CORRELATION OF OXIDATIVE AND MITOCHONDRIAL STRESS MARKERS IN NORMAL PREGNANCY AND IN PREECLAPMSIA WITH FOETAL AND MATERNAL OUTCOME.

By

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Dr. SUPRIYA H M

LIST OF ABBREVATIONS USED

MDA	**-**	**MALONDIALDEHYDE**
IMA	**-**	**ISHEMIA MODIFIED ALBUMIN**
TCO	**-**	**TOTAL CYTOCHROME OXIDASE**
TBARS	**-**	**THIOBARBITURIC ACID REACTIVE SUBSTANCES**
ELISA	**-**	**ENZYME-LINKED IMMUNO SORBENT ASSAY**
NICU	**-**	**NEONATAL INTENSIVE CARE UNIT**
ICU	**-**	**INTENSIVE CARE UNIT**
PPH	**-**	**POST PARTUM HEMORRHAGE**
IUD	**-**	**INTRAUTERINE FETAL DEMISE**
IUGR		**INTRAUTERINE FETAL GROWTH RETARDATION**
WHO	**-**	**WORLD HEALTH ORGANIZATION**
OS	**-**	**OXIDATIVE STRESS**
NADPH	**-**	**NICOTINAMIDE ADENINE DINUCLEOTIDE PHOSPHATE HYDROGEN**
SOD	**-**	**SUPER OXIDE DISMUTASE**
CU	**-**	**COPPER**
ZN	**-**	**ZINC**
GSH	**-**	**GLUTATHIONE**
NP	**-**	**NONPREGNANT**
PIH	**-**	**PREGNANCY INDUCED HYPERTENSION**
ACOG	**-**	**AMERICAN COLLEGE OF OBSTETRICIAN AND GYNECOLOGISTS**

HELLP	**-**	**HEMOLYSIS, ELEVATED LIVER ENZYMES,LOW PLATELET COUNT**
SBP	**-**	**SYSTOLIC BLOOD PRESSURE**
DBP	**-**	**DIASTOLIC BLOOD PRESSURE**
BP	**-**	**BLOOD PRESSURE**

ABSTRACT

INTRODUCTION: Hypertensive disorders complicate 5 to 10 percent of all pregnancies Preeclampsia is a multisystem disorder characterised by hypertension.

The cause remains largely unknown, but oxidative stress and a generalized inflammatory state are features of the maternal syndrome. The placenta seems to be the principal source of free radical synthesis but maternal leukocytes and the maternal endothelium are also seeming to be the likely donors. This study aims to quantify the serum OXIDATIVE STRESS markers in terms of malondialdehyde (MDA) & ischemia modified albumin(IMA) and MITOCHONDRIAL STRESS MARKER in terms of TOTAL CYTOCHROME OXIDASE and correlating these values with fetal and maternal outcome .

- **METHODS :** Pregnant women attending the out patient department of OBTETRICS AND GYNECOLOGY & admitting to labour room of RL JALAPPA Hospital and Research Center, of SRI DEVARAJ URS MEDICAL COLLEGE Tamaka, Kolar, during the period of study.
- Blood samples were taken from both case & control study population at the time of admission and measured for oxidative stress in terms of MDA(malondialdehyde), ischemic stress interms of IMA(ishemic modified albumin), mitochondrial stress in terms of TOTAL CYTOCHROME OXIDASE.
- Each women is followed up until delivary and the outcome is recorded and parameters involved with increased oxidative & mitochondrial stress are noted.
- MDA is measured by TBARS method.
- IMA is measured by turbidometric method using cobalt-II in dithiothreitol.

- TOTAL CYTOCHROME OXIDASE is measured by ELISA method.

RESULTS:

- The mean values of MDA, IMA and TOTAL CYTOCHROME OXIDASE was significantly higher in preeclampsia group as compared to the normal group (p value <0.05).
- Significant difference was seen in the distribution of abruption placenta, PPH, and eclampsia between the two groups. 19.51% of the patients in preeclampsia group had abruptio placenta as compared to 0% in normal group. Also incidence of PPH and eclampsia was significantly higher in the preeclampsia group as compared to the normal group.
- Significant association was seen in the NICU admission, low birth weight, IUD and IUGR with oxidative and mitochondrial stress markers. (p value <.05) Babies of mother with higher level of MDA, IMA and TOTAL CYTOCHROME OXIDASE had significantly higher chances of low birth weight, requirement of NICU admission, IUD and IUGR.
- Significant association was seen in abruption placenta, ICU admission and PPH with oxidative and mitochondrial stress markers. (p value <.05) Women with abruption placenta, ICU admission and PPH had significantly higher levels of oxidative and mitochondrial stress markers as compared to women without any such maternal complication

CONCLUSION: The study concludes that oxidative stress markers MDA and IMA along with mitochondrial stress marker, TOTAL CYTOCHROME OXIDASE elevated in preeclampsia in comparison with normotensive pregnants.

These markers evinced positive correlation with respect to degree of severity of maternal and fetal outcomes.

Multifarious increase of TOTAL CYTOCHROME OXIDASE observed in PE cases developed eclampsia during the course of the study where as moderate increase noticed in preeclampsia cases who has not developed eclampsia compared to normal pregnants.

KEYWORDS: Oxidative stress marker, Malondialdehyde (MDA) , ischemia modified albumin(IMA) , MITOCHONDRIAL STRESS MARKER, TOTAL CYTOCHROME OXIDASE, Preeclampsia, Proteinuria.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

INTRODUCTION

INTRODUCTION

In olden days it was accepted that “toxaemia” preceded most cases of eclampsia. The vital role of hypertension was not discovered, and after many years, it became obvious that preeclampsia was a syndrome of which hypertension was only one important facet. Still, the mechanisms by which pregnancy provokes or aggravates hypertension remain baffling. certainly, hypertensive disorders remain among the most important and intriguing unexplained problems in obstetrics[1].

Hypertensive disorders complicate 5 to 10 percent of all pregnancies, and together they are one of the deadly triad—along with haemorrhage and infection—that contributes greatly to maternal morbidity and mortality rates. The World Health Organization (WHO) systematically reviews maternal mortality worldwide, and in developed countries, 16 percent of maternal deaths were attributed to hypertensive disorders. Outstandingly, more than half of these hypertension-related deaths were deemed preventable. In India alone 8-10% incidence of preeclampsia is reported [2].

Preeclampsia being a most common and possibly threatening complication of pregnancy and is a multi-factorial and multi systemic disorder, characterized by development of hypertension after 20 weeks of gestation. The symptoms of preeclampsia can be with or without severe features. Intrauterine Foetal growth retardation, preterm delivery, maternal and prenatal morbidity and mortality are important complications[3].

It is a systemic metabolic syndrome that involves activation of endothelial cells and endothelial dysfunction and, systemic inflammatory response, oxidative stress, insulin resistance and dyslipidemia. Possible cause and mechanism behind preeclampsia remain unidentified, but the involvement of maternal, genetic factors, immune, and

placental factors have been implicated [3].

The cause remains largely unknown, but oxidative stress and a generalized inflammatory state are features of the maternal syndrome. The placenta seems to be the principal source of free radical synthesis but maternal leukocytes and the maternal endothelium are also seeming to be the likely donors [4].

Preeclampsia has largely been associated with the release of free radicals by the placenta at cellular levels. Placenta-endured oxidative and nitrosative stresses are considered as the major molecular causative factors for preeclampsia[4].

Oxidative stress (OS) is defined as "an imbalance between oxidants and antioxidants, leading to a disruption of redox signalling and control and to molecular damage". OS involves reactive oxygen species (ROS), the most common being superoxide ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2), and the hydroxyl radical (•HO). Highly reactive properties of ROS and RNS can cause structural and physiological damage to DNA, RNA, proteins, and lipids, including cell membrane-bound lipids[5].

Placental oxidative stress (OS) is present during all three trimesters in normal pregnancy and is necessary to obtain normal cell function. However, if OS reaches a certain level, pregnancy complications might arise. Preeclampsia (PE), a dangerous pregnancy specific hypertensive disorder, OS induced in the ischemic placenta causes a systemic inflammatory response and activates maternal endothelial cells[5].

During healthy pregnancy there is an increased but stable oxidative environment. If superoxide levels increase, there is an augmentation in arterial stiffness. In PE pregnancies, systemic inflammation and superoxide concentrations are higher and result in a deterioration of endothelial function.

Together, these findings support the hypothesis that vascular function is directly linked to the amount of OS and that measurement of OS in combination with vascular function tests might be used as one of the criteria in the prediction of PE[4].

Abnormally low plasma vitamin C concentrations are seen in preeclampsia, hence a combination of vitamins C and E is a promising prophylactic strategy for prevention of preeclampsia. Several multicenter randomized clinical trials are now underway to evaluate the benefits of antioxidant usage, and benefit of low-dose aspirin prophylaxis have intensified the need for a reliable predictive test for preeclampsia.

Recent reports have suggested an important role for placental trophoblast NAD(P)H oxidase in free radical generation in preeclampsia. The antioxidant vitamin E is now known to have multiple actions in addition to prevention of lipid peroxidation (ie, inhibition of NAD(P)H oxidase activation and the inflammatory response).

The newly recognized role for the involvement of NAD(P)H oxidase in the placenta represents a significant advance in our understanding of the disease. A combination of vitamins C and E, which act in synergy to prevent lipid peroxidation, may be effective in the prevention of preeclampsia. Moreover, the newly recognized anti-inflammatory properties of vitamin E may be particularly efficacious, because the multimode of action includes pathophysiological pathways associated with activation of NAD(P)H oxidase.[5]

Longitudinal studies are needed to detect an oxidative stress biomarker or a combination of these biomarkers with high sensitivity and specificity for early prediction of preeclampsia. Reference values are necessary to predict preeclampsia early in pregnancy before the onset of clinical signs and symptoms. This will help identify women at high risk who need closer monitoring during pregnancy. A

combination test involving several relevant biomarkers is likely to provide the best predictive potential and prevention of maternal and perinatal morbidity and mortality.

OBJECTIVES

AIM AND OBJECTIVES

AIM:

This study aims to quantify the serum OXIDATIVE STRESS markers in terms of MDA (malondialdehyde)& IMA (ischemia modified albumin) and MITOCHONDRIAL STRESS MARKER in terms of TOTAL CYTOCHROME OXIDASE and correlating these values with fetal and maternal outcome .

Objectives of the study:

1.To estimate MALONDIALDIHYDE (MDA) and ISHEMIA MODIFIED ALBUMIN (IMA) as oxidative stress markers in normal pregnancy and in preeclampsia cases.

2. To estimate TOTAL CYTOCHROME OXIDASE as mitochondrial stress markers in normal pregnancy and in preeclampsia cases

3.To correlate oxidative stress marker, MDA and IMA & mitochondrial stress marker, TOTAL CYTOCHROME OXIDASE with maternal & foetal outcome between normal pregnancy & preeclampsia cases.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

History of preeclampsia.

What would a millennium later become known as “preeclampsia-eclampsia” was first described by Hippocrates around 400 BC, who stated that headache accompanied by heaviness and convulsions during pregnancy was considered bad. This was the earliest suggestion that there may a specific entity associated with an unhealthy pregnancy.

Bossier de Sauvages (1710-1795) is considered the first to use the term, “eclampsia”, a Greek word meaning “lightning”, perhaps alluding to how suddenly and unexpectedly convulsions may arise.(1739) finally differentiated the seizures of eclampsia from epilepsy, noting the former was acute in nature and would resolve once the precipitating event was removed[1].

Demanet (1797) recognized the extreme swelling in eclamptic women

Pierre Rayer (1793-1867), a Frenchman, is considered the first to describe proteinuria in eclamptics, cited in his then classic text "Diseases of the Kidney".(1840) discovered protein in the urine

John Lever (1811-1859) first demonstrated that the proteinuria accompanying eclampsia was specific to that disease, and not part of a general disorder, then called Bright's disease. (1843) showed this proteinuria was specific to preeclampsia and not another kidney ailment also present in non-pregnant women.

J.Y. Simpson (1811-1870), one month later, published confirmation of Lever's finding.

By the mid 1800's, the hallmark prodromal symptoms including headache, temporary loss of vision, severe pain in the stomach, and edema in the upper body contributed to the recognition that there was a pre-eclamptic (before convulsions) state that should raise physician concern and was, in itself, a life-threatening condition.

However it was the introduction of Scipione Riva-Rocci's mercury manometer (1896) to measure blood pressure that led to the recognition that preeclampsia was a hypertensive disorder; from then until now, new onset of hypertension and proteinuria have been the major signs used in the classification of preeclampsia.

Cook and Briggs (1903) stated increase in blood pressure as the earliest sign of impending convulsions.

Zangemeister (1916), postulated that sudden increase in maternal weight is a

warning sign for development of pre eclampsia and eclampsia.[3]

Normal pregnancy is associated with a moderate increase of oxidative stress whereas the increase is marked in preeclampsia. Oxidative stress has been shown to be the causative factor for hypertension as well as causative factor for target tissue damage in hypertension[6].

A study was conducted for the measurement of oxidative stress in normal pregnancy and preeclampsia. It was observed that preeclampsia is associated increased level of MDA and thus with increased oxidative stress.[7]

J.TGohil et al performed a study on evaluation of Oxidative Stress and Antioxidant Defence in Subjects of Preeclampsia that showed increased levels of MDA are associated with preeclampsia.[8]

A study was conducted by Elisa Llubra to asses the potential role of oxidative stress as a mechanism underlying endothelial damage in PE and the pregnant woman's susceptibility to the disease. Indicative markers of lipoperoxidation and protein oxidation and

changes in antioxidant defense systems were measured in healthy pregnants and in preeclampsia cases. They concluded that significantly elevated plasma total lipid hydroperoxides, the major initial reaction products of lipid peroxidation, in severe PE. No intracellular or extracellular increases in any of the secondary end-products of lipid peroxidation, malondialdehyde or lipoperoxides[9.]

Oxidative stress is still persisting in babies of preeclamptic mothers with spontaneous vaginal delivery and vertex presentations, with appropriate placental and birth weight. The babies should be in observation and antioxidant supplementation[10.]

Mild oxidative stress in blood of preeclamptic women, as oxidative processes seem to be counteracted by the physiologic activation of antioxidant enzymes and by the high plasma vitamin E levels that would prevent further oxidative damage. These results do not permit us to conclude that oxidative stress might be a pathogenetically relevant process causally contributing to the disease.[7]

In preeclampsia there is a state of imbalance, where free radicals are high, without a compensatory increase of antioxidants. Deleterious effects may be produced due to multiple independent pathways that are activated, they contribute to the induction or the propagation of oxidative stress[7].

In a study where Forty-two pregnant women with preeclampsia and 30 healthy pregnant women were involved. The plasma concentrations of malondialdehyde, nitric oxide, and adrenomedullin were compared between the study group and the control group. In women with preeclampsia the plasma concentrations of malondialdehyde was higher while nitric oxide and adrenomedullin concentrations were lower compared to control subjects. It was observed that the plasma levels of ADM and NO are decreased while MDA levels are increased in subjects with preeclampsia and that might contribute to the pathophysiology of preeclampsia through the lack of a paracrine vasodilatory effect on uteroplacental blood flow[11].

In a study, Plasma malondialdehyde and homocysteine concentrations were measured and the correlation between them was investigated. According to the correlation found between the homocysteine and the MDA levels in preeclampsia , the supplementation of antioxidants and/or NO donors could be a chance of restoring the endothelial function in these patients[12].

