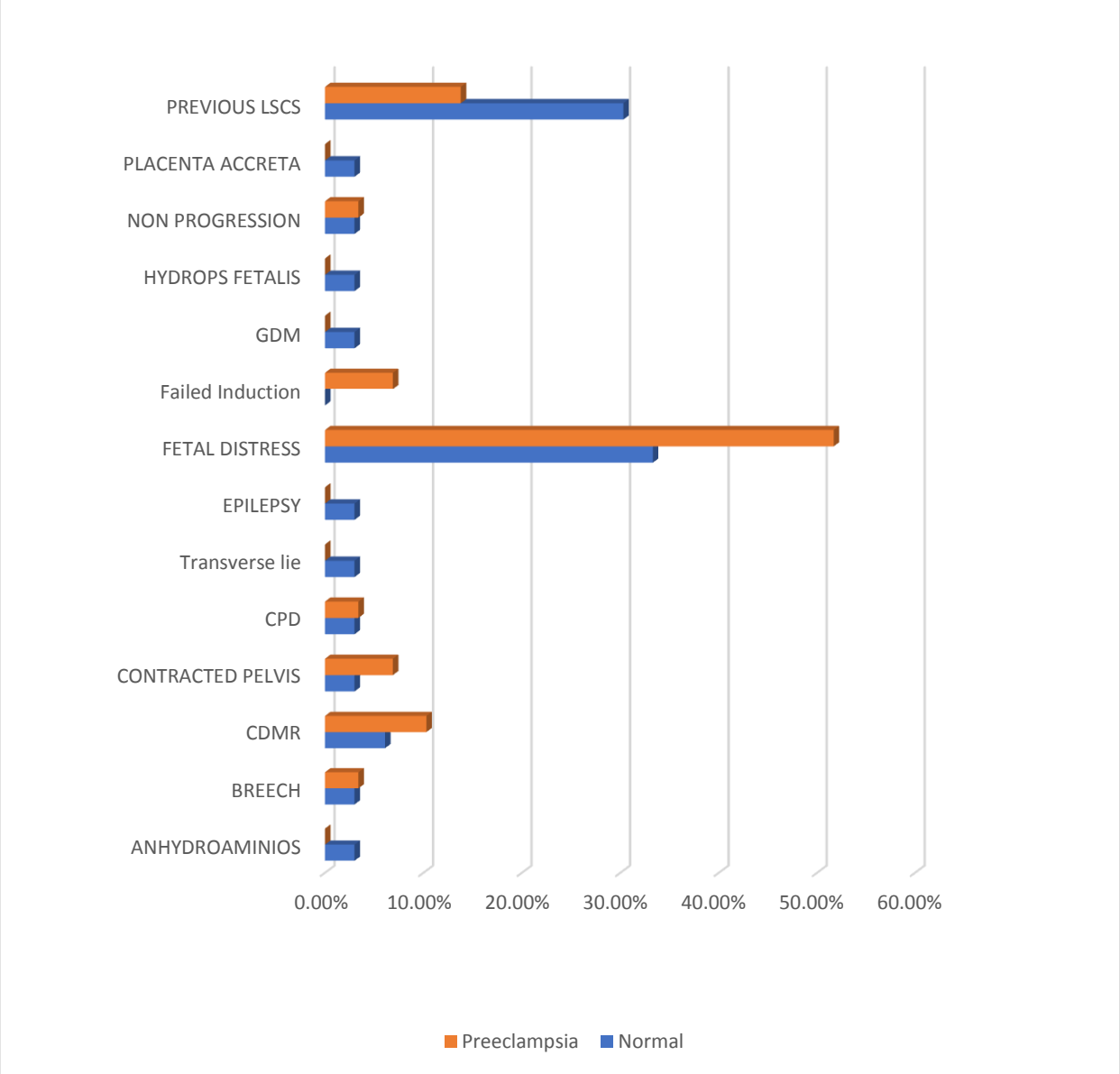


Table 7:- Distribution of subjects with preeclampsia according to severity of preeclampsia.

	N	%
Antepartum Eclampsia	1	2
Imminent eclampsia	5	10
Postpartum eclampsia	1	2
Preeclampsia	24	48
Severe preeclampsia	19	38

Figure 8:- Graph representing distribution of preeclamptic subjects according to severity of preeclampsia.

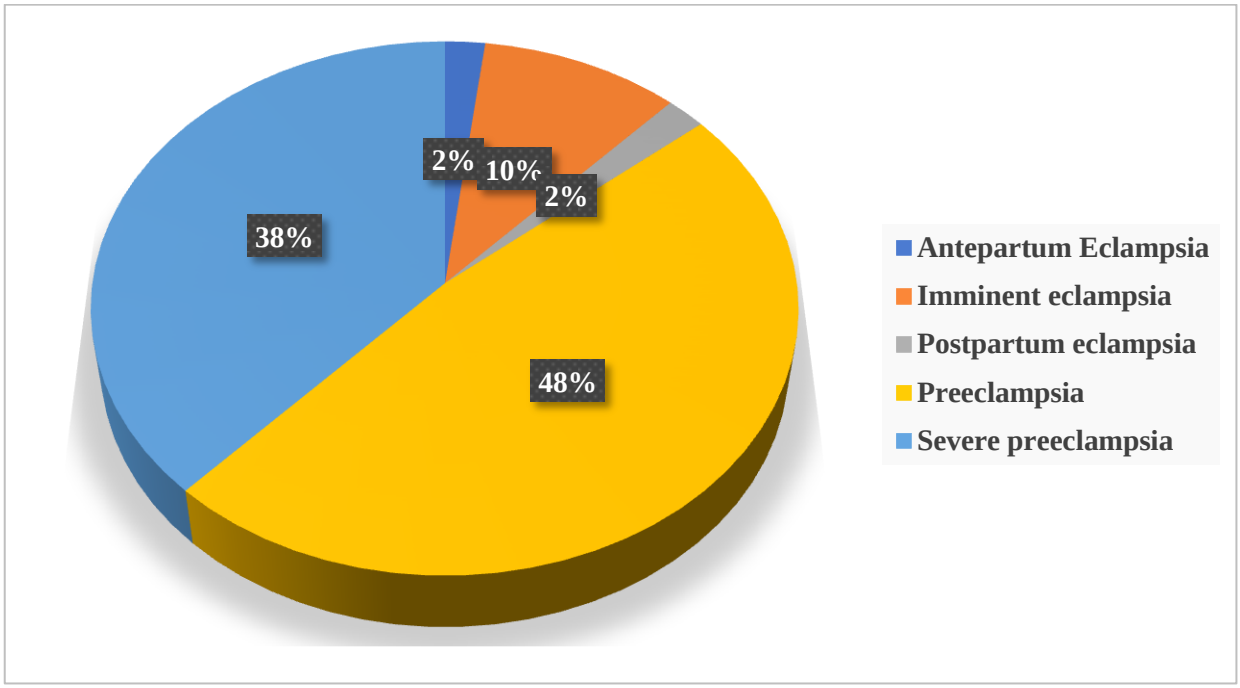


Table 8:- Distribution of subjects with preeclampsia according to fetal outcome.

	N	%
BABY MOTHER'S SIDE	28	56.0
IUD	5	10.0
NICU	17	44.0

Figure 9:- Graph representing distribution of preeclamptic subjects according to fetal outcome.