Increased free radical activity and lipid peroxidation may be implicated in the pathogenesis of preeclampsia. A study was conducted to assess antioxidant enzyme and trace metals's status in preeclampsia. The comparision was made between the pregnant women with or without preeclampsia and healthy controls in the third trimester. In the preeclamptic group malondialdehyde, Cu levels were significantly increased, while Zn and SOD levels were significantly decreased compared to normal control group and healthy pregnant women.

These evidences give support that radical scavenging SOD is consumed by the increased lipid peroxidation in preeclampsia. This information may indicate an involvement of free radicals in the pathophysiology of preeclampsia. This study suggests a relationship between increased MDA, Cu levels and decreased SOD, Zn levels in pregnancy and preeclampsia[13].

A study was done to investigate the plasma and placental levels of malondialdehyde, glutathione and superoxide dismutase in normotensive and pre-eclamptic pregnancies. mean plasma and placental levels of malondialdehyde were signficantly higher, glutathione and superoxide dismutase levels were significantly lower in pre-eclamptic compared with

normotensive patients. The plasma and placental levels of malondialdehyde significantly increased, glutathione and superoxide dismutase significantly decreased. It was found that maternal circulating and placental tissue levels of lipid peroxides increase whereas antioxidants decrease in pre-eclampsia. The extent of oxidative stress and antioxidant changes correlate well with diastolic blood pressure[14]

Placental oxidative stress and lipid peroxidation play an important role in the pathophysiology of preeclampsia. Significant association between lipid peroxidation

and pre-eclampsia and the beneficial effects of vitamin supplementation in reducing the risk of preeclampsia are observed. Biomarkers can be used to measure the efficiency of the antioxidants. Vitamins C and E supplementation may be able to further help delineate the role of oxidative stress in the etiopathogenesis of preeclampsia.[15]

Vasospasm and endothelial dysfunction is noted in preeclampsia. One of the most favoured hypotheses is the endothelial dysfunction secondary to the peroxidation of membrane lipids resulting in altered vascular reactivity, loss of vascular integrity and activation of the coagulation cascade. Elevated circulating homocysteine is a risk factor for endothelial dysfunction and vascular diseases and is found to be associated with preeclampsia. Malondialdehyde, (MDA) a metabolite of lipid peroxides detectable in plasma is used as an indicator of lipid peroxidation. A study was undertaken to find out the alterations in the circulating levels of serum malondialdehyde (MDA) in normal pregnancy and preeclampsia when compared to normal nonpregnant women.

The mean serum levels of MDA in preeclampsia patients were higher than that of normal pregnant women. Also oxidative stress plays an important role in the pathogenesis of preeclampsia. Thus identifying the risk factors and aggressive management may prove to be beneficial in these women.[16]

A study was done to investigate the changes in enzyme activities of erythrocyte superoxide dismutase (SOD), catalase, and placental glutathione peroxidase (GSH-Px), and analyze the levels of serum malondialdehyde (MDA), copper (Cu), zinc (Zn), selenium (Se), leptin and placental MDA and glutathione (GSH). It was found that

Serum levels of MDA, was markedly higher in PE women compared with HP women and NP women. Also, placental MDA level was higher Placental MDA level in PE women had significant negative correlation with serum Se level. This data demonstrate that elevation of lipid peroxides together with impaired antioxidant defense mechanisms and status of trace metals and the presence of possible interrelationship and crosstalk between those parameters may be related at least partly to the pathogenesis of preeclampsia. Additionally, lipid peroxides and blood oxidative imbalance could be part of the cytotoxic mechanisms leading to endothelial cell injury[17].

A study was done to investigate the plasma and placental levels of malondialdehyde, glutathione and superoxide dismutase in normotensive and pre-eclamptic pregnancies. The mean plasma and placental levels of malondialdehyde were sig- ni cantly higher, glutathione and superoxide dismutase levels were signicantly lower in pre-eclamptic compared with normotensive patients . The plasma and placental levels of malondialdehyde signicantly increased, glutathione and superoxide dismutase signicantly decreased with the increments in diastolic blood pressure.

It was concluded in the study that maternal circulating and placental tissue levels of lipid peroxides increase whereas antioxidants decrease in pre-eclampsia. The magnitude of oxidative stress and antioxidant changes correlate well with diastolic blood pressure[18].

Pre-eclampsia is associated with oxidative stress in the maternal circulation. There is substantial evidence to suggest that the diverse manifestations of preeclampsia, including altered vascular reactivity, vasospasm, and discrete pathology in many

organ systems, are derived from pathologic changes within the maternal vascular endothelium. The imbalance between oxidative damage and antioxidant defences in pre-eclampsia leads to endothelial cell dysfunction. Endothelial cell dysfunction appears to be a central feature in the pathophysiology of pre-eclampsia.

In order to counteract intracellular damage by free radicals, cells have developed a so called intracellular antioxidant system. This process transforms free electrons into a nonreactive form by proteins (enzymes). Antioxidants regulate oxidative reactions by inhibiting, delaying or hampering the oxidation of the substances.

The intracellular enzymes function as antioxidants are the backbone of this cellular defense system. The key antioxidant enzymes possess certain elements that shield and protect proteins. Non-enzymatic antioxidants can also neutralize radicals (e.g. water-soluble substances such as vitamin C,glutathione or fat-soluble substances such as vitamin E or vitamin A/ β- carotene). For example, the enzyme SOD transforms superoxide radicals into hydrogen peroxide, which is then broken down by catalysis into water and oxygen.

Free radicals are not exclusively damaging metabolic products, but also have a series of important functions. For example they serve in immune defense because leucocytes

and macrophages utilize their bactericidal effects: they produce free radicals and thus destroy bacteria and other foreign substances. Moreover, free radicals probably play a role in the body's tumor suppression by mediating programmed cell death (apoptosis)[17].

Immune-relevant cells also use the reactive potential of ROS as a cellular defense mechanism against entering pathogens to kill bacteria, viruses and degenerated cells.

Radicals also fulfill important physiological function such as regulating the vascular tone and those cell functions controlled by oxygen concentration. They also influence signal transmission mechanisms and trigger oxidative stress responses as well as apoptosis.

Compared with healthy pregnant women, pre-eclamptic women have low levels of several dietary antioxidants in their blood, including vitamin C, vitamin E, lycopene and

beta carotene. They also have higher levels of ROS and frequently have increased levels of uric acid, probably resulting from the body's attempt to cope with oxidative stress.

The placentas of pre-eclamptic women also have lower than normal antioxidant levels and higher than normal levels of ROS.

In overtly preeclamptic women it is impossible to deci-pher cause from effect. Nonetheless, current concepts of the genesis of preeclampsia that include endothelial dysfunction,

inflammatory activation, oxidative stress and predisposing maternal factors provide targets for nutritional aspects. The imbalance between oxidative damage and antioxidant defences in pre-eclampsia leads to endothelial cell dysfunction. A

recurrent theme is that free radical reactions, promoted by "cross-talk" between the diseased placenta and maternal dyslipidemia, promote a vicious cycle of events that make cause and effect difficult to distinguish but may

contribute to the progression of preeclampsia. Oxidative stress play a significant role in the pathophysiology of pre-eclampsia and that supplemental dietary antioxidants

may have a beneficial role in the prevention of the disease and improvement in maternal and child health[9].

Oxidative stress of the placenta is considered to be a key intermediary step in the pathogenesis of preeclampsia, but the cause for the stress remains unknown.

Hypoxia-reoxygenation (H/R) injury, as a result of intermittent placental perfusion secondary to deficient trophoblast invasion of the endometrial arteries, is a possible mechanism. In this review, we present evidence to show that there is a plausible basis from which to assume that blood flow in the intervillous space will be intermittent in all normal pregnancies. The intermittency will be exacerbated by impaired conversion of the spiral arteries, or by the presence of atherotic changes that reduce their caliber as seen in preeclampsia.

Placental oxidative stress can be the consequences of fluctuations in oxygen concentrations after H/R through the actions of reactive oxygen species. On this basis, there will be a complete spectrum of placental changes among the normal, the late onset and the early onset preeclamptic states[19].

Increased oxidative stress and antioxidative defense mechanisms may contribute to disease

processes both in preeclampsia and IUGR[20].

Hypoxia driven oxidative stress of the placenta contributes to the pathogenesis of preeclampsia. Hence Placental ischemia modified albumin may be a marker of oxidative stress in preeclampsia . Elevated levels of serum Ischemia Modified Albumin (IMA) in preeclampsia when compared with PIH and normotensive pregnancy.[21]

Sapna Vyakaranam et al did a case control study to determine the efficiency of serum IMA in differentiating hypertensive disorders of pregnancy (pregnancy induced hypertension, preeclampsia) from normal pregnancy. They concluded that serum IMA, an oxidative stress marker is elevated in PE & PIH. Hence serum IMA can undergo further evaluation as a marker of PE. [21]

Ischemia Modified Albumin is a well-known marker of cardiac Ischemia. A study was done to assess the variation in maternal serum Ischemia Modified Albumin (IMA) in preeclampsia during pre and post labour within 48 hours. A significant increase in IMA concentrations

when compared to non-pregnant women was noted. The trend of Modified albumin as IMA in preeclampsia shows the gradual increase after the delivery within 48 hrs. However the levels of IMA in normal pregnancy show a tenfold increase than the non-pregnant women[22].

TOTAL CYTOCHROME OXIDASE is of mitochondrial origin. As per the litertature reviewed information on serum TOTAL CYTOCHROME OXIDASE in normal pregnants and in preeclamsia is limited and seldom. However there is a report

on placental TOTAL CYTOCHROME OXIDASE in a study carried out by Liping H et al., titled, Reduced amount of TOTAL CYTOCHROME OXIDASE subunit I messenger RNA in placentas from pregnancies complicated by preeclampsia.

TOTAL CYTOCHROME OXIDASE is a marker enzyme of the mitochondrial inner membrane. A change in the structure and activity of TOTAL CYTOCHROME OXIDASE may alter the electron transport in the inner membrane, leading to insufficient adenosine triphosphate (ATP) production. ATP is essential for maintaining the function of cells. A study was done to compare the expression of TOTAL CYTOCHROME OXIDASE subunit I mRNA in placentas from normal and preeclamptic pregnancies. The study demonstrates a reduced amount of TOTAL CYTOCHROME OXIDASE subunit I mRNA in preeclamptic placentas compared to control placentas. They have concluded reduced expression may play a role in the pathophysiology of preeclampsia[23] .

Hypertensive disorders of pregnancy

Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and perinatal mortality worldwide. It has been estimated that preeclampsia complicates 2–8% of pregnancies globally.

In Latin America and the Caribbean, hypertensive disorders are responsible for almost 26% of maternal deaths, whereas in Africa and Asia they contribute to 9% of deaths. Although maternal mortality is much lower in high-income countries than in developing countries, 16% of maternal deaths can be attributed to hypertensive disorders. In the United States, the rate of preeclampsia increased by 25% between 1987 and 2004. Moreover, in comparison with women giving birth in 1980, those giving birth in 2003

were at 6.7-fold increased risk of severe preeclampsia.

American College of Obstetrician and Gynecologists (ACOG) committee on terminology in 2013, described Hypertensive diseases into four categories .

1. Gestational hypertension
2. Preeclampsia and Eclampsia syndrome
3. Chronic Hypertension of any etiology
4. Preeclampsia superimposed on chronic hypertension.

This classification well differentiates the preeclampsia syndrome from other hypertensive disorders.

ETIOPATHOGENESIS [24]

1. Normal and Abnormal Trophoblastic invasion

In normal pregnancy during implantation, extensive remodeling of the uterine arteries occurs due to the invasion of the Endovascular Trophoblasts. These trophoblasts replace the endothelial and muscular layers of the vessel wall to enlarge the diameter of the vessel thus, increasing its capacitance. This physiological change takes place in two phases.

PHASE I- This phase starts at the time of early implantation and ends by 12 to 14 weeks of gestation. In this phase the Trophoblastic tissue invades the Myometrial segment of the vasculature.

PHASE II- This phase begins at 12-14weeks of gestation and proceeds on till 20 to 24 weeks of gestation. During this phase there is further invasion of trophoblastic tissue into the Myometrial segment of the spiral arteries. This leads to dilataion of the arteries, by increasing their capacitance and there by converting high resistance system into low resistance system. This facilitates better exchange of gases and nutrients across the maternal-fetal circulation leading to enhanced intra uterine fetal growth.

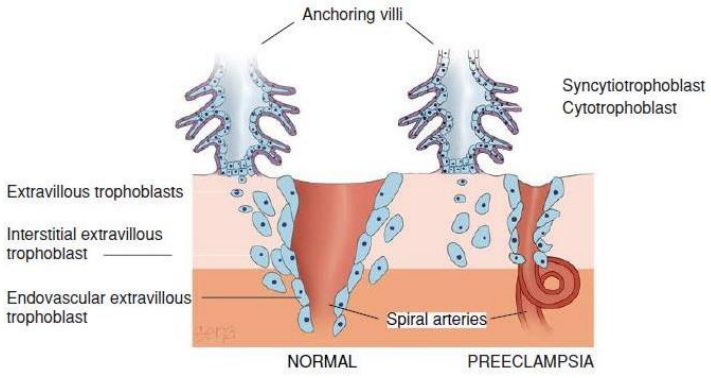


FIGURE -1:Schematic representation of normal placental invasion and Defective Trophoblastic invasion

Trophoblastic invasion of the maternal Decidua takes place by two different pathways [26]

1. Interstitial pathway-vessels are invaded by the interstistial trophoblastic cells and then these are further termed as the „Endovascular Trophoblasts".
2. Endovascular Pathway - The Endovascular trophoblastic cells migrate in retrograde direction i.e., in the direction opposite to the arterial flow.

Hence, the phenotypic expression of Preeclampsia syndrome is a "Two Stage Disorder"

Atherosis in a blood vessel from a placental bed. Photomicrograph shows disruption of the endothelium that results in a narrowed lumen because of subendothelial accumulation of plasma proteins and foamy macrophages. Some of the foamy macrophagesare shown by curved arrows, and straight arrows highlight areas of endothelial disruption.

All the above changes which occur physiologically in the spiral arteries replace the Musculo-Elastic Tunica media layer of the vessel wall by the "Mononuclear Trophoblasts embedded in the Fibrinoid". This converts the original Low capacitance- High resistance vessels into High capacitance –Low resistance vessels leading to increased blood flow to the inter villous space.

In normal pregnancy, this physiological conversion is seen in majority of the vessels at term, while only 1/3 rd of the arteries show myometrial invasion at 16-18 weeks of pregnancy. In hypertensive disorders, failure to complete late conversion i.e.,failure of invasion by trophoblasts is the pathological cause

underlying in majority cases.

2. Immunological Factors[25]

Maternal immune system show physiological change in its immune tolerance to the Fetal and placental antigens by producing blocking Antibodies. Production of these Blocking Antibodies is impaired in patients with risk factors for Preeclampsia.MCH Class I and II play a important role in the immune activity.

3. Genetic Factors

Studies show that hereditary hypertension is a risk factor for Preeclampsia and thus tendency for Preeclampsia –Eclampsia is inherited.

Genes involved with Preeclampsia are

- HLA Antigen- involved in immune tolerance
- Factor V (Leiden)
- MTHFR gene-Methylene Tetra Hydrofolate reductase
- NOS3-helps in nitric oxide production in Endothelium
- AGT(M235 T)- Angiotensinogen
- F2-Prothrombin (Factor II)

4. Inflammatory and Angiogenic Factors[26]

In response to the ischemic changes placental factors are released intiating a cascade of events.

- Preeclampsia is a state in which leucocytes are activated to their extremes in the

maternal circulation.

- Reduced expression of HLA-G(immune suppressive Human Leucocute Antigen).

- Increase in cytokines Th1(Pro inflammatory cytokines) and Th2 (Anti-inflammatory cytokines).

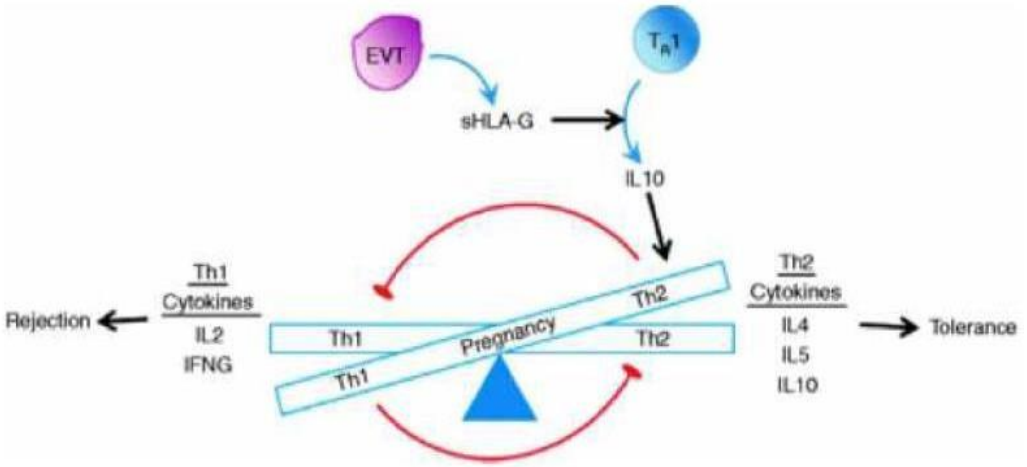


FIGURE-2: Schematic representation of immune factors in Preeclampsia

5. Endothelial Cell Activation[27]

Due to the hypoxia leading to the ischemic changes various inflammatory changes takes place leading to the cascade of events releasing anti Angiogenic and metabolic factors and other leucocyte mediators which provoke systemic endothelial cell injury which ultimately causes Endothelial cell activation or dysfunction.

PATHOGENESIS:

1. **Vasospasm**

   Vasoconstriction and increase in resistance to the flow is seen as a result of endothelial activation leading to Hypertension.

2. **Increased vasopressor response**

   In normal pregnancy, physiological development of resistance to the vasopressors is seen which is reduced in Preeclampsia cases as there is increase sensitivity to the Vasopressors due to various factors.

3. **Prostaglandins**[28]

   In individuals predisposed to Preeclampsia, PGI2 (prostacyclin) levels decreases and TXA2 (Thromboxane) levels increases which ultimately leads to increased sensitivity to the vasopressors.

4. **Nitric Oxide**[29]

   Synthesis of Nitric oxide mimics the scenario of Preeclamsia by reducing Heart rate and increasing Mean arterial pressure.

5. **Angiogenic and Anti Angiogenic proteins**

   In normal pregnancy,increase in Endothelin -1(ET-1) levels are observed whose levels are more exaggerated in preeclampsia.

   Increased levels of sFlt-1, sEng (Soluble Endoglin) begin to increase before the development of clinical features.

   SFlt-soluble fms-like

tyrosine kinase PIGF-

placental growth factor

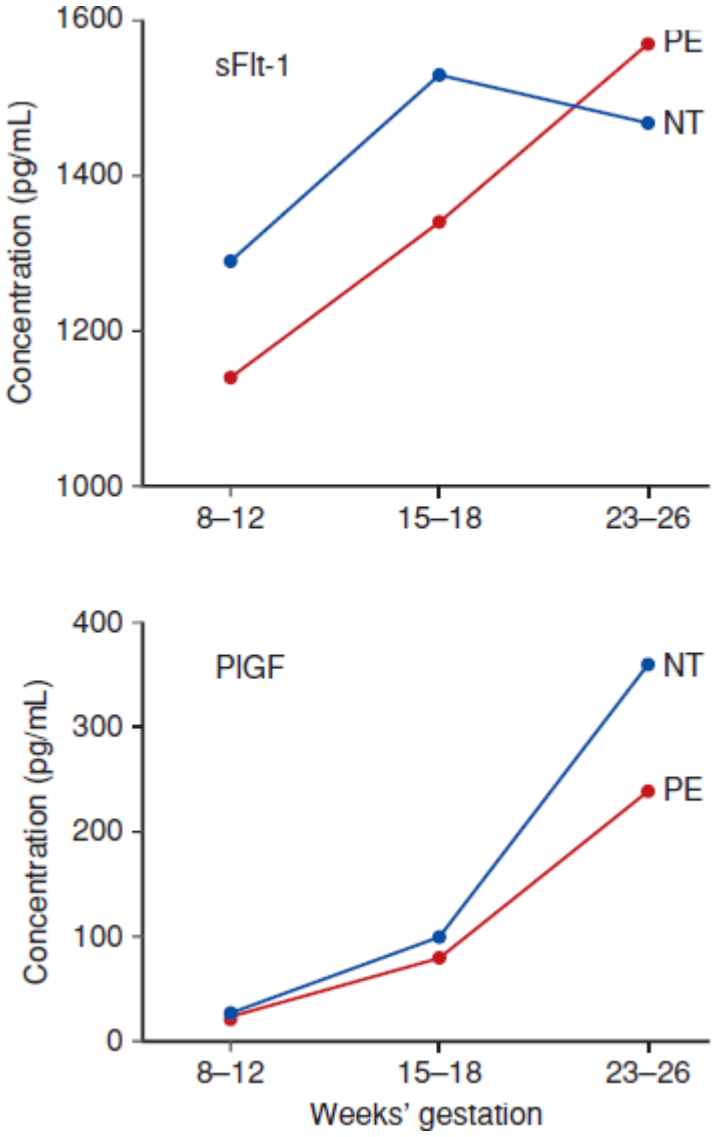


FIGURE-3:Angiogenic and Anti Angiogenic factors in Normotensive and Preeclamptic women

PATHOPHYSIOLOGY[30]

Preeclampsia manifests as a muliorgan dysfunction affecting the cardiovascular system majorly.

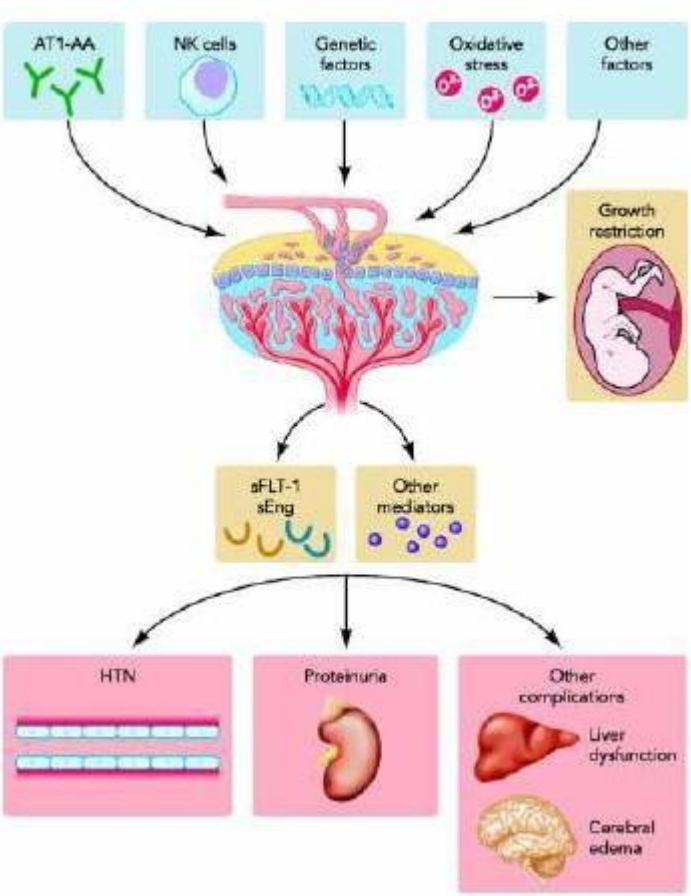


FIGURE-4:SCHEMATIC REPRESENTATION OF PATHOPHYSIOLOGY IN PREECLAMPSIA.

Cardiovascular system[31]

- Increase in the cardiac afterload due to hypertension
- Reduced Cardiac preload, due to pathologically diminished volume expansion.
- Endothelial activation leading to the inter endothelial extravasation of intravacular fluid into extravascular space especially the lungs.

Hemodynamic changes and Cardiac function [32]

- Increase in the peripheral resistance due to decrease in the capacitance of the vessels.
- Decrease in the cardiac output.

Myocardial function

- Ventricular remodelling leading to Diastolic Dysfunction
- Diastolic dysfunction leads to cardiogenic pulmonary oedema

Hematological changes

- Hemoconcentration is the Hallmark of Eclampsia
- Fall in the Hematocrit level but shows false high hematocrit value.
- Maternal Thrombocytopenia- Platelet count < 1,00,000 cells/cu.mm
- Hemolysis of cells seen in HELLP syndrome

Hepatic changes [33]

- Elevated liver enzymes levels especially the serum Transaminases.
- Charectaristic Hepatic lesions are regions of Periportal hemorrhages in the periphery,ischemic lesions and fibrin depositions.
- Hepatic infarctions and subcapsular liver Hematomas are not uncommon.

Renal changes

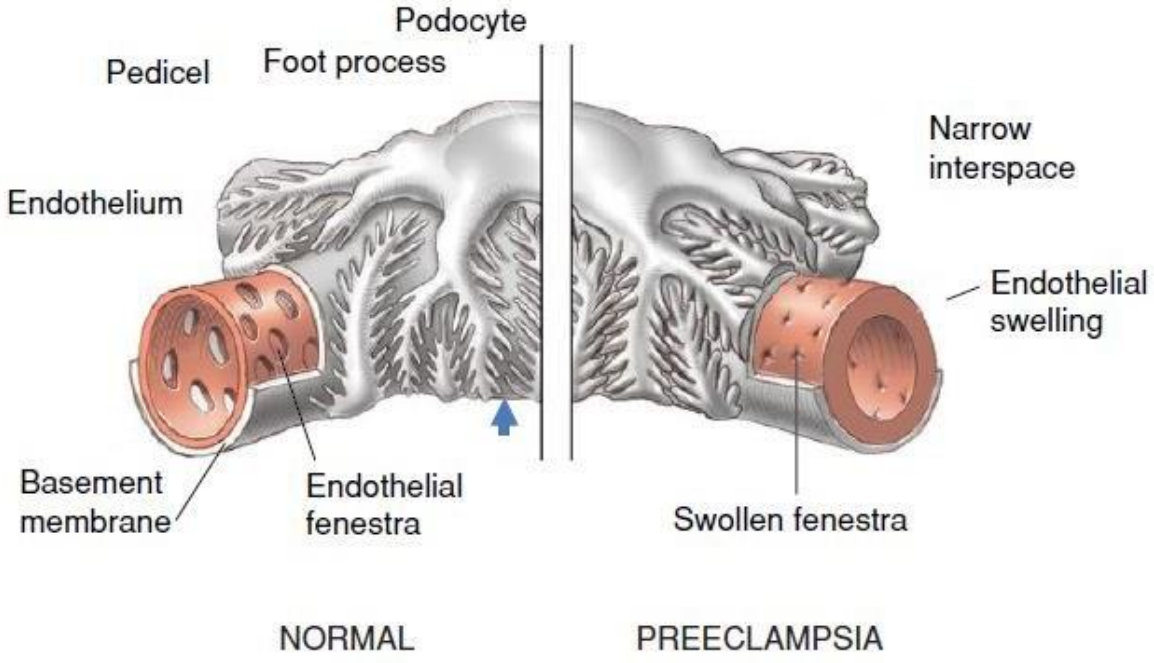


FIGURE-5:Schematic representation showing glomerular capillary Endotheliosis

- Decreased glomerular filtration rate is seen in Preeclampsia due to Vasospasm leading to decreased renal perfusion.

- Reduction in the GFR leads to decreased tubular reabsorption causing elevated plasma Uric acid levels.
- Morphology of kidney shows characteristic “Glomerular Endotheliosis”
- Increase in the urine osmolality is seen along with the Oliguria**.**
- **PROTEINURIA**[34]**-** detection of proteinuria helps to establish preeclampsia 24 hour urine excretion exceeding 300 mg urine protein: Creatinine ratio > 0.3 >/= +1 dipstick

- Acute tubular necrosis is seen in some of the cases

Central nervous system

- Headache and visual disturbances are the most common with Severe Preeclampsia.
- Associations with convulsions diagnose Eclampsia.
- Vasospasm in Preeclampsia attributes to Hypertensive Encephalopathy.
- Radiological studies show cerebral oedema, hemorrhagic lesions particularly in the posterior hemispheres.
- Some patients present with altered mentation.

Placenta[35]

- Compromised Uteroplacental perfusion is seen attributed to the high resistance

vessels.

- Chorionic villi congestion is seen with Proliferative Endarteritis and cytotrophoblastic celss proliferation
- Increased incidence of infarcts and hematomas.

Diagnosis of Hypertensive disorders- ACOG-2013

Hypertension is diagnosed when systolic Blood pressure exceeds 140 mm Hg or diastolic blood pressure exceeds 90 mm Hg in previously normotensive patients in two occassions atleast 4 hours apart, after 20 weeks of gestation.

To define diastolic pressure korotkoff phase V (i.e, disappearance of sounds) is used. Blood pressure is checked either in sitting position or in left lateral position with arm at the level of the heart with the appropriate sized cuff.

Gestational Hypertension

Elevation of the blood pressure to 140/90 mm of Hg or greater for the first time after the mid pregnancy with absent proteinuria and the blood pressure returns to normal after 12 weeks postpartum.

Preeclampsia superimposed with Chronic Hypertension

It is the sudden increase in proteinuria or BP or platelet count less than 1 lakh per ml in women with hypertension and proteinuria before 20 weeks of Gestation.[23]

Preeclampsia and Eclampsia syndrome

It is best described as the pregnancy specific disorder which causes multi organ dysfunction. It is characterised by increased blood pressure during pregnancy

after 20 weeks of gestation associated with proteinuria (> 300 mg per 24 hours or Dip stick > +1).

Eclampsia

It is the presence of new onset Grand mal seizures in a woman with pre existing Preeclampsia excluding other causes of seizures. Eclampsia can occur before, during or after labour.

Risk Factors for Preeclampsia[36]

- Nulliparity
- Multifetal gestations
- Preeclampsia in a previous pregnancy
- Chronic hypertension
- Pregestational diabetes
- Gestational diabetes
- Thrombophilia
- Systemic lupus erythematosus
- Prepregnancy body mass index greater than 30
- Antiphospholipid antibody syndrome
- Maternal age 35 years or older
- Kidney disease
- Assisted reproductive technology
- Obstructive sleep apnea

Diagnostic criteria for Preeclampsia

Blood pressure	• Greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure • Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy
and	
Proteinuria	• Greater than or equal to 300 mg per 24-hour urine collection (or this amount extrapolated from a timed collection) or • Protein/creatinine ratio greater than or equal to 0.3* • Dipstick reading of 1+ (used only if other quantitative methods not available)
Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:	
Thrombocytopenia	• Platelet count less than 100,000/microliter
Renal insufficiency	• Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease
Impaired liver function	• Elevated blood concentrations of liver transaminases to twice normal concentration
Pulmonary edema	
Cerebral or visual symptoms	

* Each measured as mg/dL.

Preeclampsia is further classified into Non Severe and Severe Preeclampsia on the basis of following criteria.