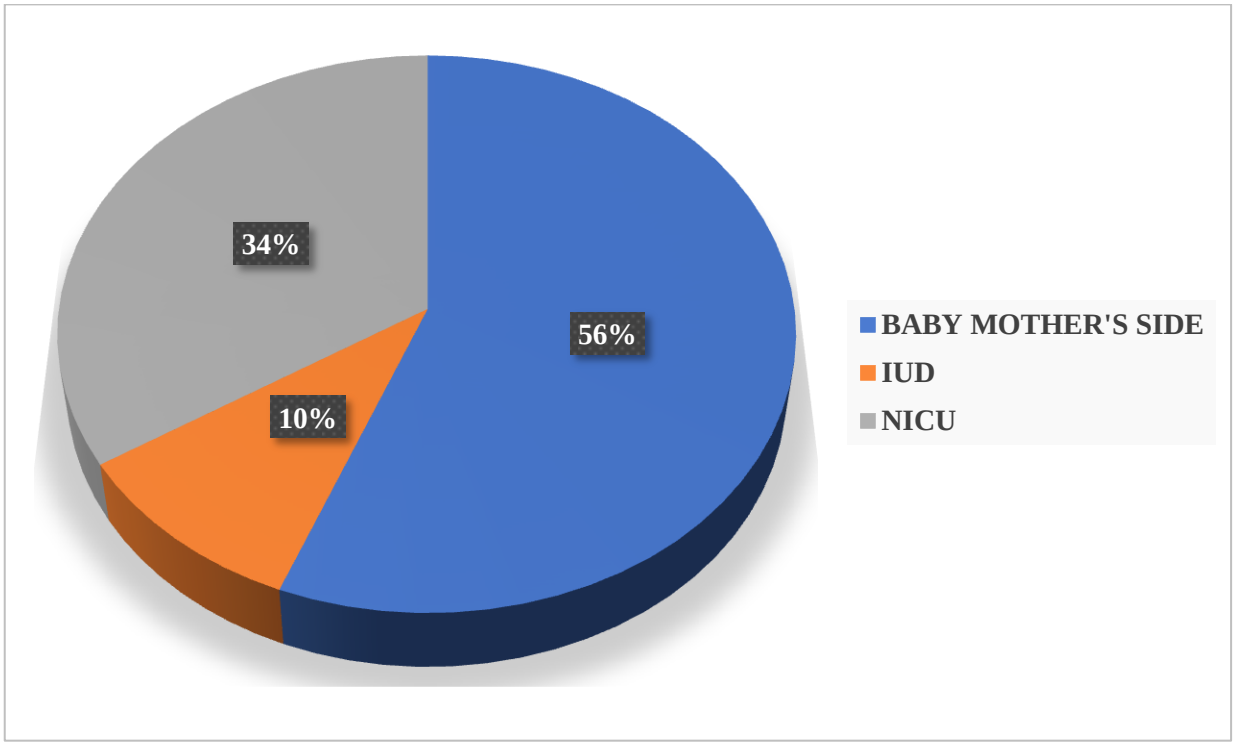


Table 9:- Comparison of mean CA 125 between two groups

	Mean	Std. Deviation	P Value
Normal	24.24	13.71	**0.033**
Preeclampsia	30.61	15.69	

Mean CA 125 among normal subjects was 24.24±13.71 IU/ml and Mean CA 125 among Preeclampsia subjects was 30.61± 15.69IU/ml. There was a statistical significance found between two groups with respect to CA 125.

In preeclampsia, CA125 was increased by around 126.27% more compared to normotensive group. This indicates the importance in estimation of preeclampsia. The same has been determined with significant p-value.

Figure 10:- Graph representing comparison of mean CA 125 between two groups.

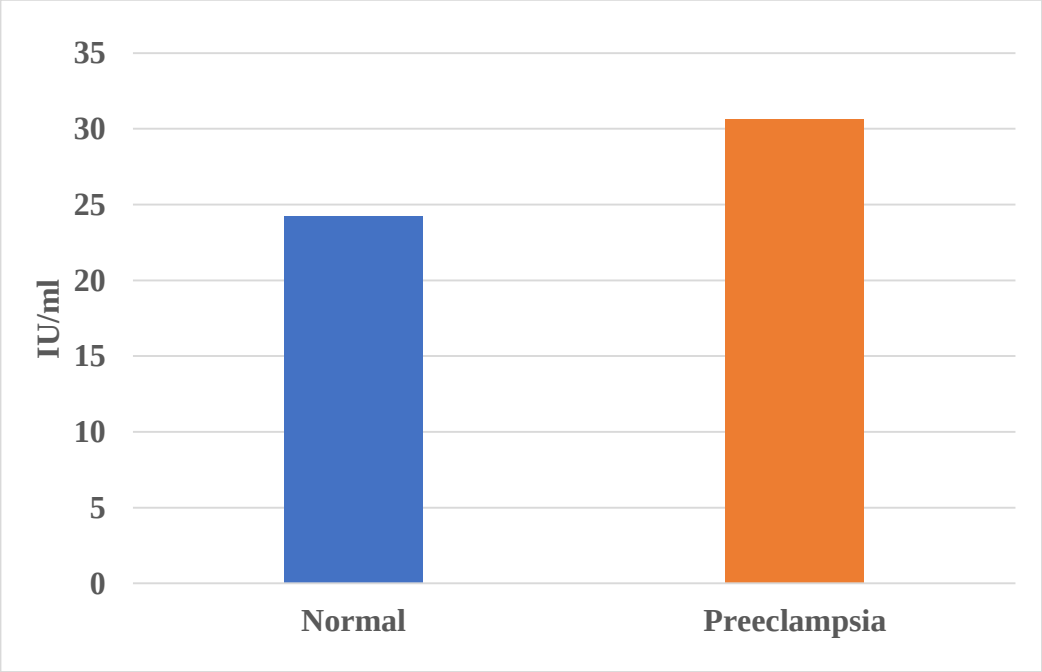


Table 10:- Subgroup classification of preeclampsia and CA125 value:

	Mean	Std. Deviation	p value
Preeclampsia	24.10	9.59	p value <0.001
Severe preeclampsia	32.77	12.97	
Imminent eclampsia	58.28	9.53	
Antepartum/ Postpartum Eclampsia	65.80	0.71	

p-value less than 0.001, indicates statistical significance found between severities of preeclampsia with respect to CA 125.

Among the subgroup classification in present study, we documented CA125 levels highest among antepartum/postpartum eclampsia compared to preeclampsia where it has elevated around 2.73 times, which indicatesCA125 to be a better predictor in antepartum/postpartum eclampsia

Figure 11:- Graph showing Comparison of mean CA 125 according to severity of preeclampsia.

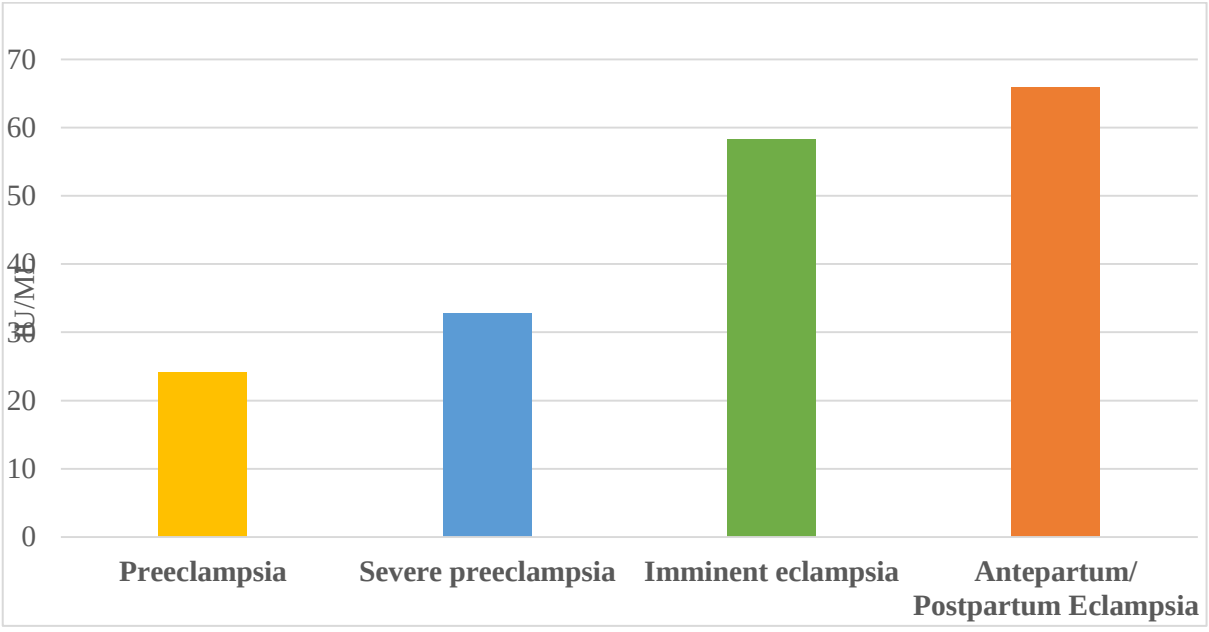
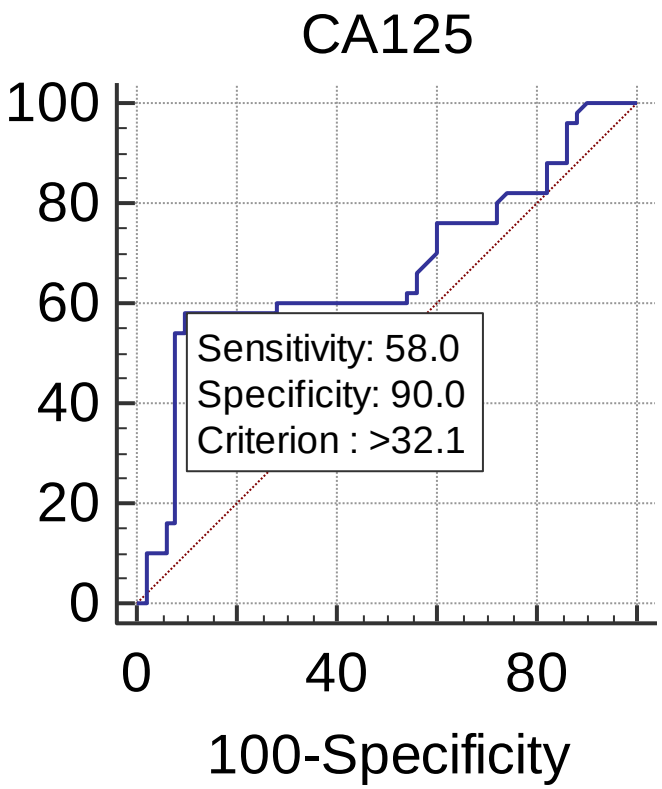


Figure 10:- ROC curve for CA 125 in predicting Preeclampsia



With respect to receiver operating curve for CA125, it has been observed in our study that CA125 is a specific marker with a specificity value of 90% and sensitivity of 58%. However, the sensitivity depends on various factors and observer bias; specificity helps clinicians to make a critical decision in preeclampsia and use CA125 as a good predictor.