Indicators of severity of Gestational Hypertensive disorders[37]:

ABNORMALITY	**NONSEVERE PE**	**SEVERE PE**
Diastolic BP	<110 mm of Hg	>110 mm of Hg
Systolic BP	<160 mm of Hg	>160 mm of Hg
Proteinuria	None to positive	None to positive
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper abdominal pain	Absent	Present

Oliguria	Absent	Present
Convulsions(Eclampsia)	Absent	Present
Serum Creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
Serum Transaminases elevation	Minimal	Marked
Fetal growth restriction	Absent	Present
Pulmonary oedema	Absent	Present
Gestational age	Late	Early

Severe Features of Preeclampsia[38].

• Systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensivetherapy is initiated before this time)

• Thrombocytopenia (platelet count less than 100,000/microliter)

• Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both

• Progressive renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)

• Pulmonary edema

• New-onset cerebral or visual disturbances

HELLP SYNDROME[28,39]

This is the severe form of preeclampsia with the acronym of Hemolysis (H), Elevated Liver enzymes (EL)and low Platelet count(LP).

Diagnostic criteria for HELLP syndrome

1. Hemolysis
   - Bilirubin levels >1.2mg/dl
   - Elevated LDH levels(>600 U/L)
   - Abnormal peripheral smear(with Burr cells ,schizonts)
2. Elevated Liver enzymes
   - Elevated LDH levels(>600 U/L)
   - Serum AST(Aspartate transaminase) >70 U/L
3. Low Platelet count-less than 1,00,000/mm^3

MANAGEMENT OF PREECLAMPSIA[40]

According to the ACOG criteria (2013), the first consideration in the management of Preeclampsia without severe features i.e., non severe Preeclampsia is safety of both mother and the fetus where as in case of severe Preeclampsia safety of the mother is considered more important.

Mild /Non severe Preeclampsia

- Once the diagnosis of mild Gestational hypertension has been established ,further management depends upon the maternal and Fetal investigations, Gestational age, presence of fetal membranes, stage of labour ,vaginal bleeding and other co morbidities.
- CRITERIA FOR HOME MANAGMENT OF MILD PREECLAMPSIA [41]

  -Ability to comply with the recommendations

  -DBP <100 mm of Hg

  -SBP <160 mm of Hg

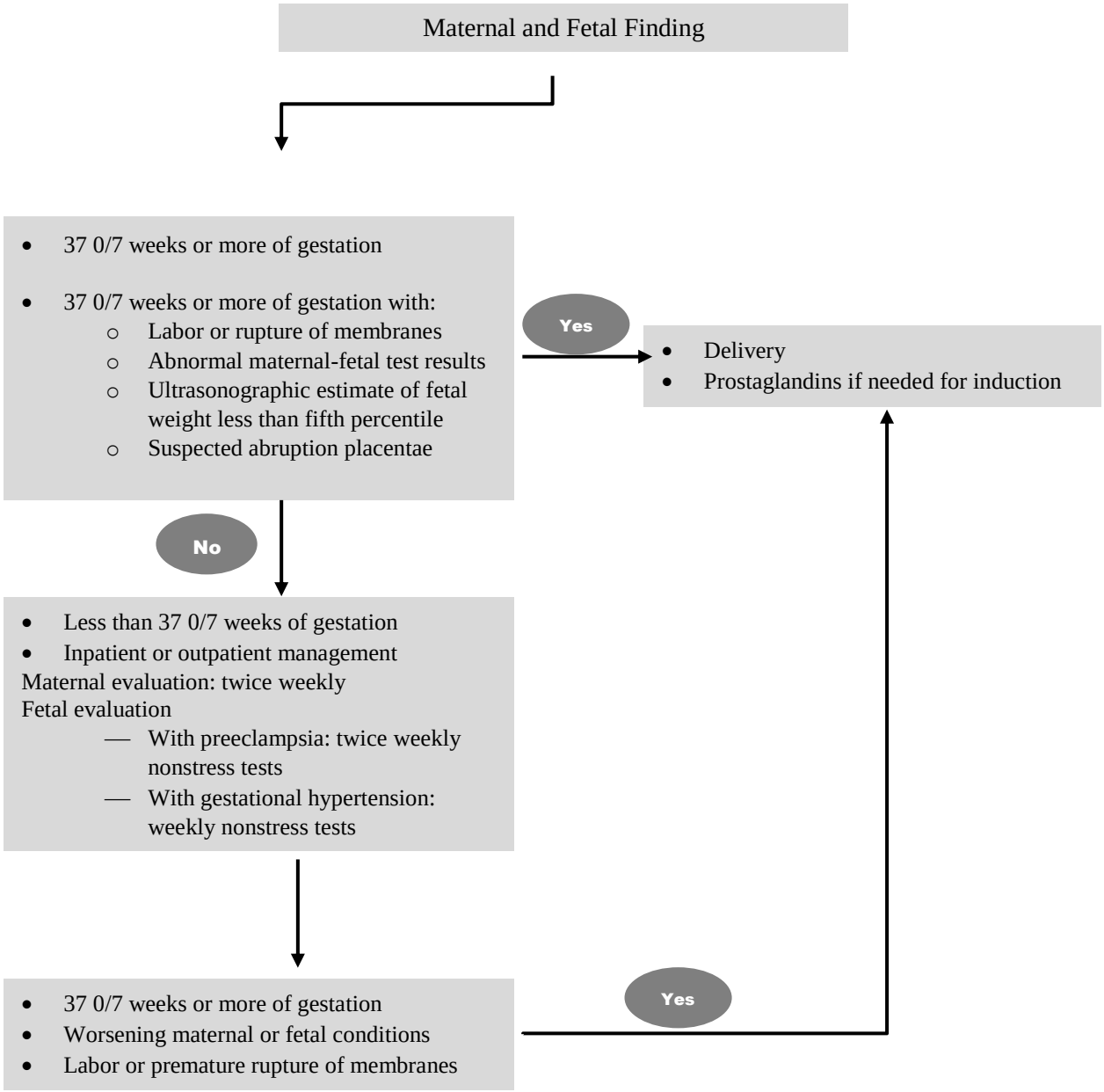
  -normal laboratory tests and no maternal symptoms

  -reassuring fetal status with appropriate growth

  - Urine protein 1 gm or less in 24 hours.

 If the patient doesnot fullfill the above mentioned criteria then the patient is managed by the hospital admission.

Management of mild gestation hypertension or preeclampsia without severe features.



Management of mild gestation hypertension or preeclampsia without severe features.

The preferred mode of delivery is vaginal. Caesarean section is considered only in the presence of other Obstetrical indications.

MANAGEMENT OF SEVERE PREECLAMPSIA[41]

- Severe Preeclampsia can result in both acute and long term complications in both mother and the newborn. Maternal complications of severe Preeclampsia include Pulmonary oedema, Myocardial Infarction, stroke, severe renal failure, acute Respuratory distress syndrome, coagulopathy and Retinal injury.These complications are more likely to occur in the presence of preexistent medical disorders and with acute maternal organ dysfunction related from exposure to uteroplacental insufficiency or from preterm birth or both.
- All women should undergo investigations for complete blood picture (CBC) with Hematocrit, assessment of serum Creatinine, Liver Function tests, 24 hour urine protein levels and detailed history is taken for any imminent signs or signs of severe Preeclampsia.
- Fetal evaluation is done for Estimated fetal weight and Amniotic fluid index by Ultrasonography, Non stress test (NST), Biophysical profile (BPP).

- Consider deliver in women >34 weeks of gestation.
- Patients at 32-34 weeks administer steroids and plan for delivery.
- Patients at 23-32 weeks of gestation, expectant management is done
- Women with non viable fetus should be presented with the option of pregnancy Termination

-

- Observe in labor and delivery for first 24-48 hours
- Corticosteroids, magnesium sulphate prophylaxis, and antihypertensive medications
- Ultrasonography, monitoring of fetal heart rate, symptoms, and laboratory tests

Contraindications to continued expectant management

- Eclampsia
- Pulmonary Edema
- Disseminated intravascular coagulation
- Uncontrollable severe hypertension
- Non viable fetus
- Abnormal fetal test results
- Abruptio placentae
- Intrapartum feral diarrhea

Ye → Delivery once maternal condition is stable

Are these additional expectant complications?

- Greater than or equal to 33 5/7 weeks of gestation
- Persistent symptoms
- HELLP or partial HELLP syndrome
- Fetal growth restriction (less than fifth percentile)
- Sever oligohydramnios
- Reversed end-diastolic flow (umbilical artery Doppler studies)
- Labor or premature rupture of membrane
- Significant renal dysfunction

Ye → Corticosteroids for fetal maturation
Delivery after 48 hours

Expectant Management

- Facilities with adequate maternal and neonatal intensive care resources
- Fetal visibility – 33 6/7 weeks of gestation
- Inpatient only and stop magnesium sulfate
- Daily maternal-fetal tests
- Vital signs, symptoms and blood tests
- Oral antihypertensive drugs

- Achievement of 34 0/7 weeks of gestation
- New-onset contraindications to expectant management
- Abnormal maternal-fetal test results
- Labor or premature rupture of membrane

Ye → Delivery

Management of severe preeclampsia

Guidelines for expeditious delivery within 48-72 hours in severe Preeclampsia[42]

Maternal

- Uncontrolled severe hypertension (SBP>160 mm of Hg ,DBP>/= 110 mm of Hg) despite maximum 2 doses of two anti Hypertensives.
- Eclampsia or persistent cerebral symptoms.
- Pulmonary oedema
- Placental Abruption
- Thrombocytopenia (platelet count less than 1 lakh per ml) or elevated liver enzymes(HELLP).
- Serum Creatinine of 1.5 mg/dl or more or oliguria(< 0.5 ml/kg/hr).

Fetal

- Severe fetal growth restriction (< 5 th percentile for gestational age).
- Persistent oligohydramnios amniotic fluid index of < 2 cm on atleast two occasions more than 24 hours apart.
- Umbilical artery Doppler studies with persistet reverse end diastolic flow.
- Biophysical profile < 4 on two occasions 4 hours apart.
- Repetitive Late declerations or prolonged variable decelerations or loss of beat to beat variability.

Anti Hypertensive Agents

Anti hypertensive agents used for Acute control of hypertension in pregnancy

DRUG	**DOSE**	**COMMENTS**
Labetolol (Selective alpha- and nonselective beta-antagoist)	10-20 mg IV,then 20-80 mg every 20- 30 min to a maximum dose of 300 mg or constant infusion of 1-2mg/Hr.	-First line of agent –reflex Tachycardia and hypotension is less common contraindicated in patients with asthma, heart disease
Hydralazine (Arterial vasodilator)	5 mg IV or IM,then 5-10 mg IV every 20-40 min or constant infusion 0.5-10 mg/Hr ,.	Higher dosage associated with maternal hypotension, fetal distress, head aches
Nifedepine (Calcium channel blocker)	10-20 mg orally, repeat in 30min if needed, then 10-20 mg every 6 to 8 hours	Reflex tachycardia and head aches

Common oral anti Hypertensive agents in pregnancy

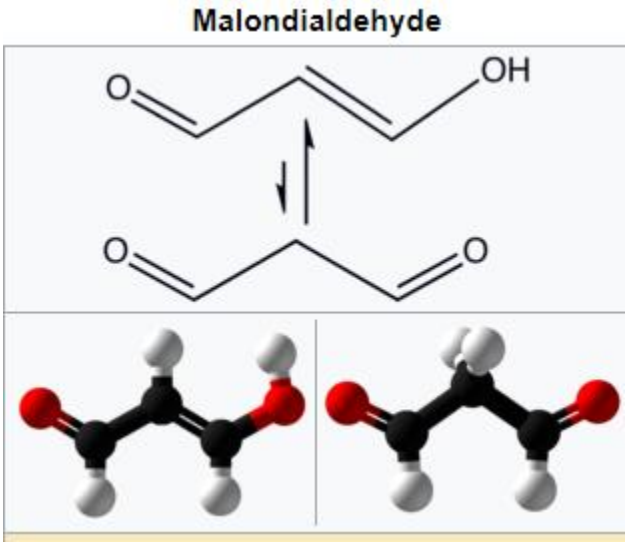
DRUG	**DOSAGE**	**COMMENTS**
Labetolol	200-2,400 mg/day orally in two to three divided doses	Well tolerated Potential bronchio constrictive effects
Nifedipine	30-120 mg/day orally of a slow release preparation	Do not use sublingual form
Methyl dopa	0.5 -3 gm/day orally in two to three divided doses.	May not be as effective in control of severe Hypertension
Thiazide Diuretics	Depends on agents	Second line agent
ACE inhibitors		Associated with anomalies, hence contraindicated in pregnancy and pre conceptional period.

Malondialdehyde

Malondialdehyde (MDA) is the organic compound with the nominal formula $CH_2(CHO)_2$. A colorless liquid, malondialdehyde is a highly reactive compound that occurs as the enol. It occurs naturally and is a marker for oxidative stress[45].

Structure and synthesis

Malondialdehyde mainly exists as the enol.



CH2(CHO)2 → HOC(H)=CH-CHO

In organic solvents, the cis-isomer is favored, whereas in water the trans-isomer predominates. The equilibrium is rapid and is inconsequential for many purposes.

Biosynthesis and reactivity

Malondialdehyde results from lipid peroxidation of polyunsaturated fatty acids. It is a prominent product in thromboxane A2 synthesis where in cyclooxygenase 1 or cycloxygenase 2 metabolizes arachidonic acid to prostaglandin H2 by platelets and a wide array of other cell types and tissues. This product is further metabolized by thromboxane synthase to thromboxane A2, 12-hydroxyheptadecatrienoic acid, and malonyldialdehyde. Alternatively, it may rearrange non-enzymatically to a mixture of 8-cis and 8-trans isomers of 12-hydroxyeicosaheptaenoic acid plus malonyldialdehyde. The degree of lipid peroxidation can be estimated by the amount of malondialdehyde in tissues[46].

Reactive oxygen species degrade polyunsaturated lipids, forming malondialdehyde.This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts referred to as advanced lipoxidation end-products (ALE), in analogy to advanced glycation end-products (AGE). The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an organism.

Analysis

Malondialdehyde and other thiobarbituric reactive substances (TBARS) condense with two equivalents of thiobarbituric acid to give a fluorescent red derivative that can be assayed spectrophotometrically. 1-Methyl-2-phenylindole is an alternative more selective reagent.

MDA was estimated using the thiobarbituric acid (TBA) method. In short, MDA present in serum is precipitated with weak trichloroacetic acid and boiled for 30 min with 0.67% TBA in 2M sodium sulfate reagent in acidic medium (0.05M H2SO4) which results in hydrolysis of C = N bonds of conjugated Schiff's base of MDA protein adduct. The liberated MDA couples with TBA to form a pink 1:2 (MDA: TBA) adduct. This chromogen is extracted with n-Butanol on cooling and absorbance measured at 532 nm.

The results are presented as mean ± standard deviation MDA levels as well as a number of participants (frequency) in a specified range of MDA.

In women with preeclampsia, there is a significant elevation of plasma MDA level and reduction of serum SOD level which suggests significant oxidative stress in pregnancy leading to endothelial dysfunction, which may be responsible for PIH[22. 47].