Table 11:- Area under ROC curve

Area under ROC curve	0.67
95% Confidence interval	0.52 to 0.71
p value	**0.003**

Table 12:- Distribution of subjects according to CA 125 cut off as 32.1 between two groups.

	Normal	Preeclampsia	Total
≤32.1	45	24	69
	90.0%	48.0%	69.0%
>32.1	5	26	31
	10.0%	52.0%	31.0%
Total	50	50	100
	100.0%	100.0%	100.0%

Among the 31 subjects whose CA125 is >32.1 IU/ml , most of them (twenty six study subjects) belonged to preeclamptic group.

Figure 13:- Graph showing Distribution of subjects according to CA 125 cut off as 32.1 between two groups:

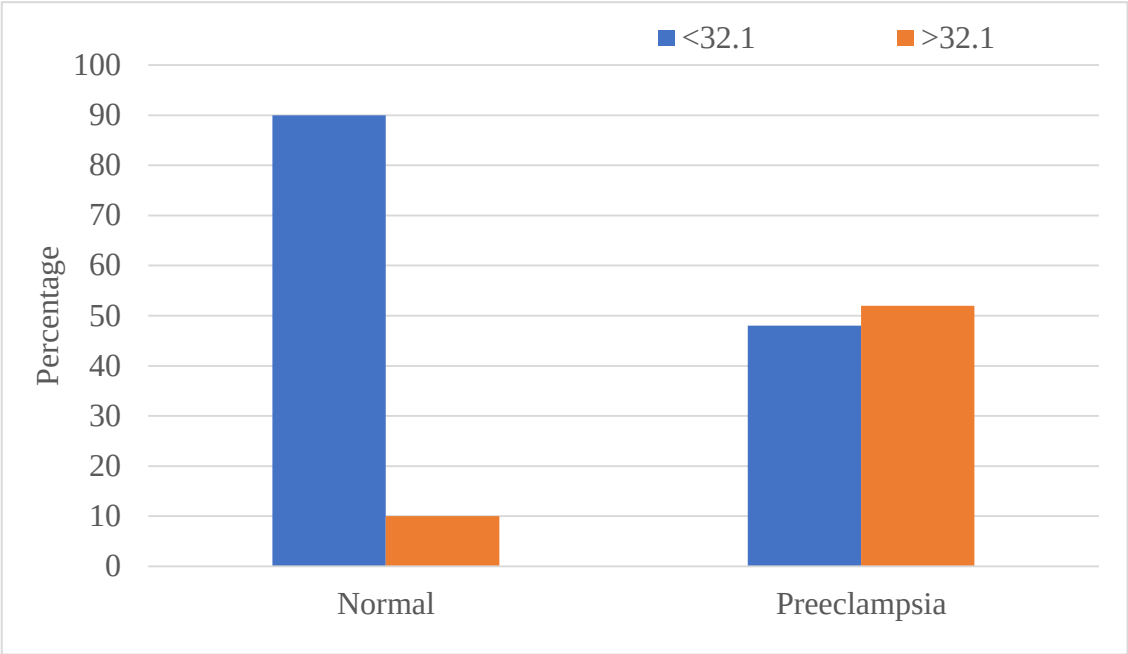


TABLE 13: Fetal outcome in preeclampsia according to CA 125 cut off as 32.1:

	≤32.1	>32.1
BABY MOTHER'S SIDE	19 (32.26%)	9 (36.84%)
NICU	10 (61.29%)	7 (47.37%)
IUD	2 (6.45%)	3 (15.79%)

p-value 0.47, no statistical significance in fetal outcome among two group with CA 125 cut off as 32.1. But among five IUD babies, three had CA 125 cut off >32.1IU/ml. Among six low birth weight (complication in preeclampsia) babies which got shifted to NICU , four babies had CA 125 cut off >32.1IU/ml.

Table 14:- Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value of CA 125 in predicting preeclampsia at cut-off 32.1

	Value	**95% CI**
Sensitivity	52.00%	37.4-66.3%
Specificity	90.00%	78.2 - 96.7%
Positive Predictive Value	83.9%	68.3 - 92.5%
Negative Predictive Value	65.2%	58.7 - 71.4%

This study signifies that, The association of CA125 level in preeclampsia is highly specific (90%) with (i)positive predictive value 83.9% but less sensitive (52%) and (ii)negative predictive value 65.2%.

DISCUSSION

DISCUSSION

Preeclampsia is a hypertensive pregnancy disease that puts mother and intrauterine fetus in many complications and even death. The specific pathophysiology of this illness is unknown, however it may produce vasoconstrictive chemicals that cause broad harm to the maternal vascular endothelium, kidneys, and liver.[42] Thus, process of understanding the syndrome divided as follows:

Stage I: Predisposes the placenta to hypoxia with enhanced release of cytokines.

1. Stage II: effect of cytokines leading to injury of the vascular endothelial cells, altered vascular reactivity, reduction of tissue perfusion, and onset of inflammatory processes leading to thrombotic microangiopathy.

Maternal susceptibility to changes was crucial consideration. Due to the absence of immunological tolerance during pregnancy, the placenta and fetus's paternal antigens may be the target of an immune reaction. As a result, the process of placentation is stopped, and the invasion of cytotrophoblasts is reduced. As a result, the placenta experiences hypoxia and starts to release inflammatory mediators that have an impact on the vascular endothelium.[43,44] On the surface of cells, there is an antigen called CA 125 which is a glycoprotein. Rise in CA 125 concentrations that were found during antenatal period and in postpartum may be caused by fetal membrane, liquor amnii, or maternal endometrial lining, according to some research. This shows that the dissolution of the maternal decidual may be one of the causes of raised CA 125 concentration.[45] The etiology of pregnancies complicated by preeclampsia may be suggested by the same mechanism. The failure in invasion of the trophoblasts and activation of inflammation in the placenta are thought as potential causes of CA 125 expression.

Clinical investigations conducted by Cebesoy FB et al., in 2009, have examined the biochemical and clinical evidence of CA 125 expression augmentation.[14]

Lindheimer MD et al., in 2010, have shown that pregnancy-specific preeclampsia is a multisystemic disorder.[42] Cebesoy FB et al., in 2009, observed that in preeclampsia, decreased migration of trophoblasts into the maternal decidua results in persistent inflammatory reaction, which increases CA-125 expression.[14] Observations of Karaman E, et al., in 2014., have asserted that clinical diseases common in poor and underdeveloped nations include eclampsia and pre-eclampsia.[37]

In this study, we have categorized pregnancy into Normal and Preeclampsia. This is based on the age group: 18-22 years [13 (26.0%) Normal and 24(48.0%) Preeclampsia] followed by 23-27 years [23 (46.0%) Normal and 13(26.0%), Preeclampsia], 28-32 years [12 (24.0%) Normal and 9 (18.0%) Preeclampsia] and 33-37years [2 Normal (4.0%) and 4 Preeclampsia (8.0%)]. p-value 0.067, no statistical significance found among two groups in aspect of age. Study subjects were divided into three groups for the 2012 study by Ozat M et al., controls, study subjects with moderate preeclampsia and study subjects with severe preeclampsia.[12]

Maternal age, period of gestation and body mass index, were compared among the three study groups. Gottipati G et al. conducted a 2019 study in which study subjects were divided up into three groups that were comparable in terms of: age, past obstetric history, and period of gestation. When compared to gestational hypertension group, mean gestational age at starting point of disease in preeclampsia group reported as 31 weeks as opposed to 35 weeks, indicating an early disease onset (p-value = 0.000).[15] In a 2018 study by Gbemisola E et al., no statistical significance in maternal age($p = 0.40$), parity($p = 0.71$), or period of gestation at

enrollment (p = 0.98) between normotensive subjects and subjects with preeclampsia.[39] Mukherjee B et al case-control research from 2020 included 40 antenatal subjects of pre-eclampsia with no severe features, 40 antenatal subjects with severe features of pre-eclampsia, and 40 antenatal subjects who were healthy and matched for age, parity, and period of gestation at recruitment.[40]

Study subjects in current study categorized into Normal and Preeclampsia based on Parity: Primigravida [20 (40.0%) Normal and 30 (60.0%) Preeclampsia] followed by Gravida 2 [17 (34.0%) Normal and 12 (24.0%) Preeclampsia], Gravida 3 [6 (12.0%) Normal and 6 (12.0%) Preeclampsia] and Gravida 4 [7 (14.0%) Normal and 2 (4.0%) Preeclampsia]. p value compared with all four groups based on parity had no statistical significance (p-value of 0.131).