ISCHEMIA MODIFIED ALBUMIN

Ischemia-modified albumin (IMA) has emerged as a new biomarker of myocardial ischemia. Currently, no information is available on maternal IMA levels during normal and complicated pregnancy. Preeclampsia is associated with ischemia and increased formation of free radicals in the placenta. We therefore hypothesized that production of IMA may occur in women with preeclampsia.[45]

- Hypoxia driven oxidative stress of the placenta contributes to the pathogenesis of preeclampsia. Serum Ischemia Modified Albumin (IMA) has recently emerged as an oxidative stress marker, used in diagnosis of cardiac ischemia. Studies were done to determine the efficiency of serum IMA in differentiating hypertensive disorders of pregnancy (pregnancy induced hypertension, preeclampsia) from normal pregnancy. And they observed that serum IMA, an oxidative stress marker is elevated in PE & PIH. Hence serum IMA can undergo further evaluation as a marker of PE[49].
- In few studies increased serum IMA was attributed to the overproduction or decreased clearance. Though albuminuria is characteristic of preeclampsia, IMA was not present in the urine indicating an extra renal clearance.
    - Serum IMA is formed in response to hypoxia or free radical injury to N terminus (asp-ala-his-lys) of albumin. It is been used as a marker of cardiac ischemia. Its levels are also elevated in conditions related to oxidative stress like scleroderma, end stage renal disease, peripheral vascular disorders and any events associated with hypoxia[50].

Preeclampsia is characterized by poor placental perfusion due to vasospasm of uterine spiral arteries, which generate hypoxia and oxidative stress. Hence serum IMA a marker of oxidative stress and hypoxia is elevated in preeclampsia. [23 46]

ISHEMIA MODIFIED ALBUMIN was measured by 100µl of patient sample and 50 µl of cobalt chloride (Co (II)) are incubated for 5 minutes. During this incubation, the Co (II), which is a transitional metal that binds to the N-terminal residues of unaltered albumin in the sample; albumin for which the N- terminal residues is altered as a result of ischemic process binds to the Co (II) to a far lesser extent. 25µl of Dithiothreitol (DTT) forms a colored complex with Co (II) that is not bound to the modified N-terminal residues of albumin and this complex is measured at 470nm.

The trend of Modified albumin as IMA in preeclampsia shows the gradual increase before the delivery. However, the levels of IMA in non-pregnancy shows 3.2- 10 fold decrease than the normal pregnant women and preeclampsia group. Increased IMA concentrations in preeclampsia before and after delivery.

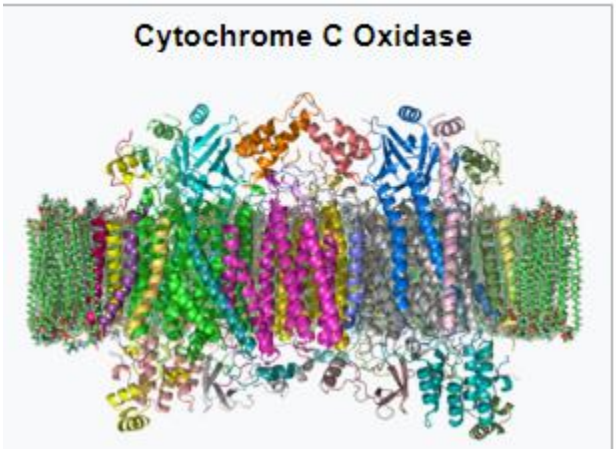
TOTAL CYTOCHROME OXIDASE

TOTAL CYTOCHROME OXIDASE, also known as complex IV, is the terminal, or final, enzyme of the electron transport system (this does not include ATP synthase). **TOTAL CYTOCHROME OXIDASE** is a transmembrane molecule found in the mitochondria of eukaryotes and in the cellular space of aerobic prokaryotes.

TOTAL CYTOCHROME OXIDASE, also known as complex IV, is the terminal, or final, enzyme of the electron transport system (this does not include ATP synthase). Total cytochrome oxidase is a transmembrane molecule found in the mitochondria of eukaryotes and in the cellular space of aerobic prokaryotes. This molecule is a proton pump that plays a vital role in producing energy, in the form of ATP, via the ETS. In the last steps of the energy production process, total cytochrome oxidase oxidizes the waste products from the end of the energy making process, converting reactive species, H^+ and dioxygen (O_2), to a more stable molecule, water (H_2O). In the absence of TOTAL CYTOCHROME OXIDASE, this energetically favorable reaction could be explosive and no energy production would occur.[2] total cytochrome oxidase allows this reaction to occur safely while harnessing energy to form the H^+ ion gradient. This energy produced from the reaction is used to pump H^+ ions from the matrix to the intermembrane space of the mitochondria.

Total cytochrome oxidase is a dimer meaning it is made up of two identical proteins. The two proteins in total cytochrome oxidase mirror one another. The system uses multiple metals to complete its function including the two irons in the two hemes, three coppers,

one magnesium, and one zinc. The irons in the two hemes and the three copper molecules are vital to the success of the enzyme in aerobic respiration.[52]



The crystal structure of bovine TOTAL CYTOCHROME OXIDASE in a phospholipid bilayer. The intermembrane space lies to top of the image.

METHODOLOGY

METHODOLOGY

Materials

- **Source of data:** Pregnant women attending the out patient department of OBTETRICS AND GYNECOLOGY & admitting to labour room of RL JALAPPA Hospital and Research Center, of SRI DEVARAJ URS MEDICAL COLLEGE Tamaka, Kolar, during the period of study. Study population includes 41 normal pregnant women as controls and 41 severe preeclamptic women in whom hypertension was developed after 20 weeks of gestation as cases.

Ethical clearance is obtained from the Institutional Ethics committee .

SUBJECTS:

In a comparative observational study,a total number of 82 subjects were enrolled in the study after obtaining patient information consent after 20 weeks of gestation period. And were categorized in to 41 subjects as normal pregnancy and 41 were preeclampsia cases. The study period covered was between January 2018-December 2018**.**

Method of collection of data:

Inclusion Criteria:

- Age between 18 to 35 years
- gestational age between 20-40 weeks
- Singleton pregnancy

Exclusion Criteria:

- Gestational diabetics,
- Chronic hypertensives,
- Multiple gestations

Pregnant women fulfilling the inclusion criteria are registered for the study.

Detailed history regarding age, parity, gestational age, menstrual history, obstetric history and any complications in present pregnancy is taken. General clinical examination, complete obstetric examination and necessary investigations are done.

Sample size:

Sample size was based on the mean difference in serum MDA levels observed with preeclampsia & in normal pregnancy in a study by Vanitha Gowda MN et al ,2009, observed the varience estimate of 0.1369 in MDA to detect an effect size of 87% increase in MDA in preeclamptic women. With 95% confidence interval with 80% power to detect n increase of 86% increase in MDA among peeclamptic women.

Sample size was calculated using the software G power. Keeping α=0.05 and β=0.8

The calculated sample size was found to be 82

Group A- 41 cases- normal pregnancy cases.

Group B-41 cases- preeclampsia cases.

SAMPLE COLLECTION:

Five milliliter of Venous blood samples is collected from Ante Cubital vein under aseptic condition from normal pregnancy group and preeclampsia group after 20 weeks of gestational age .The samples are allowed to retract at room temperature for 10 minutes, and then samples are centrifuged at 3000 rpm for 10 minutes to obtain clear serum. Thus obtained clear serum samples were stored at – 20 ^{0}C and later analysed for MDA, IMA and TOTAL CYTOCHROME OXIDASE LEVELS.

Methods:

- Pregnant women attending the out patient department of OBTETRICS AND GYNECOLOGY & admitting to labour room of RL JALAPPA Hospital and Research Center, of SRI DEVARAJ URS MEDICAL COLLEGE Tamaka, Kolar, during the period of study.
- At the time of enrolment, an informed written consent would be obtained from the patients.
- Blood samples were taken from both case & control study population at the time of admission and measured for oxidative stress in terms of MDA(malondialdehyde), ischemic stress interms of IMA(ishemic modified albumin), mitochondrial stress in terms of TOTAL CYTOCHROME OXIDASE.
- Each women is followed up until delivary and the outcome is recorded and parameters involved with increased oxidative & mitochondrial stress are noted.
- MDA is measured by TBARS method.
- IMA is measured by turbidometric method using cobalt-II in dithothreitol.
- TOTAL CYTOCHROME OXIDASE is measured by ELISA method.

Malondialdehyde

MDA was estimated using the thiobarbituric acid (TBA) method. In short, MDA present in serum is precipitated with weak trichloroacetic acid and boiled for 30 min with 0.67% TBA in 2M sodium sulfate reagent in acidic medium (0.05M H_2SO_4) which results in hydrolysis of C = N bonds of conjugated Schiff's base of MDA protein adduct. The liberated MDA couples with TBA to form a pink 1:2 (MDA: TBA) adduct. This chromogen is extracted with n-Butanol on cooling and absorbance measured at 535 nm.

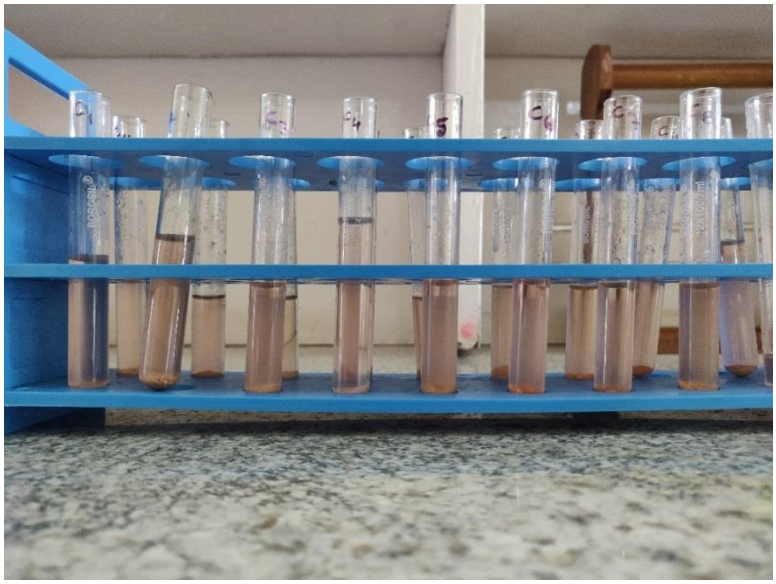


FIGURE-6: Estimation of MDA

Ischemia modified albumin

Ischemia modified albumin was determined by addition of a known amount of cobalt(II) to a serum specimen and measured unbound cobalt (II) by colorimetric assay using dithiothreitol. The absorbance of the intensity of the colour produced measured against a control at 470nm.

Assay for IMA

Principle

ACB assay for determination of the level of IMA in serum is done by addition of a known amount of cobalt (II) to a serum specimen and measurement of the unbound cobalt (II) from the absorbance of the coloured complex between dithiothreitol (DTT) and free

cobalt by spectrophotometer which is indicative of the level of IMA [13]. Intensity of the coloured complex varies inversely with the ACB.

Assay protocol

A volume of 200 μL of serum was mixed with 50 μL of 1 g/l cobalt chloride (CoCl2) solution. Vigorous mixing was done followed by incubation for 10 min. Then 50 μL of 1.5g/l solution of dithothreitol(DTT) was added and mixed following which an incubation for 2 min. Finally, 1 ml of 9 g/l of Nacl was added, and absorbance was read at 470 nm in a spectrophotometer .The blank was prepared similarly with the exclusion of DTT. Standard curve was prepared using different concentrations of CoCl2.

FIGURE-7: Estimation of IMA

TOTAL CYTOCHROME OXIDASE

Human TOTAL CYTOCHROME OXIDASE (CO) concentration determined by ELISA as per the procedure provided by the Sincere Biotech Co., Ltd, Beijing, China.

The procedure is based on the principle of coated heme CO antibody to micro plate wells to make solid phase antibody, then serum sample containing CO added to the wells. Combined Human CO antibody with HRP labelled added to get solid phase antibody-antigen- antibody – enzyme complex. After washing completely 33’ 55’ tetra methyl bentidine(TMB) chromogenic substrate added. HRP enzyme catalyzes TMB in to blue colour, reaction is terminated by addition of sulphuric acid. Later the colour changes to yellow is measured at 450 nm wavelength.

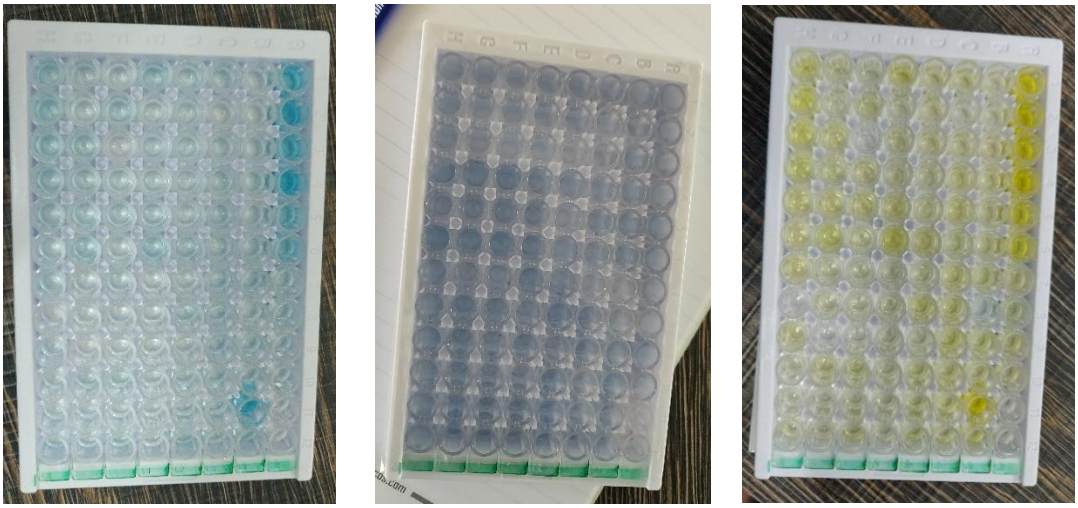


FIGURE-8: Estimation of total Cytochrome oxidase

STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.

Statistical tests were applied as follows-

1. Quantitative variables were compared using Independent t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups and ANOVA was used for comparison between three groups.

2. Qualitative variables were associated using Chi-Square test/Fisher's Exact test.

3. Pearson correlation coefficient was used to assess the correlation of oxidative and mitochondrial stress markers with outcome.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

RESULTS

RESULTS AND OBSERVATIONS

Table 1:- Comparison of age between normal and preeclampsia group.

Age distribution(years)	**Group**		**Total**	**P value**
	Normal(n=41)	**Preeclampsia(n=41)**		
19-20	5 (12.20%)	5 (12.20%)	10 (12.20%)	0.802*
21-25	16 (39.02%)	20 (48.78%)	36 (43.90%)	
26-30	14 (34.15%)	12 (29.27%)	26 (31.71%)	
31-35	6 (14.63%)	4 (9.76%)	10 (12.20%)	
Mean ± SD	25.88 ± 4.11	24.71 ± 3.7	25.29 ± 3.93	0.179#
Median(IQR)	25(23 - 28.250)	24(22 - 27)	25(22 - 28)	

Note- p value <0.05 considered as statistically significant.