Mukherjee B et al. conducted 2020 study based on evaluation of CA-125 values among subjects with mild preeclampsia, moderate preeclampsia, preeclampsia with severe features and control group. Serum uric acid and CA-125 levels significantly higher in group containing preeclampsia with severe features.[40]

We distributed the study subjects based on gestational age: <33weeks [5 (10.0%) Normal and 6 (12.0%) Preeclampsia] followed by 33-37weeks [3 (6.0%) Normal and 13 (26.0%) Preeclampsia] and >37weeks [42 (84.0%) Normal and 31 (62.0%) Preeclampsia]. p-value of 0.018, indicates that statistical significance between two groups with respect to gestational age was present. Gbemisola E et al. (2018) divided all consenting eligible women into two different study groups ie; seventy preeclamptic subjects in study group and seventy healthy antenatal subjects in control group) and matched them for maternal age, parity of each study subject, and period of gestation. They discovered no discernible differences in the

individuals' period of gestation and maternal age at enrollment, lending credence to the two groups' similarities.[39] The mean gestational age at illness onset was thirty-one weeks in preeclampsia group and thirty-five weeks in gestational hypertension group in a 2019 study by Gottipati G et al., indicating that preeclampsia had an early onset of illness (p-value = 0.000).[15]

Our study findings were consistent with findings of the study done by Gottipati G et al.[15] We documented Antepartum Eclampsia [1 (2.0%) Preeclampsia] followed by Imminent eclampsia [5 (10.0%) Preeclampsia], Postpartum eclampsia [1 (2.0%) Preeclampsia], Preeclampsia [24 (48.0%) Preeclampsia] and Severe preeclampsia [19 (38.0%) Preeclampsia]. Comparison of mean CA 125 according to severity of Preeclampsia: Preeclampsia (Mean 24.10 and Std. Deviation 9.59), severe preeclampsia (Mean 32.77 and Std. Deviation 12.97), imminent eclampsia (Mean 58.20 and Std. Deviation 9.53) and antepartum/ postpartum eclampsia (Mean 65.80 and Std. Deviation .7071). p-value less than 0.001, indicating a statistical significance among severities of preeclampsia and CA 125.

According to research by Mukherjee B et al. published in 2020, pre-eclampsia severity increases are associated with lower levels of maternal platelets and smaller babies at birth. Their findings highlighted the potential role of CA125 as a biochemical in prediction of disease severity.[40] By Gottipati G et al., study, 2019 The preeclampsia group's mean birth weight was 2.1 kg thus indicating a low birth weight which is likely caused by either preterm births brought on by labor induction to end the pregnancy or fetal development restriction, which is one of the disease's symptoms.[15]This disparity is most likely due to one of the drawbacks in their inclusion criteria, as the population for their study included only antenatal mothers over 32 weeks of gestation.[15]

In our study, among the 50 preeclamptic study subjects, there were 5 (10%) fetuses who died intrauterine and 17(44%) of them were shifted to neonatal intensive care unit after delivery. Whereas 28(56%) of them were shifted to mother's side after delivery showing that in this study more than fifty percent of the preeclamptic pregnant women were well managed antenatally leading to good fetal outcomes. Among the five intrauterine demises, three had CA125 cut off >32.1IU/ml. Among the six low birth weight born babies, four had CA125 cut off >32.1IU/ml.

"Karaman E et al., assessed ninty one subjects who had given birth to singleton babies in a study conducted in 2014. CA-125 levels in serum were measured in study subjects of pre-eclampsia with severe features group (n = 34) and those subjects with mild pre-eclampsia (n = 24). The CA-125 was significantly higher in severe pre-eclampsia group when compared to mild pre-eclampsia and control groups (p-value of 0.05). There was no discernible difference in CA-125 levels between groups with mild pre-eclampsia and controls.[37]"

In our study comparison of mean CA-125 between two groups: Normal [Mean+/-Standard deviation 24.24+/-13.71 and Preeclampsia [Mean+/-Std. Deviation (30.61+/-15.69)] and p-value 0.033. There was a statistical significance between two groups with respect to CA 125.

Sayyadi BM et al. discovered that there is a significant difference in CA125 among subjects having mild and severe pre-eclampsia in a 2020 study, with CA125 levels likely to be higher in pre-eclampsia with severe features group than mild features of pre-eclampsia group.[46] Department's standard operating procedure (SOP) was followed when treating study participants with severe pre-eclampsia, and they were sufficiently prepared for birth. Mild features of pre-eclampsia affects 15% to 20% of pregnancies, while severe features of pre-eclampsia affects 1% to 2%, according to a study by Aziz R. and colleagues.[47] Pre-

eclampsia with severe features where diagnosed when blood pressure of 160/110 mmHg or more along with other complications.[48]

In the current study , we diagnosed study subjects as preeclampsia with severe features when systolic blood pressure recorded as 160mmHg and diastolic blood pressure recorded as 110mmhg with presence of proteins in urine with or without fetomaternal complications.

In their research, Bhattacharya, Saha, and Karaman E et al. discovered that study subjects of moderate preeclampsia group, severe features of pre-eclampsia group, and eclampsia group contained higher serum CA125 level than those study subjects of normal pregnancy group.[36, 37]

"According to Gottipati G et al study .'s from 2019, the average serum CA-125 level of preeclampsia group was reported as 56.6 IU/mL, which was close to Bhattacharya and Saha's (58.5 IU/mL), but slightly higher in value than Karaman et al's (38.8 IU/mL).[15,37] In our study, mean CA 125 among normal subjects was 24.24+/-13.71 IU/ml and Mean CA 125 among Preeclampsia subjects was 30.61+/- 15.69IU/ml. The above said difference in mean can be explained by a large difference in the current study's standard deviation when compared to other two studies, as higher values of CA-125 were observed in a few patients with increasing severity of preeclampsia (Bhattacharya and Karaman).[36,37] According to a 2020 study by Aremu Kasumu et al., the average CA-125 level during a normal pregnancy was 24.53 ± 9.42 IU/ml, whereas moderate preeclampsia was associated with a mean of 21.94± 13.18 IU/mL and severe preeclampsia with a mean level of 45.68 ±23.38 IU/mL.[41] In a study published in 2014, Karaman E et al. found that the mean CA125 concentration was 18.8+/-8.4 IU/mL in moderate pre-eclamptics and 38.8+/-20.9 IU/mL in severe preeclamptics.[37] Our study observed mean CA125 level as 24.10+/-9.59 IU/ ml in preeclampsia, 32.77+/-12.96IU/ml in severe preeclampsia, 58.28+/-9.53IU/ml in imminent

eclampsia and 65.8+/-0.70 IU/ml in antepartum/postpartum eclampsia. Thus a p value <0.001 , there was a statistical significance found between severities of preeclampsia and CA125 level. Study by In normal pregnancies, Ozat M et al. (2011) determined a mean of 48.25 3.34 IU/mL.[12] Miami et al. observed a significantly lower amount, with a mean of 13.70 ± 8.44 IU/mL.[15] We could get a mean concentration of 24.24+/-13.71 IU/ml in normotensive subjects."

In our study, CA 125 in determining preeclampsia at cut off 32.1: Sensitivity [Value (52.0%) and 95% CI (37.4-66.3%)], Specificity [Value (90.0%) and 95% CI (78.2 - 96.7%)], Positive Predictive Value [Value (83.9%) and 95% CI (68.3 - 92.5%)] and Negative Predictive Value [Value (65.2%) and 95% CI (58.7 - 71.4%)] which were consistent with previous studies. Sensitivity value of 70.1% and specificity value of 62.0% were reported from a 2018 study by Gbemisola E et al using ROC curve to analyze connection between maternal CA125 and increased blood pressure readings.[39]

With a sensitivity value and specificity value of 83.6% and 98.2%, Gottipati G.'s cut off value for CA-125 was established to 23.7 IU/mL, which is lower than that of other studies.[15] With a limit value to be 50 IU/mL and sensitivity and specificity of 93.7% and 88%, Ozat et al., Specificity was shown to be higher when comparing our sensitivity and sensitivity to the work of Ozat et al.[12] Utilizing 35 IU/mL cut-off, Cebesoy et al. did not assess the sensitivity or specificity of their approach.

Study by Mukherjee B et al., in 2020, Sensitivity and specificity 92.1% and 97.1%, with cut-off 35 IU/ml serum CA-125. 95.5% of predictions were correct, whereas 94.4% of predictions were incorrect.[40]

In our study, the subjects were distributed according to mode of delivery between two groups: LSCS [38 (76.0%) Normal and 29 (58.0%) Preeclampsia] and NVD [12 (24.0%) Normal and 21 (42.0%) Preeclampsia]. p-value of 0.088, there was no statistical significance reported among two groups based on mode of termination of pregnancy. In our study the comparison of indications for LSCS between two groups: Anhydramnios [1 (3.0%) Normal and 0 (0%) Preeclampsia] followed by Breech [1 (3.0%) Normal and 1 (3.4.0%) Preeclampsia], Caesarean delivery under maternal request [2 (6.1%) Normal and 3 (10.3%) Preeclampsia], Contracted Pelvis [1 (3.0%) Normal and 2 (6.9%) Preeclampsia], Cephalopelvic disproportion [1 (3.0%) Normal and 1 (3.4%) Preeclampsia], Transverse lie [1 (3.0%) Normal and 0 (0%) Preeclampsia], Epilepsy [1 (3.0%) Normal and 0 (0%) Preeclampsia], Fetal Distress [11 (33.3%) Normal and 15 (51.7%) Preeclampsia], failed induction [0 (0%) Normal and 2 (6.9%) Preeclampsia], GDM [1 (3.0%) Normal and 0 (0%) Preeclampsia], Hydrops Fetalis [1 (3.0%) Normal and 0 (0%) Preeclampsia], Non Progression of labour [1 (3.0%%) Normal and 1 (3.4%) Preeclampsia], Placenta Accreta [1 (3.0%) Normal and 0 (0%) Preeclampsia] and Previous LSCS [10 (30.3%) Normal and 4 (13.8%) Preeclampsia]. In contrast to these two parameters of mode of delivery and comparison of indications for LSCS between two groups, studies conducted elsewhere did not include these two parameters to justify the results compared to our study.

"Recent studies suggested that maternal serum CA-125 could distinguish between severe preeclampsia group and mild preeclampsia group using blood pressure, presenting symptoms, and blood parameters to guide treatment decisions.[52] There is a significant correlation between serum concentration of CA-125 and with severity of preeclampsia, according to a study by Boroumand F et al. that measured CA-125 in preeclampsia.[53] This biomarker can be used to distinguish mild from severe types. The level of this biomarker is

normal in non-severe preeclampsia and in normal pregnancy, but it rises in relation to the severity of preeclampsia, according to further comparisons made between normal pregnancy and severe features of preeclampsia and mild features of preeclampsia.[37] Study by Osanyin GE, et al., in 2018., showed that both severe and non-severe forms of preeclampsia have higher-than-normal CA-125 levels.[39] From the study by Sane S et al., in 2021., It was shown that the level of CA-125 in non-severe preeclampsia and normal pregnancy did not vary significantly. The difference between severe and non-severe preeclampsia was negligible.[54"]

Pre-eclampsia and its complications are estimated to cause more than 63,000 lives in women each year, with up to 98% maternal deaths in developing nations.[51] The clinical appearance in pre-eclamptics is caused by pathological alterations, which cause endothelial dysfunction. Patients with benign pelvic problems and ovarian malignancies express the chemical marker CA-125.[36] It is yet unknown if the fetus plays a role in CA-125 release or other factors that occur after birth.[36] Pre-eclampsia subjects differed significantly from controls in a meta-analysis of nine trials involving 977 antenatal mothers (Mean value of 15.86 IU/mL, 95% Confidence interval ranged between 9.03-22.69).[55] In comparison to study participants in pre-eclampsia with moderate features, study participants in pre-eclampsia with severe features reported significantly high CA-125. According to a meta-regression analysis, 34 weeks as period of gestation may have a favorable impact on the relationship between CA125 and preeclampsia.[55] According to research, CA125 is a potential biomarker for pre-eclampsia that had the capability to be utilized for diagnosis and follow-up, and it strongly corresponds with severity of pre-eclampsia.[36] Fetal growth is restricted and is lowered as a result of poor placental perfusion. Premature birth is a significant preeclampsia complication that happens after treatment to end the pregnancy and results in fetal harm, neurodevelopmental impairment, and fetal death. The duration of pregnancy can

be prolonged with good antenatal management in the case of preterm fetuses with the addition of CA125 to the therapeutic modality when the rest fails to avoid termination of pregnancy.

Preeclampsia affects young and nulliparous women more frequently than older antenatal women, who also have increased risk of developing preeclampsia and become chronic hypertension after delivery. Preeclampsia risk factors have also been identified.[56] New clinical methods, advanced knowledge and good experience, needed in generalizing findings of evidence-based clinical studies on patient management and survival. During preeclampsia-related pregnancies, inability of trophoblast penetration and onset of inflammation in the placenta result in production of biomarkers, with CA-125 predominating. As a result, CA-125 is biomarker of magnitude of inflammation in preeclampsia and fit to be used as supplement test as well as surrogate test to detect preeclampsia with atypical features or to detect its severity early.[52]

CONCLUSION

CONCLUSION:

In the current study, we found a statistical significance in gestational age between two groups. The mean CA-125 among pregnancies with normal study subjects was observed to be significantly low when compared with preeclamptics in this study. Furthermore, a connection was identified between serum concentration of CA-125 and severity of preeclampsia.

CA125 has been identified as a potential biomarker that can be used for pre-eclampsia diagnosis and follow-up, and it matches up markedly with the severity of pre-eclampsia.

As a result, we recommend that more robust longitudinal studies with maternal CA125 patterns in pregnancy be conducted to assess its applicability as a predictive marker for preeclampsia and to establish an acceptable cut-off value, particularly among Indian women who have a proclivity to present with severe disease and a poor pregnancy outcome.

LIMITATION:

Small sample size, and generalising results requires evidence from comparable large studies.

RECOMMENDATION:

The use of CA125 for timely identification of preeclampsia is recommended in this study so that effective management methods can be initiated as soon as possible for good maternal and neonatal outcomes.

SUMMARY

SUMMARY:

This two year cross sectional study was conducted on all antenatal mothers between 20 -40 weeks gestational age getting admitted RLJH and research centre Tamaka (Jan 2021- Dec 2022), for the period of 2 years who fulfilled inclusion and exclusion criteria.

The data were recorded into a Microsoft Office excel sheet and analyzed with SPSS 22 software. Frequencies and proportions were used to represent categorical data. As a significance analysis for qualitative data, the Chi-square test or Fischer's exact test were used. The mean and standard deviation were used to represent continuous data. The independent t test was used as a statistical significance test to determine the mean between two quantitative variables. Receiver operating characteristic(ROC) curve was constructed for CA 125 and preeclampsia. For the estimation of sensitivity value, specificity value, positive predictive value and negative predictive value, the receiver operating characteristic (ROC) curve and optimal cut-off points were chosen. A test with an area under ROC curve of 0.5 helps in prediction of an outcome no better than chance. An area under ROC curve greater than 0.8 indicated reasonably good prediction. MS Excel and MS Word were used to create various graphs. After applying all rules of statistical test, p value ie; probability that the result is true of less than 0.05 was considered statistically significant. To analyze data, MS Excel and SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA) were used.