*-Chi square test

#-Independent t test

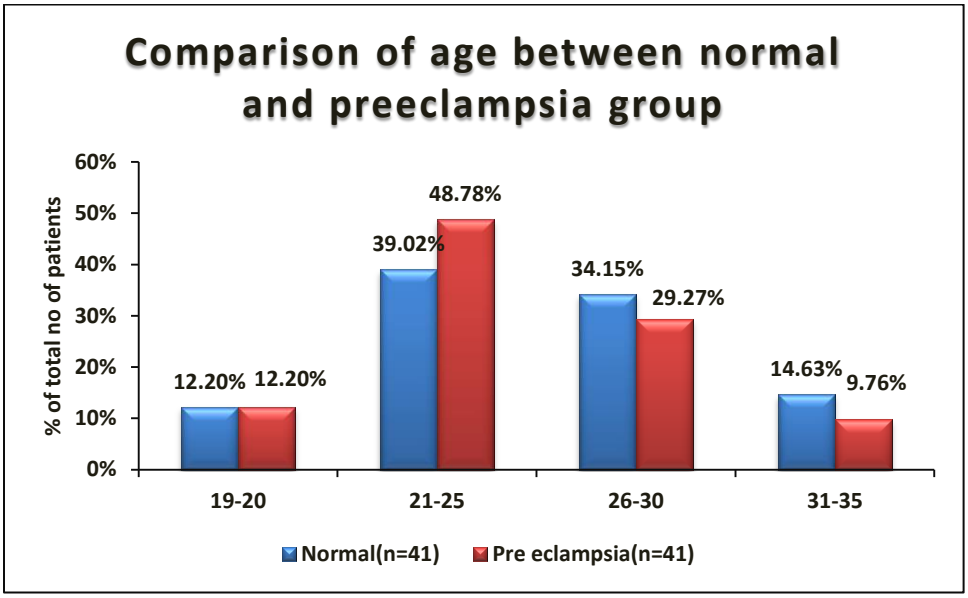


Figure 1:- Comparison of age between normal and preeclampsia group.

Table 1 and figure 1 depicts age group of the subjects in the study. Results showed that no significant difference was seen in age distribution between normal and preeclampsia group. (p value >.05) Majority of the women in both the groups belonged to 21 to 25 years of age group; 39.02% in normal group and 48.78% of patients in preeclampsia group. 34.15% of patients in normal group and 29.27% of patients in preeclampsia group belonged to 26 to 30 years of age group. Very few patients belonged to 19 to 20 and 31 to 35 years of age group. Mean value of age of patients in normal group was 25.88 ± 4.11 years and in preeclampsia group was 24.71 ± 3.7 years. (Table 1, Figure 1)

Table 2:- Comparison of booked/referred between normal and preeclampsia group.

Booked/Referred	Group		Total	P value
	Normal(n=41)	Preeclampsia(n=41)		
Booked	30 (73.17%)	3 (7.32%)	33 (40.24%)	<.0001*
Referred	11 (26.83%)	38 (92.68%)	49 (59.76%)	
Total	41 (100.00%)	41 (100.00%)	82 (100.00%)	

***-Fisher's exact test**

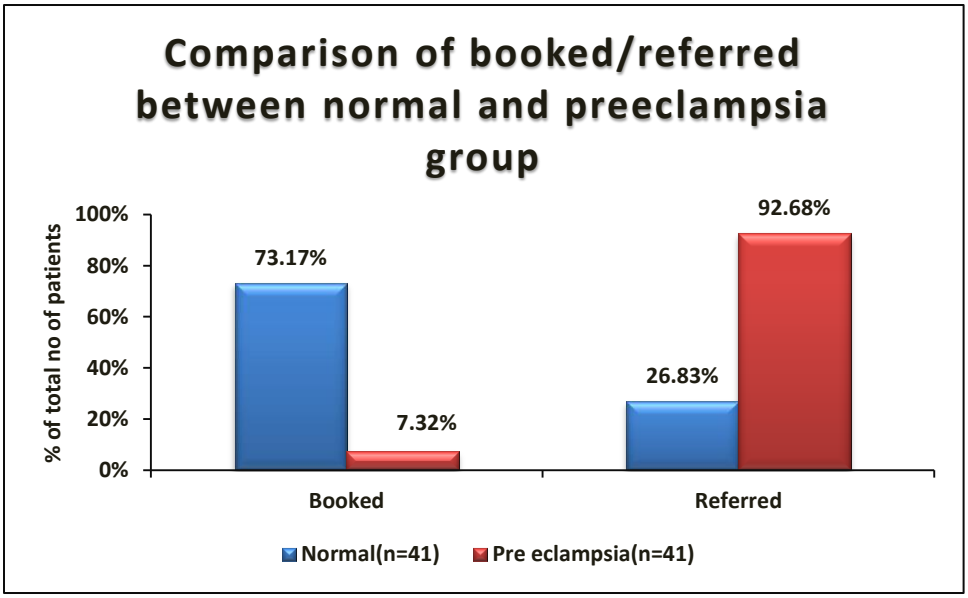


Figure 2:- Comparison of booked/referred between normal and preeclampsia group.

Significant difference was seen in the distribution of booked or referred between normal and preeclampsia group. (p value <.05) 92.68% of women in preeclampsia group were referred as compared to 26.83% of women in normal group and on the other hand, 73.17% of the women in normal group were booked as compared to only 7.32% of the women in preeclampsia group. So we can say that proportion of referred patients were significantly higher in preeclampsia group as compared to normal group. (Table 2, Figure 2)

Table 3:- Comparison of obstetric index between normal and preeclampsia group.

Obstetric index	Group		Total	P value
	Normal(n=41)	Preeclampsia(n=41)		
Primigravida	19 (46.34%)	25 (60.98%)	44 (53.66%)	0.184*
Multigravida	22 (53.66%)	16 (39.02%)	38 (46.34%)	
Total	41 (100.00%)	41 (100.00%)	82 (100.00%)	

Note- p value <0.05 considered as statistically significant.

***-Chi square test**

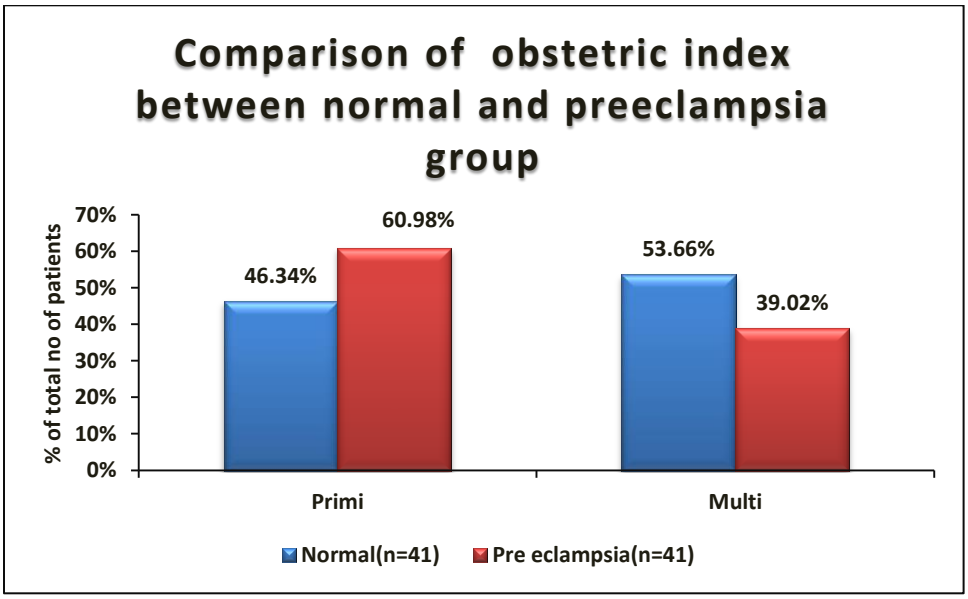


Figure 3:- Comparison of obstetric index between normal and preeclampsia group.

No significant difference was seen in the distribution of obstetric history of the patients between the two groups. (p value >.05) 60.98% of the preeclampsia women and 46.34% of the women in normal group were primi. (Table 3, Figure 3)

Table 4:- Comparison of gestational age in weeks between normal and preeclampsia group.

Gestational age in weeks		Group		Total	P value
		Normal(n= 41)	Preeclampsia(n=41)		
Early preterm/late preterm/early term/full term	Early preterm	0 (0.00%)	8 (19.51%)	8 (9.76%)	0.0002*
	Late preterm	3 (7.32%)	9 (21.95%)	12 (14.63%)	
	Early term	9 (21.95%)	13 (31.71%)	22 (26.83%)	
	Full term	29 (70.73%)	11 (26.83%)	40 (48.78%)	
Preterm/Term	Preterm	3 (7.32%)	17 (41.46%)	20 (24.39%)	0.0006#
	Term	38 (92.68%)	24 (58.54%)	62 (75.61%)	
Gestational age	Mean ± SD	39.1 ± 1.19	36.54 ± 3.41	37.82 ± 2.84	<.0001@
	Median(IQR)	39.43(38.71 4 - 40)	37.86(35.107 - 39)	38.86(37.286 - 40)	

Note- p value <0.05 considered as statistically significant.

***-Chi square test**

#-Fisher's Exact test

@-Independent t test

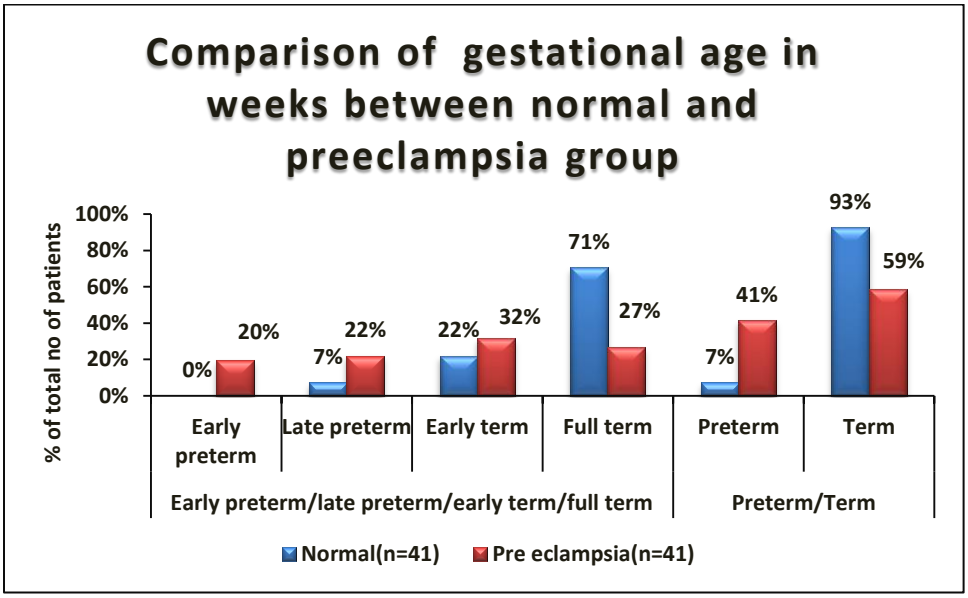


Figure 4(a):- Comparison of gestational age between normal and preeclampsia group.

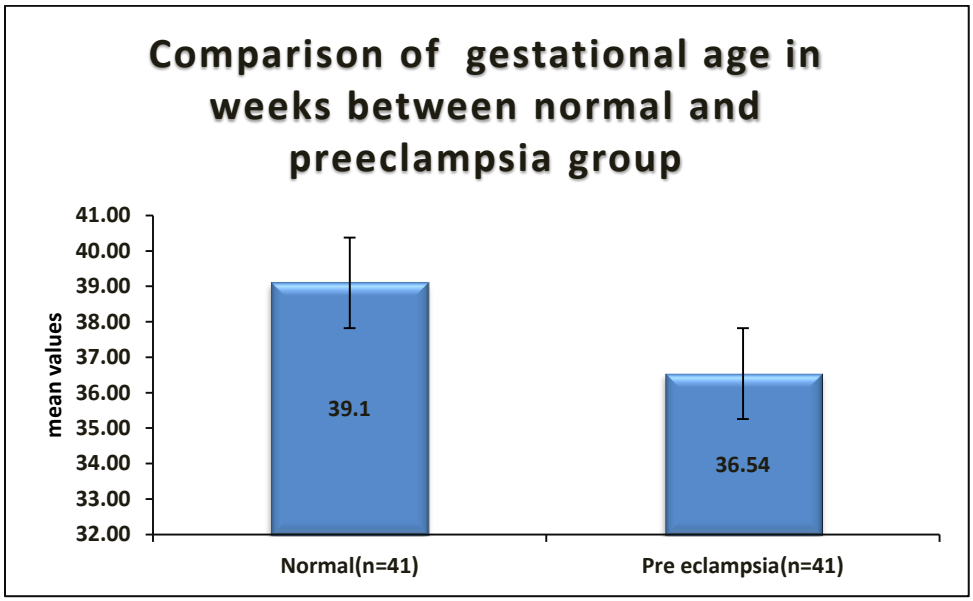


Figure 4(b):- Comparison of gestational age in weeks between normal and preeclampsia group.

Significant difference was seen in the gestational age between the two groups. (p value <.05) Gestational age of around 70% of the women in normal group was full term as compared to only 26.83% in preeclampsia group and on the other hand, early term and late preterm was seen in 31.71% and 21.95% of the women in preeclampsia group as compared to only 21.95% and 7.32% in normal group respectively. Also on categorisation of gestational age into term and preterm, women with preeclampsia had significantly higher proportion of preterm birth as compared to women in normal group; 41.46% versus 7.32%. Also mean value of gestational age in normal group was 39.1 ± 1.19 weeks and in preeclampsia group was 36.54 ± 3.41 weeks. So it can be concluded that gestational age was significantly lower in women with preeclampsia as compared to normal women. (Table 4, Figure 4(a), 4(b))

Table 5:- Comparison of blood pressure between normal and preeclampsia group.

Blood pressure(mmHg)	Normal(n=41)		Preeclampsia(n=41)		P value *
	Mean ± SD	Median(IQR)	Mean ± SD	Median(IQR)	
Systolic blood pressure(mmHg)	116.34 ± 5.36	120(110 - 120)	157.42 ± 13.12	160(150 - 170)	<.0001
Diastolic blood pressure(mmHg)	75.12 ± 5.14	76(70 - 80)	103.27 ± 6.73	100(100 - 110)	<.0001

Note- p value <0.05 considered as statistically significant.

***-Mann Whitney test**

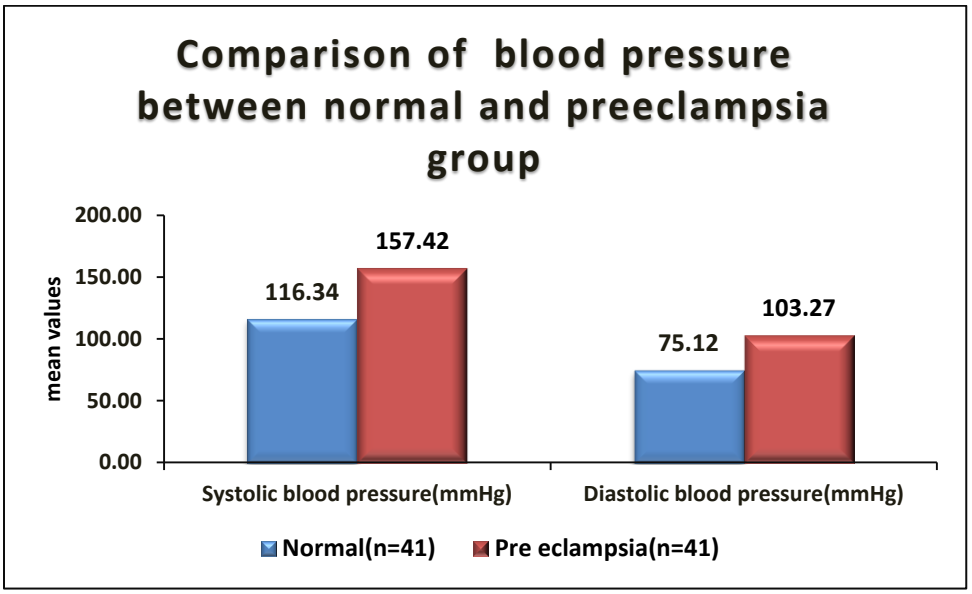


Figure 5:- Comparison of blood pressure between normal and preeclampsia group.