According to gestational age between two groups: <33weeks [5 (10.0%) Normal and 6 (12.0%) Preeclampsia] followed by 33-37weeks [3 (6.0%) Normal and 13 (26.0%) Preeclampsia] and >37weeks [42 (84.0%) Normal and 31 (62.0%) Preeclampsia], p-value was statistically significant. The comparison of distribution of subjects with preeclampsia according to severity of preeclampsia: Antepartum Eclampsia [1 (2.0%) Preeclampsia] followed by Imminent eclampsia [5 (10.0%) Preeclampsia], Postpartum eclampsia [1 (2.0%) Preeclampsia], Preeclampsia [24 (48.0%) Preeclampsia] and Severe preeclampsia [19

(38.0%) Preeclampsia]. Comparison of mean CA 125 according to severity of Preeclampsia: Preeclampsia (Mean 24.10 and Std. Deviation 9.59), Severe preeclampsia (Mean 32.77 and Std. Deviation 12.97), Imminent eclampsia (Mean 58.28 and Std. Deviation 9.53) and Antepartum/ Postpartum Eclampsia (Mean 65.800000 and Std. Deviation .7071068). p-value less than 0.001 indicates a significant statistical difference between preeclampsia severity groups in relation to CA 125. Distribution of subjects with preeclampsia according to fetal outcome: BABY MOTHER'S SIDE [28 (56.0%)] followed by IUD [5 (10.0%)] and NICU [17 (44.0%).

Comparison of mean CA 125 between two groups: Normal [Mean 24.24 and Std. Deviation (13.71) and Preeclampsia [Mean 30.61 and Std. Deviation (15.69)] and p value is 0.033. Mean CA 125 among normal subjects was 24.24+13.71 IU/ml and Mean CA 125 among Preeclampsia subjects was 30.61+ 15.69IU/ml. In terms of CA 125, the results showed statistical significance between two groups.

In our study sensitivity value, specificity value, positive predictive value and negative predictive value of CA 125 in predicting preeclampsia at cut-off 32.1: Sensitivity [Value (52.0%) and 95% CI (37.4-66.3%)], Specificity [Value (90.0%) and 95% CI (78.2 - 96.7%)], Positive Predictive Value [Value (83.9%) and 95% CI (68.3 - 92.5%)] and Negative Predictive Value [Value (65.2%) and 95% CI (58.7 - 71.4%)]. CA125 has been found to be a potential biomarker that can be used for diagnosis and follow-up in pre-eclampsia and correlates significantly with the degree of pre-eclampsia.

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ANNEXURES

PROFORMA

Serum CA 125 level in normotensive and pre eclamptic pregnancies in a tertiary care hospital

NAME:

AGE:

ADDRESS:

UHID NO:

I.P NO:

DATE/ TIME OF ADMISSION:

DATE/ TIME OF DISCHARGE:

CHIEF COMPLAINTS:

OBSTETRICAL HISTORY: Booked/ Unbooked/ Referred

Married Life:

Consanguinous marriage: Yes/ No

Obstetrical Score:

MENSTRUAL HISTORY:

LMP:

EDD:

POG:

cEDD:

PAST HISTORY:

PERSONAL HISTORY:

FAMILY HISTORY:

GENERAL PHYSICAL EXAMINATION:

Pallor/ Icterus/ Cyanosis/ Clubbing/ Lymphadenopathy/ Edema

Pulse: BP:

RR: Temp:

CNS:

CVS:

RS:

Per Abdomen:

Per Speculum:

Per Vagina:

PROVISIONAL DIAGNOSIS:

INVESTIGATIONS:

Date of testing CA 125 level:

Serum CA 125 level result:

Other specific investigation results:

PATIENT INFORMATION SHEET

STUDY TITLE: . SERUM CA 125 LEVEL IN NORMOTENSIVE AND PREECLAMPTIC PREGNANCIES IN A RURAL TERTIARY CARE HOSPITAL"

STUDY SITE: R.L Jalappa Hospital and Research Centre, Tamaka, Kolar.

This is to inform you that, you require SERUM CA 125 LEVEL for

Making the diagnosis of the disease, extent of the disease and for planning of the treatment in pre eclampsia patients.

We are conducting this study to predict the onset and severity of this condition.

If you are willing you will be enrolled in this study and we will send CA 125 level and other relevant investigations which are required for diagnosis and treatment of pre eclampsia

This will facilitate identifying PREECLAMPSIA in an early stage and treating it and thereby preventing further complications associated with pre eclampsia.. You are free to opt-out of the study at any time if you are not satisfied or apprehensive to be a part of the study. Your treatment and care will not be compromised if you refuse to be a part of the study. The study will not add any risk or financial burden to you if you are part of the study. In case of any complication during surgery patient will be treated accordingly.

Your identity and clinical details will be confidential. You will not receive any financial benefit for being part of the study. You are free to contact Dr. SAHITHYA S or any other member of the above research team for any doubt or clarification you have.

Dr. SAHITHYA S

Mobile no: 7299908222

E-mail id: sahilaksh96@gmail.com

Dr. SHEELA S.R.

Mobile no: 9845217277

E-mail id: drsrsheela@gmail.com

INFORMED CONSENT FORM

I Mr./Mrs. _____ have been explained in my own understandable language, that I will be included in a study which is **"SERUM CA 125 LEVEL IN NORMOTENSIVE AND PREECLAMPTIC PREGNANCIES IN A RURAL TERTIARY CARE HOSPITAL"**

I have been explained that my clinical findings, investigations, postoperative findings will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary, and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have been explained about the interventions needed possible benefits and adversities due to interventions, in my own understandable language.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I have principal investigator mobile number for enquiries.

I in my sound mind give full consent to be added in the part of this study.

Signature of the patient: Signature of the witness:

Name: Name:

Date: Relation to patient:

Place:

KEY TO MASTER CHART

GROUP	NORMOTENSIVE	N
	PREECLAMPTIC	P

AGE GROUP	18-22yrs	1
	23-27yrs	2
	28-32yrs	3
	33-37yrs	4

PARITY	PRIMIGRAVIDA	PRIMI
	GRAVIDA 2	2
	GRAVIDA 3	3
	GRAVIDA 4	4

GESTATIONAL AGE	29-32weeks	1
	33-36weeks	2
	37-40weeks	3
	41-44weeks	4

MODE OF DELIVERY	Lower segmen caesarean section	LSCS
	Vaginal delivery	NVD

GROUP	AGE	AGE GROUP	PARITY	GESTATIONAL AGE	GA	MODE OF DELIVERY	INDIICATION FOR LSCS	FETAL OUTCOME	CA125	SEVERITY OF PREECLAMPSIA
N	31	3	3	38+3	1	LSCS			7.3	NORMAL
N	22	1	2	40	3	LSCS	CONTRACTED PELVIS		9.8	NORMAL
N	26	2	PRIMI	39	2	LSCS	PREVIOUS LSCS		9.8	NORMAL
N	27	2	2	37 WEEKS 6DAYS	3	NVD			9.8	NORMAL
N	21	1	3	29	1	LSCS	PLACENTA ACCRETA		10.1	NORMAL
N	28	3	3	39	3	LSCS	CPD		10.2	NORMAL
P	21	1	PRIMI	37WEEKS 3 DAYS	3	LSCS	CDMR	BABY MOTHER'S SIDE	10.2	Preeclampsia
P	21	1	2	39 WEEKS 4 DAYS	3	LSCS	FETAL DISTRESS	NICU	10.5	Severe preeclampsia
N	22	1	3	39+2	2	LSCS			10.8	NORMAL
P	23	2	PRIMI	37 WEEKS	3	NVD		BABY MOTHER'S SIDE	10.9	Preeclampsia
P	20	1	PRIMI	29 WEEKS 6 DAYS	1	NVD		NICU	11.6	Severe preeclampsia
P	22	1	PRIMI	39 WEEKS	2	NVD		BABY MOTHER'S SIDE	12.3	Preeclampsia
P	22	1	3	35 WEEKS	2	NVD		BABY MOTHER'S SIDE	12.5	Preeclampsia
N	30	3	2	39+1	3	LSCS	FETAL DISTRESS		12.6	NORMAL
N	26	2	PRIMI	40+4	3	LSCS	NON PROGRESSION		12.6	NORMAL
P	19	1	PRIMI	40 WEEKS 4 DAYS	3	LSCS	CDMR	BABY MOTHER'S SIDE	13.4	Preeclampsia
P	26	2	PRIMI	38 weeks	3	LSCS	CONTRACTED PELVIS	BABY MOTHER'S SIDE	13.6	Preeclampsia
P	26	2	4	32 WEEKS 5DAYS	1	NVD		NICU	14	Severe preeclampsia
N	30	3	PRIMI	38	3	LSCS	CDMR		14.8	NORMAL
N	27	2	PRIMI	40 WEEKS	3	NVD			15.3	NORMAL
N	33	4	4	40	3	NVD			15.3	NORMAL
N	20	1	PRIMI	34+4	2	NVD			16.9	NORMAL
N	21	1	PRIMI	40	3	NVD	EPILEPSY		17.3	NORMAL
P	24	2	PRIMI	40 WEEKS +2DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	17.3	Preeclampsia
P	27	3	PRIMI	33 WEEKS	2	NVD		IUD	17.9	Preeclampsia
P	35	4	PRIMI	38 WEEKS 6DAYS	3	LSCS	CONTRACTED PELVIS	NICU	17.9	Severe preeclampsia
N	21	1	2	40	3	NVD			18	NORMAL
N	30	3	4	38+1	3	NVD			18	NORMAL
N	20	1	PRIMI	39+3	3	NVD			18.2	NORMAL
N	26	2	PRIMI	41	1	LSCS	FETAL DISTRESS		18.7	NORMAL
N	26	2	PRIMI	38+6	2	LSCS	FETAL DISTRESS		18.8	NORMAL
N	25	2	PRIMI	40	3	NVD			19.9	NORMAL
P	22	2	PRIMI	39	3	NVD		BABY MOTHER'S SIDE	20	Preeclampsia
P	28	3	2	37 WEEKS 5DAYS	3	LSCS	PREVIOUS LSCS	BABY MOTHER'S SIDE	20	Severe preeclampsia
P	22	1	3	38 WEEKS 5 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	20.9	Severe preeclampsia
N	22	1	PRIMI	41+4	2	LSCS	FETAL DISTRESS		21	NORMAL
P	23	2	PRIMI	38 WEEKS 4 DAYS	3	NVD		BABY MOTHER'S SIDE	21	Preeclampsia
N	20	1	2	38	3	LSCS	FETAL DISTRESS		21.1	NORMAL
P	20	1	2	38WEEKS 2 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	21.1	Preeclampsia
P	34	4	PRIMI	34WEEKS	2	LSCS	BREECH	LBW	21.4	Preeclampsia
P	27	2	2	39 weeks 2 days	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	21.5	Preeclampsia
N	28	3	4	40+4	3	LSCS	FETAL DISTRESS		21.7	NORMAL
P	24	2	PRIMI	39 WEEKS 1DAY	3	LSCS	FETAL DISTRESS	NICU	21.8	Preeclampsia
N	30	3	2	38+4	3	LSCS	PREVIOUS LSCS		21.9	NORMAL
N	24	2	2	40	3	LSCS	CDMR		22.3	NORMAL
N	25	2	2	39+6	3	LSCS			22.3	NORMAL
N	20	1	PRIMI	37	3	NVD			22.4	NORMAL
N	23	2	2	39+4	3	LSCS	PREVIOUS LSCS		23.1	NORMAL
N	27	3	3	38+2	3	LSCS	PREVIOUS LSCS		23.6	NORMAL
N	28	3	2	40	3	LSCS			23.6	NORMAL
N	25	2	4	29+4	1	LSCS	TRANSVERSE LIE		23.8	NORMAL
N	21	1	PRIMI	37	3	LSCS	FETAL DISTRESS		25	NORMAL

GROUP	AGE	AGE GROUP	PARITY	GESTATIONAL AGE	GA	MODE OF DELIVERY	INDIICATION FOR LSCS	FETAL OUTCOME	CA125	SEVERITY OF PREECLAMPSIA
N	25	2	2	38+4	3	LSCS	PREVIOUS LSCS		25	NORMAL
N	25	2	4	37+3	3	LSCS			27.1	NORMAL
N	19	1	PRIMI	37 WEEKS 5DAYS	3	NVD			27.2	NORMAL
N	25	2	4	35+3	2	LSCS	FETAL DISTRESS		27.5	NORMAL
P	28	3	2	36 WEEKS 1 DAY	2	LSCS	PREVIOUS LSCS	LBW	28	Preeclampsia
N	26	2	PRIMI	40	3	LSCS	FETAL DISTRESS		28.1	NORMAL
N	29	3	3	29+4	1	LSCS	HYDROPS FETALIS		28.3	NORMAL
N	23	2	2	40	3	LSCS	FETAL DISTRESS		28.4	NORMAL
N	24	2	PRIMI	38+3	3	LSCS			28.7	NORMAL
N	28	3	PRIMI	32+5	1	LSCS	PREVIOUS LSCS		29.8	NORMAL
N	37	4	4	39+3	3	LSCS	PREVIOUS LSCS		31.2	NORMAL
N	27	2	2	37	3	NVD			31.4	NORMAL
N	23	2	PRIMI	39	3	LSCS	FETAL DISTRESS		32.1	NORMAL
N	29	3	2	35+3	2	LSCS	GDM		32.1	NORMAL
P	26	2	3	35WEEKS 6 DAYS	2	LSCS	PREVIOUS LSCS	LBW	32.8	Preeclampsia
P	21	1	PRIMI	35WEEKS 3 DAYS	2	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	32.8	Severe preeclampsia
N	25	2	PRIMI	38+1	3	LSCS	PREVIOUS LSCS		33.1	NORMAL
P	26	2	2	36 WEEKS 5 DAYS	2	LSCS	CDMR	BABY MOTHER'S SIDE	34	Preeclampsia
P	21	1	2	34WEEKS 4 DAYS	2	NVD		LBW	34.1	Preeclampsia
P	26	2	PRIMI	37 WEEKS	3	LSCS	NON PROGRESSION	BABY MOTHER'S SIDE	34.1	Severe preeclampsia
P	30	3	3	39 WEEKS	3	LSCS	FAILED INDUCTION	BABY MOTHER'S SIDE	34.2	Preeclampsia
P	26	2	PRIMI	40 WEEKS 5 DAYS	3	NVD		BABY MOTHER'S SIDE	35	Preeclampsia
P	34	4	PRIMI	38 WEEKS 4 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	35	Severe preeclampsia
P	29	3	2	38 WEEKS	3	NVD		BABY MOTHER'S SIDE	35.9	Preeclampsia
P	30	3	2	36 WEEKS 3 DAYS	2	LSCS	FETAL DISTRESS	NICU	35.9	Severe preeclampsia
P	22	1	PRIMI	40 WEEKS 3 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	36.2	Preeclampsia
P	20	1	PRIMI	40 WEEKS 1 DAY	3	LSCS	CPD	BABY MOTHER'S SIDE	36.5	Preeclampsia
P	30	3	4	36 WEEKS 4 DAYS	2	NVD		BABY MOTHER'S SIDE	36.8	Preeclampsia
P	19	1	PRIMI	39 WEEKS	3	LSCS	FETAL DISTRESS	NICU	38.6	Severe preeclampsia
P	29	3	PRIMI	38 WEEKS	3	NVD		NICU	38.6	Severe preeclampsia
P	20	1	PRIMI	38 WEEKS 5 DAYS	3	LSCS	PREVIOUS LSCS	BABY MOTHER'S SIDE	40	Severe preeclampsia
P	22	1	2	32 WEEKS 4 DAYS	1	NVD		IUD	41	Severe preeclampsia
P	29	3	PRIMI	38 WEEKS 4 DAYS	3	NVD		NICU	42	Severe preeclampsia
P	18	1	PRIMI	35 WEEKS	2	NVD		LBW	42.7	Severe preeclampsia
P	29	3	PRIMI	39 WEEKS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	46	IMMINENT ECLAMPSIA
P	21	1	PRIMI	32 WEEKS	1	LSCS	FAILED INDUCTION	LBW	46.3	Severe preeclampsia
N	23	2	2	37	3	LSCS	PREVIOUS LSCS		46.7	NORMAL
P	22	1	2	29 WEEKS 1 DAY	1	NVD		IUD	48	Severe preeclampsia
P	18	1	2	29 WEEKS 2 DAYS	1	NVD		IUD	50.5	IMMINENT ECLAMPSIA
P	35	4	3	37+5WEEKS	2	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	52.8	Severe preeclampsia
N	27	2	2	29 weeks	1	LSCS	ANHYDROAMINIOS		55.5	NORMAL
N	30	3	PRIMI	37+5	3	LSCS	BREECH		56	NORMAL
P	20	1	PRIMI	38 WEEKS	3	NVD		BABY MOTHER'S SIDE	61.5	IMMINENT ECLAMPSIA
P	18	1	PRIMI	40 WEEKS 3 DAYS	3	NVD		NICU	65.3	Antepartum Eclampsia
P	20	1	PRIMI	35 WEEKS 2 DAYS	2	LSCS	FETAL DISTRESS	NICU	66.3	Antepartum Eclampsia
P	18	1	PRIMI	40 WEEKS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	66.7	IMMINENT ECLAMPSIA
P	23	2	3	34 WEEKS 6DAYS	2	NVD		IUD	66.7	IMMINENT ECLAMPSIA
N	21	1	2	39	3	LSCS	PREVIOUS LSCS		87.8	NORMAL