Significant difference was seen in the blood pressure between the normal and preeclampsia patients. (p value <.05) Median(IQR) value of systolic and diastolic blood pressure in normal women was 120(110 - 120) mmHg and 76(70 - 80) mmHg respectively and in women with preeclampsia was 160(150 - 170) mmHg and 100(100 - 110) mmHg respectively. So it was evident that both systolic and diastolic blood pressure was significantly higher in preeclampsia women as compared to normal women. (Table 5, Figure 5)

Table 6:- Comparison of MDA, IMA and TOTAL CYTOCHROME OXIDASE between normal and preeclampsia group.

MDA, IMA and TOTAL CYTOCHROME OXIDASE	**Normal(n=41)**		**Preeclampsia(n=41)**		**P value***
	Mean ± SD	**Median(IQR)**	**Mean ± SD**	**Median(IQR)**	
Malondialdehyde(µ mole/liter)	0.35 ± 0.1	0.33(0.276 - 0.380)	0.61 ± 0.2	0.55(0.421 - 0.765)	<.0001
Ishemia modified albumin(ABSU)	0.29 ± 0.12	0.29(0.193 - 0.345)	0.96 ± 0.39	1(0.632 - 1.060)	<.0001
TOTAL CYTOCHROME OXIDASE(ng/ml)	1.78 ± 1.05	1.83(1.071 - 2.246)	5.55 ± 2.04	5.78(4.075 - 7.060)	<.0001

Note- p value <0.05 considered as statistically significant.

***-Independent t test**

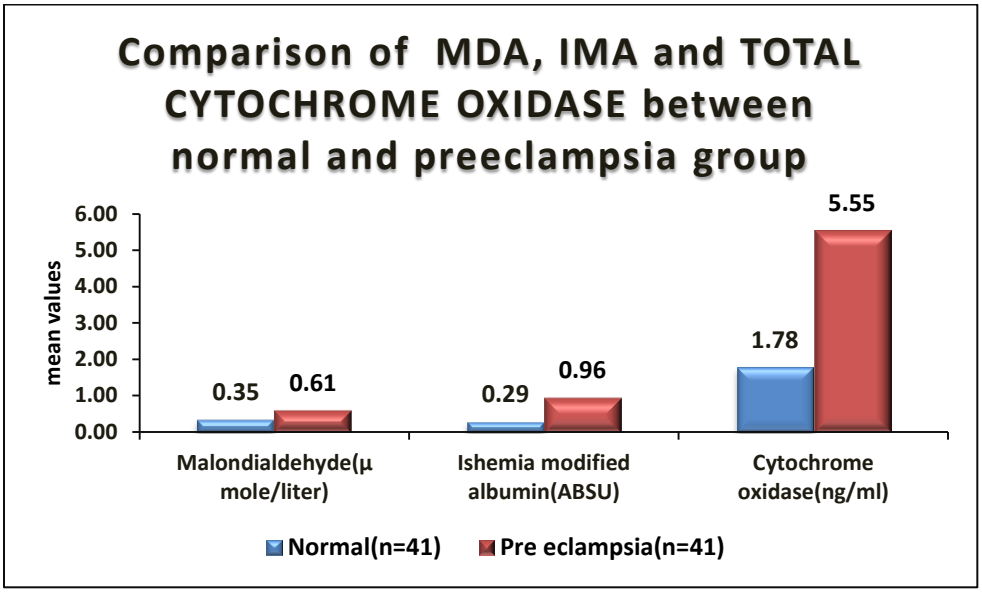


Figure 6:- Comparison of MDA, IMA and TOTAL CYTOCHROME OXIDASE between normal and preeclampsia group.

Significant difference was seen in the mean levels of MDA, IMA and TOTAL CYTOCHROME OXIDASE. (p value <.05) Mean values of MDA, IMA and TOTAL CYTOCHROME OXIDASE in normal women was 0.35 ± 0.1 µmole/liter, 0.29 ± 0.12 ABSU and 1.78 ± 1.05 ng/ml respectively and in preeclampsia women was 0.61 ± 0.2 µmole/liter, 0.96 ± 0.39 ABSU and 5.55 ± 2.04 ng/ml respectively. So it was evident that the mean values of MDA, IMA and TOTAL CYTOCHROME OXIDASE was significantly higher in preeclampsia group as compared to the normal group. (Table 6, Figure 6)

Table 7:- Comparison of urine albumin between normal and preeclampsia group.

Urine albumin	Group		Total	P value*
	Normal(n=41)	Preeclampsia(n=41)		
Nil	41 (100.00%)	0 (0.00%)	41 (50.00%)	<.0001
Traces	0 (0.00%)	1 (2.44%)	1 (1.22%)	
1+	0 (0.00%)	9 (21.95%)	9 (10.98%)	
2+	0 (0.00%)	22 (53.66%)	22 (26.83%)	
3+	0 (0.00%)	9 (21.95%)	9 (10.98%)	
Total	41 (100.00%)	41 (100.00%)	82 (100.00%)	

Note- p value <0.05 considered as statistically significant.

***-Chi square test**

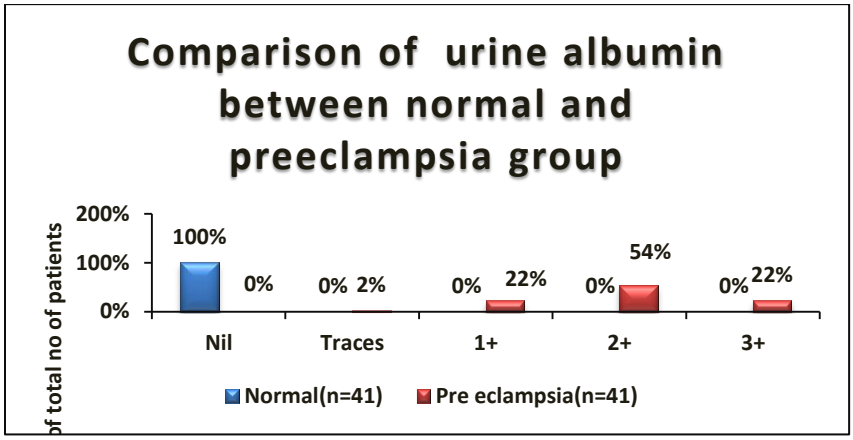


Figure 7:- Comparison of urine albumin between normal and preeclampsia group.

Significant difference was seen in the distribution of urine albumin between normal and preeclampsia women. (p value <.05) Urine albumin was nil in all the patients of normal women as compared to 0% in preeclampsia women and on the other hand, majority of the women in preeclampsia group had 2+ urine albumin followed by 1+ and 3 +.(Table 7, Figure 7)

Table 8:- Comparison of indication for LSCS between normal and preeclampsia group.

Indication for LSCS	Group		Total	P value
	Normal(n=41)	Preeclampsia(n=41)		
Fetal distress	5 (12.20%)	3 (7.32%)	8 (9.76%)	0.712*
Oligohydramnios	3 (7.32%)	3 (7.32%)	6 (7.32%)	1.000*
Maternal desire	1 (2.44%)	1 (2.44%)	2 (2.44%)	1.000*
Previous LSCS	6 (14.63%)	6 (14.63%)	12 (14.63%)	1.000#
IUGR with doppler changes	1 (2.44%)	7 (17.07%)	8 (9.76%)	0.057*
Failed induction	0 (0.00%)	1 (2.44%)	1 (1.22%)	1.000*
Antepartum eclampsia with unfavourable cervix	0 (0.00%)	2 (4.88%)	2 (2.44%)	0.494*
Contracted pelvis	1 (2.44%)	1 (2.44%)	2 (2.44%)	1.000*
Cephalopelvic disproportion	6 (14.63%)	0 (0.00%)	6 (7.32%)	0.026*
Imminent eclampsia	0 (0.00%)	3 (7.32%)	3 (3.66%)	0.241*
Abruptio placenta	0 (0.00%)	1 (2.44%)	1 (1.22%)	1.000*

Note- p value <0.05 considered as statistically significant.

***-Fisher's exact test**

#-Chi square test

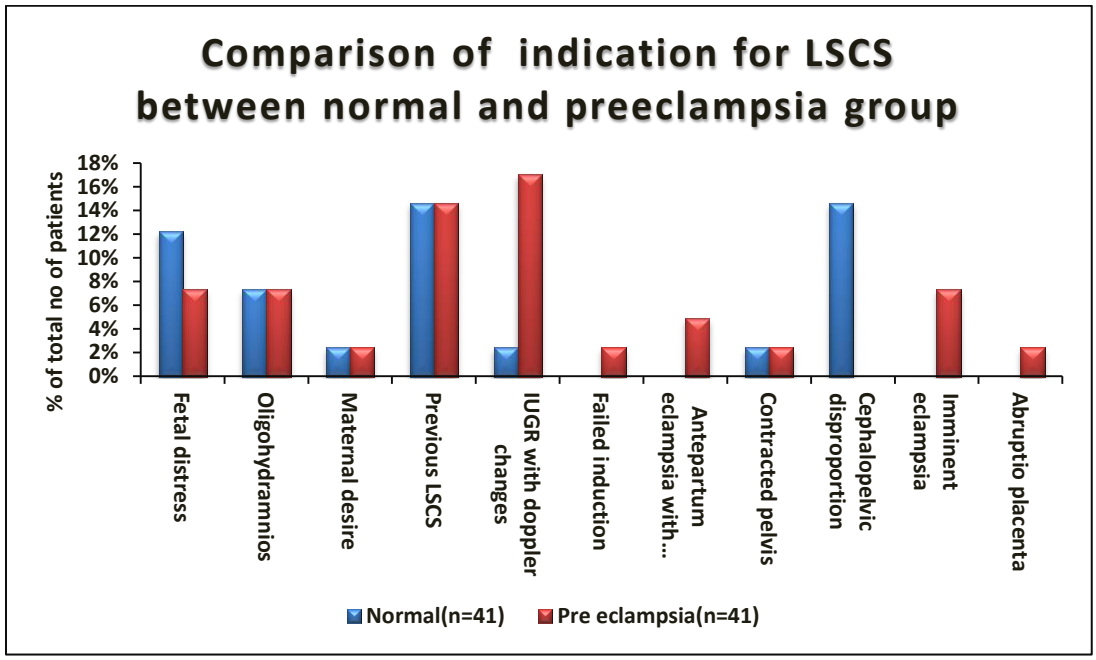


Figure 8:- Comparison of indication for LSCS between normal and preeclampsia group.

No significant difference was seen in the distribution of indication for LSCS between normal and preeclampsia women (p value >.05) except for cephalopelvic disproportion. Proportion of patients with cephalopelvic disproportion as indication of LSCS was significantly higher in normal group as compared to preeclampsia group (14.63% vs 0%). (p value <.05) (Table 8, Figure 8)

Table 9:- Comparison of fetal outcome between normal and preeclampsia group.

Fetal outcome		Group		Total	P value
		Normal	Preeclampsia		
Mode of delivery	LSCS	22 (53.66%)	26 (63.41%)	48 (58.54%)	0.370*
	Vaginal delivery	19 (46.34%)	15 (36.59%)	34 (41.46%)	
APGAR Score at 5 minutes	<7	2 (4.88%)	12 (33.33%)	14 (18.18%)	0.002#
	>=7	39 (95.12%)	24 (66.67%)	63 (81.82%)	
	Mean ± SD	8.78 ± 0.82	7.53 ± 1.34	8.2 ± 1.26	<.0001$
	Median(IQR)	9(9 - 9)	8(6 - 9)	9(7 - 9)	
NICU admission	No	35 (85.37%)	19 (52.78%)	54 (70.13%)	0.002*
	Yes	6 (14.63%)	17 (47.22%)	23 (29.87%)	
	Mean ± SD	3.17 ± 1.72	6.35 ± 3.16	5.52 ± 3.16	0.030@
	Median(IQR)	3(2 - 4)	5(4 - 7.250)	5(3.250 - 7)	
Birth weight(kg)	<2.5	6 (14.63%)	22 (53.66%)	28 (34.15%)	0.0002*
	>=2.5	35 (85.37%)	19 (46.34%)	54 (65.85%)	
	Mean ± SD	2.8 ± 0.33	2.39 ± 0.66	2.6 ± 0.56	0.001@
	Median(IQR)	2.9(2.600 - 3)	2.3(1.915 - 2.985)	2.8(2.200 - 3)	
IUD		0 (0.00%)	5 (12.20%)	5 (6.10%)	0.055#
IUGR		1 (2.44%)	17 (41.46%)	18 (21.95%)	<.0001#
Respiratory distress		6 (14.63%)	7 (17.07%)	13 (15.85%)	0.762*
Small for gestational age		0 (0.00%)	7 (17.07%)	7 (8.54%)	0.012#
Perinatal mortality		0 (0.00%)	2 (5.56%)	2 (2.60%)	0.215#
Causes of perinatal mortality					
Respiratory failure		0 (0.00%)	2 (4.88%)	2 (2.44%)	0.494#
Sepsis		0 (0.00%)	1 (2.44%)	1 (1.22%)	1.000#

Note- p value <0.05 considered as statistically significant.

***-Chi square teat**

#-Fisher's exact test

@-Independent t test

$-Mann Whitney test

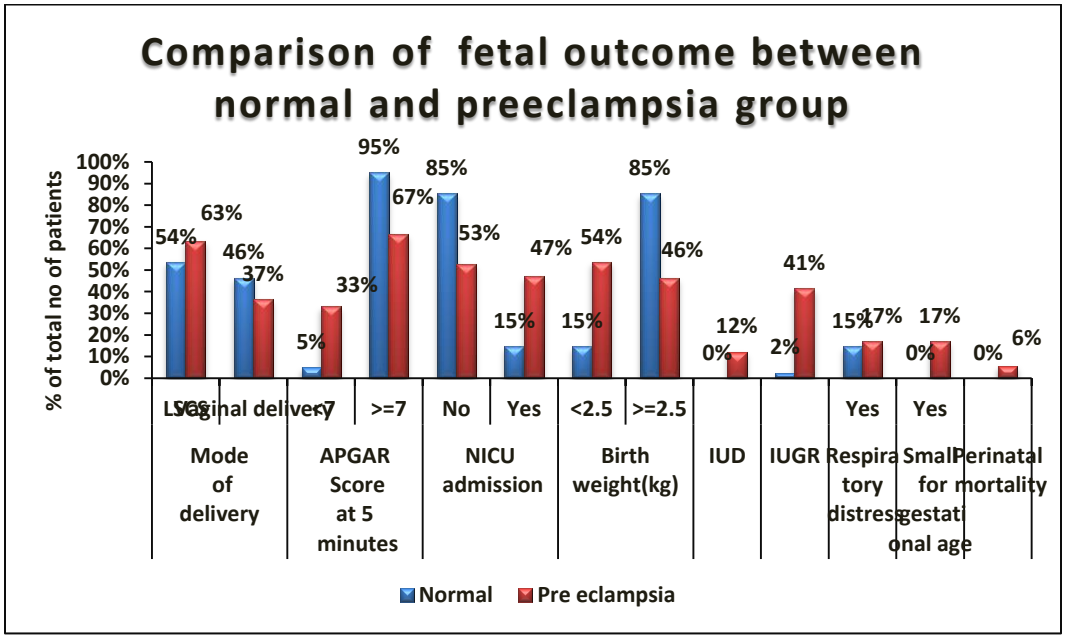


Figure 9(a):- Comparison of fetal outcome between normal and preeclampsia group.