GROUP	AGE	AGE GROUP	PARITY	GESTATIONAL AGE	GA	MODE OF DELIVERY	INDIICATION FOR LSCS	FETAL OUTCOME	CA125	SEVERITY OF PREECLAMPSIA
P	28	3	2	36 WEEKS 1 DAY	3	LSCS	PREVIOUS LSCS	LBW	8	Preeclampsia
P	19	1	PRIMI	39 WEEKS	3	LSCS	FETAL DISTRESS	NICU	9.9	Severe preeclampsia
P	21	1	PRIMI	37WEEKS 3 DAYS	3	LSCS	CDMR	BABY MOTHER'S SIDE	10.2	Preeclampsia
P	21	1	2	39 WEEKS 4 DAYS	3	LSCS	FETAL DISTRESS	NICU	10.5	Severe preeclampsia
P	23	2	PRIMI	37 WEEKS	3	NVD		BABY MOTHER'S SIDE	10.9	Preeclampsia
P	20	1	PRIMI	29 WEEKS 6 DAYS	1	NVD		NICU	11.6	Severe preeclampsia
P	22	1	PRIMI	39 WEEKS	3	NVD		BABY MOTHER'S SIDE	12.3	Preeclampsia
P	22	1	3	35 WEEKS	2	NVD		BABY MOTHER'S SIDE	12.5	Preeclampsia
P	19	1	PRIMI	40 WEEKS 4 DAYS	3	LSCS	CDMR	BABY MOTHER'S SIDE	13.4	Preeclampsia
P	18	1	PRIMI	40 WEEKS 3 DAYS	3	NVD		NICU	13.6	POSTPARTUM ECLAMPSIA
P	26	2	4	32 WEEKS 5DAYS	1	NVD		NICU	14	Severe preeclampsia
P	20	1	PRIMI	38 WEEKS	3	NVD		BABY MOTHER'S SIDE	14	IMMINENT ECLAMPSIA
P	18	1	2	29 WEEKS 2 DAYS	1	NVD		IUD	14	IMMINENT ECLAMPSIA
P	24	2	PRIMI	40 WEEKS +2DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	17.3	Preeclampsia
P	35	4	PRIMI	38 WEEKS 6DAYS	3	LSCS	CONTRACTED PELVIS	NICU	17.9	Severe preeclampsia
P	27	2	PRIMI	33 WEEKS	2	NVD		IUD	17.9	Preeclampsia
P	28	3	2	37 WEEKS 5DAYS	3	LSCS	PREVIOUS LSCS	BABY MOTHER'S SIDE	20	Severe preeclampsia
P	22	1	PRIMI	39	3	NVD		BABY MOTHER'S SIDE	20	Preeclampsia
P	22	1	3	38 WEEKS 5 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	20.9	Severe preeclampsia
P	23	2	PRIMI	38 WEEKS 4 DAYS	3	NVD		BABY MOTHER'S SIDE	21	Preeclampsia
P	20	1	2	38WEEKS 2 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	21.1	Preeclampsia
P	34	4	PRIMI	34WEEKS	2	LSCS	BREECH	LBW	21.4	Preeclampsia
P	27	2	2	39 weeks 2 days	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	21.5	Preeclampsia
P	24	2	PRIMI	39 WEEKS 1DAY	3	LSCS	FETAL DISTRESS	NICU	21.8	Preeclampsia
P	26	2	PRIMI	37 WEEKS	3	LSCS	NON PROGRESSION	BABY MOTHER'S SIDE	22.2	Severe preeclampsia
P	34	4	PRIMI	38 WEEKS 4 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	25.3	Severe preeclampsia
P	20	1	PRIMI	40 WEEKS 1 DAY	3	LSCS	CPD	BABY MOTHER'S SIDE	26.5	Preeclampsia
P	30	3	4	36 WEEKS 4 DAYS	2	NVD		BABY MOTHER'S SIDE	26.8	Preeclampsia
P	21	1	PRIMI	35WEEKS 3 DAYS	2	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	27.2	Severe preeclampsia
P	30	3	3	39 WEEKS	3	LSCS	FAILED INDUCTION	BABY MOTHER'S SIDE	27.2	Preeclampsia
P	29	3	PRIMI	38 WEEKS	3	NVD		NICU	28.6	Severe preeclampsia
P	26	2	2	36 WEEKS 5 DAYS	2	LSCS	CDMR	BABY MOTHER'S SIDE	34	Preeclampsia
P	30	3	2	36 WEEKS 3 DAYS	2	LSCS	FETAL DISTRESS	NICU	35.9	Severe preeclampsia
P	22	1	PRIMI	40 WEEKS 3 DAYS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	36.2	Preeclampsia
P	18	1	PRIMI	40 WEEKS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	40	IMMINENT ECLAMPSIA
P	20	1	PRIMI	38 WEEKS 5 DAYS	3	LSCS	PREVIOUS LSCS	BABY MOTHER'S SIDE	40	Severe preeclampsia
P	22	1	2	32 WEEKS 4 DAYS	1	NVD		IUD	41	Severe preeclampsia
P	29	3	PRIMI	38 WEEKS 4 DAYS	3	NVD		NICU	42	Severe preeclampsia

P	18	1	PRIMI	35 WEEKS	2	NVD		LBW	42.7	Severe preeclampsia
P	23	2	3	34 WEEKS 6DAYS	2	NVD		IUD	43.2	IMMINENT ECLAMPSIA
P	29	3	PRIMI	39 WEEKS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	46	IMMINENT ECLAMPSIA
P	20	1	PRIMI	35 WEEKS 2 DAYS	2	LSCS	FETAL DISTRESS	NICU	46.3	Antepartum Eclampsia
P	21	1	PRIMI	32 WEEKS	1	LSCS	FAILED INDUCTION	LBW	46.3	Severe preeclampsia
P	26	2	PRIMI	38 weeks	3	LSCS	CONTRACTED PELVIS	BABY MOTHER'S SIDE	47.3	Preeclampsia
P	22	1	2	29 WEEKS 1 DAY	1	NVD		IUD	48	Severe preeclampsia
P	26	3	3	35WEEKS 6 DAYS	2	LSCS	PREVIOUS LSCS	LBW	50.5	Preeclampsia
P	35	4	3	37+5WEEKS	3	LSCS	FETAL DISTRESS	BABY MOTHER'S SIDE	52.8	Severe preeclampsia
P	21	1	2	34WEEKS 4 DAYS	2	NVD		LBW	61.5	Preeclampsia
P	29	3	2	38 WEEKS	3	NVD		BABY MOTHER'S SIDE	66.7	Preeclampsia
P	26	3	PRIMI	40 WEEKS 5 DAYS	3	NVD		BABY MOTHER'S SIDE	66.7	Preeclampsia

GROUP	INDIICATION FOR LSCS			
N	ANHYDROAMINIOS		N	ANHYDROAMINIOS
N	BREECH		N	BREECH
N	CDMR		N	CDMR
N	CDMR		N	CDMR
N	CONTRACTED PELVIS		N	CONTRACTED PELVIS
N	CPD		N	CPD
N	DCDA TWIN		N	TRANSVERSE LIE
N	EPILEPSY		N	EPILEPSY
N	FETAL DISTRESS		N	FETAL DISTRESS
N	FETAL DISTRESS		N	FETAL DISTRESS
N	FETAL DISTRESS		N	FETAL DISTRESS
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N	FETAL DISTRESS		N	FETAL DISTRESS
N	FETAL DISTRESS		N	FETAL DISTRESS
N	GDM		N	GDM
N	HYDROPS FETALIS		N	HYDROPS FETALIS
N	NON PROGRESSION		N	NON PROGRESSION
N	PLACENTA ACCRETA		N	PLACENTA ACCRETA
N	PREVIOUS LSCS		N	PREVIOUS LSCS
N	PREVIOUS LSCS		N	PREVIOUS LSCS

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N	PREVIOUS LSCS		N	PREVIOUS LSCS
P	BREECH		P	BREECH
P	CDMR		P	CDMR
P	CDMR		P	CDMR
P	CDMR		P	CDMR
P	CONTRACTED PELVIS		P	CONTRACTED PELVIS
P	CONTRACTED PELVIS		P	CONTRACTED PELVIS
P	CPD		P	CPD
P	FETAL DISTRESS		P	FETAL DISTRESS
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P	FETAL DISTRESS		P	FETAL DISTRESS
P	FOOTLING BREECH		P	FAILED INDUCTION
P	FOOTLING BREECH		P	FAILED INDUCTION
P	NON PROGRESSION		P	NON PROGRESSION
P	PREVIOUS LSCS		P	PREVIOUS LSCS
P	PREVIOUS LSCS		P	PREVIOUS LSCS
P	PREVIOUS LSCS		P	PREVIOUS LSCS
P	PREVIOUS LSCS		P	PREVIOUS LSCS