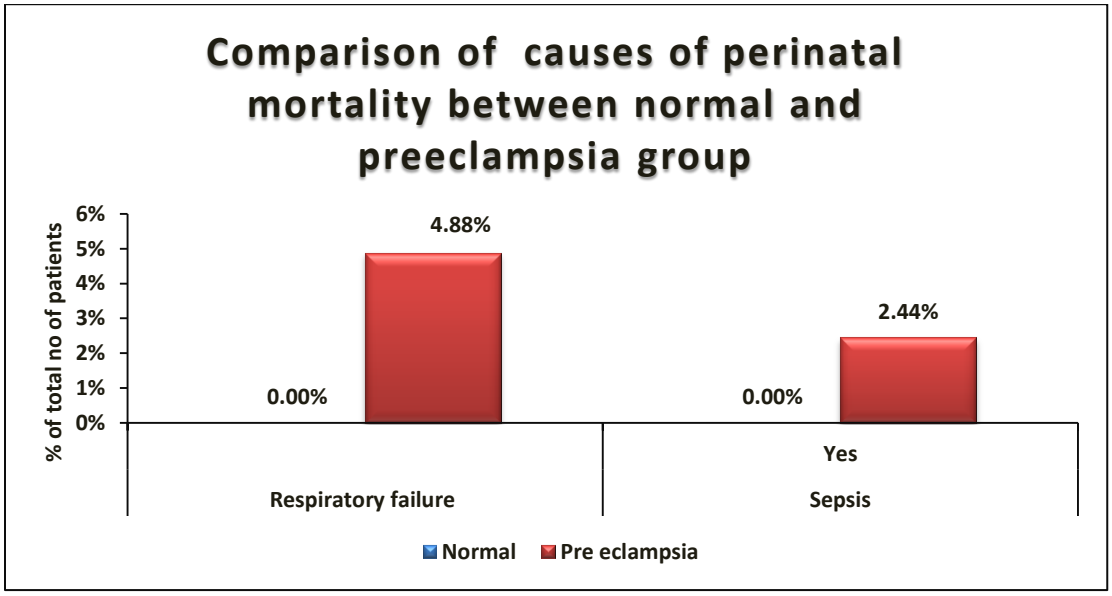


Figure 9(b):- Comparison of causes of perinatal mortality between normal and preeclampsia group.

On comparing the fetal outcome between normal and preeclampsia women no significant difference was seen in the distribution of the mode of delivery, respiratory distress, perinatal mortality and causes of perinatal mortality between the two groups (p value >.05). However, significant difference was seen in the APGAR score at 5 minutes, NICU admission, birth weight, IUGR and small for gestational age between normal and preeclampsia group (p value <.05) APGAR score at 5 minutes <7 was found in 33.33% of the babies in preeclampsia group as compared to only 4.88% of babies in normal group. Median(IQR) value of APGAR score at 5 minutes in preeclampsia group was 8(6 - 9) and in normal group was 9(9 - 9). Also the proportion of the babies who required NICU admission was significantly higher in preeclampsia group as compared to the normal group (47.22% versus 14.63%) with significantly higher mean value of days of NICU admission. Low birth weight was also seen in preeclampsia group significantly more as compared to the normal group (53.66% versus 14.63%) with mean value of birth weight in preeclampsia group as 2.39 ± 0.66 kg and in normal group as 2.8 ± 0.33 kg. Around 41% of the babies in preeclampsia group were IUGR as compared to only 2.44% of the babies in normal group. Small for gestational age was also significantly higher in preeclampsia group as compared to normal group (17.07% versus 0%). (Table 9, Figure 9(a), (b))

Table 10:- Comparison of maternal complications between normal and preeclampsia group.

Maternal complications		Group		Total	P value
		Normal	Preeclampsia		
Abruptio placenta		0 (0.00%)	8 (19.51%)	8 (9.76%)	0.005*
Anaemia		2 (50.00%)	5 (41.67%)	7 (43.75%)	0.432*
PRES		0 (0.00%)	3 (25.00%)	3 (18.75%)	0.241*
Maternal mortality		0 (0.00%)	0 (0.00%)	0 (0.00%)	-
Antepartum hemorrhage		0 (0.00%)	1 (8.33%)	1 (6.25%)	1*
Choriangimoga		0 (0.00%)	1 (8.33%)	1 (6.25%)	1*
Oligohydramnios		0 (0.00%)	2 (16.67%)	2 (12.50%)	0.494*
ICU admission		0 (0.00%)	5 (12.20%)	5 (6.10%)	0.055*
PPH		1 (2.44%)	8 (19.51%)	9 (10.98%)	0.029*
Eclampsia	**No**	41 (100.00%)	30 (73.17%)	71 (86.59%)	0.0005*
	Yes	0 (0.00%)	11 (26.83%)	11 (13.41%)	
Types of eclampsia	**Antepartum eclampsia**	0 (0.00%)	3 (27.27%)	3 (27.27%)	-
	Imminent eclampsia	0 (0.00%)	4 (36.36%)	4 (36.36%)	
	Intra partum eclampsia	0 (0.00%)	2 (18.18%)	2 (18.18%)	
	Post partum eclampsia	0 (0.00%)	2 (18.18%)	2 (18.18%)	
HELLP syndrome	**No**	41 (100.00%)	37 (90.24%)	78 (95.12%)	$0.122^{\#}$
	Partial	0 (0.00%)	2 (4.88%)	2 (2.44%)	
	Complete	0 (0.00%)	2 (4.88%)	2 (2.44%)	

Note- p value <0.05 considered as statistically significant.

***-Fisher's exact test, *-Chi square test**

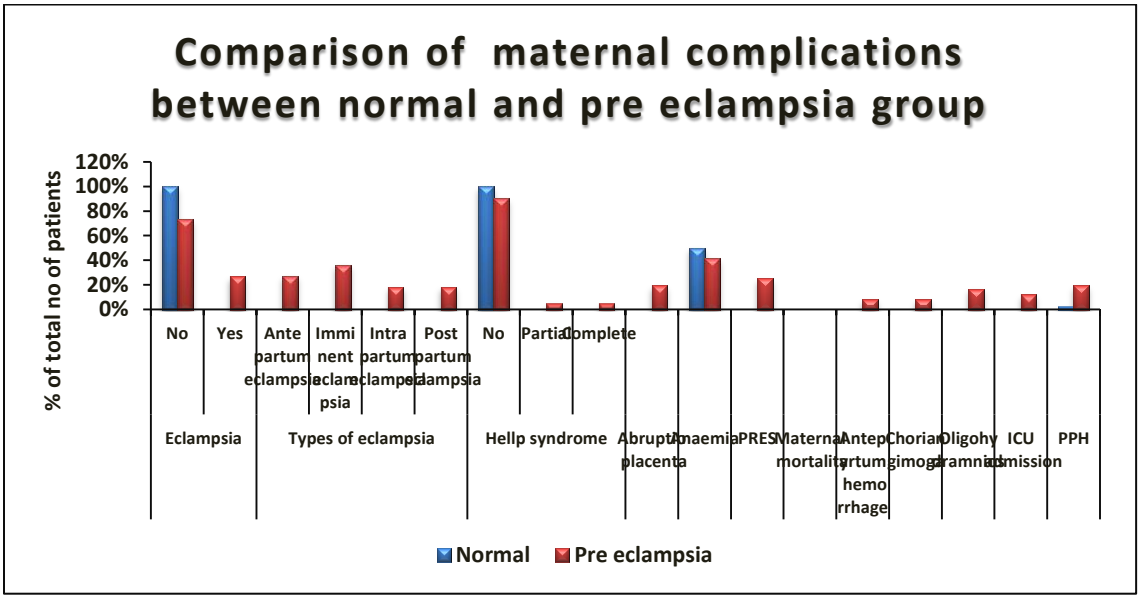


Figure 10:- Comparison of maternal complications between normal and preeclampsia group.

On comparing maternal complications between normal and preeclampsia group, no significant difference was seen in the distribution of anaemia, PRES, maternal mortality, antepartum haemorrhage, chorioangioma, oligohydramnios, ICU admission and HELLP syndrome between the two groups. (p value >.05) Significant difference was seen in the distribution of abruption placenta, PPH, and eclampsia between the two groups. 19.51% of the patients in preeclampsia group had abruptio placenta as compared to 0% in normal group. Also incidence of PPH and eclampsia was significantly higher in the preeclampsia group as compared to the normal group. (Table 10, Figure 10)

Table 11:- Comparison of maternal outcome between normal and preeclampsia group.

Maternal outcome	Group		Total	P value*
	Normal(n=41)	Preeclampsia(n=41)		
Need of blood products	3 (7.32%)	11 (26.83%)	14 (17.07%)	0.037
Antihypertensives	1 (2.44%)	33 (80.49%)	34 (41.46%)	<.0001

Note- p value <0.05 considered as statistically significant.

***-Fisher's exact test**

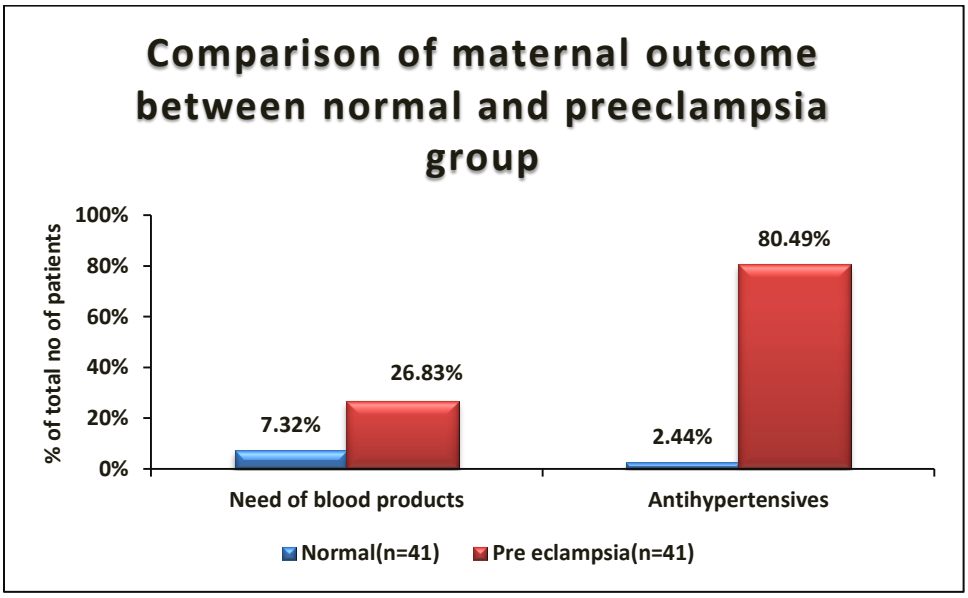


Figure 11:- Comparison of maternal outcome between normal and preeclampsia group.

Significant difference was seen in the maternal outcome between normal and preeclampsia group. (p value <.05) 26.83% and 80.49% of the patients in preeclampsia group required blood products and antihypertensives as compared to 7.32% and 2.44% in the normal group respectively. So we can say that the maternal outcome was significantly better in normal group as compared to the preeclampsia group. (Table 11, Figure 11)

Table 12:- Association of fetal outcome with ishemia modified albumin , TOTAL CYTOCHROME OXIDASE and malondialdehyde.

Fetal outcome		**Malondialdehyde(micro mole/liter)**	**Ishemia modified albumin(ABSU)**	**TOTAL CYTOCHROME OXIDASE(ng/ml)**
Mode of delivery				
LSCS(n=48)	**Mean ± SD**	0.47 ± 0.19	0.6 ± 0.39	3.52 ± 2.26
	Median(IQR)	0.42(0.320 - 0.544)	0.48(0.312 - 0.987)	3.16(1.697 - 5.363)
Vaginal delivery(n=34)	**Mean ± SD**	0.49 ± 0.23	0.66 ± 0.51	3.86 ± 2.8
	Median(IQR)	0.42(0.302 - 0.689)	0.43(0.215 - 1.029)	2.4(1.830 - 6.121)
p value*		0.649	0.567	0.543
APGAR score at 5 minutes				
<7(n=14)	**Mean ± SD**	0.6 ± 0.21	0.93 ± 0.43	5.14 ± 2.15
	Median(IQR)	0.54(0.474 - 0.775)	0.96(0.731 - 1.081)	5.11(3.921 - 7.026)
>=7(n=63)	**Mean ± SD**	0.42 ± 0.17	0.51 ± 0.38	3.02 ± 2.18
	Median(IQR)	0.37(0.302 - 0.468)	0.39(0.231 - 0.593)	2.31(1.466 - 4.144)
p value*		0.001	0.001	0.002
NICU admission				
No(n=54)	**Mean ± SD**	0.41 ± 0.17	0.5 ± 0.4	2.86 ± 2.12
	Median(IQR)	0.37(0.299 - 0.453)	0.32(0.215 - 0.549)	2.19(1.460 - 3.815)
Yes(n=23)	**Mean ± SD**	0.56 ± 0.2	0.79 ± 0.4	4.68 ± 2.3
	Median(IQR)	0.53(0.384 - 0.738)	0.82(0.445 - 1.029)	5.04(3.018 - 6.289)
p value*		0.002	0.004	0.001
Birth weight (kg)				
<2.5(n=28)	**Mean ± SD**	0.6 ± 0.21	0.87 ± 0.43	5.08 ± 2.44
	Median(IQR)	0.54(0.437 - 0.764)	0.92(0.501 - 1.056)	5.14(3.601 - 6.913)

>=2.5(n=54)	**Mean ± SD**	0.41 ± 0.18	0.5 ± 0.39	2.93 ± 2.2
	Median(IQR)	0.36(0.291 - 0.453)	0.32(0.215 - 0.549)	2.27(1.485 - 3.815)
p value*		0.0001	0.0002	0.0001
IUD				
No(n=77)	**Mean ± SD**	0.46 ± 0.19	0.58 ± 0.42	3.4 ± 2.31
	Median(IQR)	0.41(0.306 - 0.544)	0.43(0.280 - 0.946)	2.6(1.651 - 5.175)
Yes(n=5)	**Mean ± SD**	0.8 ± 0.17	1.26 ± 0.27	7.65 ± 1.64
	Median(IQR)	0.79(0.707 - 0.947)	1.39(0.995 - 1.451)	8.59(6.388 - 8.807)
p value*		0.002	0.006	0.001
IUGR				
No(n=64)	**Mean ± SD**	0.44 ± 0.19	0.56 ± 0.45	3.1 ± 2.27
	Median(IQR)	0.37(0.304 - 0.519)	0.33(0.216 - 0.955)	2.36(1.472 - 4.526)
Yes(n=18)	**Mean ± SD**	0.61 ± 0.2	0.87 ± 0.34	5.68 ± 2.21
	Median(IQR)	0.6(0.474 - 0.762)	0.92(0.561 - 1.031)	5.98(4.329 - 7.162)
p value*		0.001	0.001	0.0002
Respiratory distress				
No(n=69)	**Mean ± SD**	0.48 ± 0.21	0.61 ± 0.44	3.62 ± 2.5
	Median(IQR)	0.42(0.315 - 0.585)	0.43(0.280 - 1.003)	2.6(1.706 - 5.835)
Yes(n=13)	**Mean ± SD**	0.47 ± 0.18	0.69 ± 0.44	3.88 ± 2.5
	Median(IQR)	0.45(0.306 - 0.562)	0.51(0.369 - 0.949)	3.92(1.890 - 5.175)
p value*		0.889	0.378	0.804
Small for gestational age				
No(n=75)	**Mean ± SD**	0.46 ± 0.21	0.61 ± 0.45	3.5 ± 2.47
	Median(IQR)	0.41(0.306 - 0.545)	0.43(0.274 - 1.002)	2.6(1.594 - 5.530)
Yes(n=7)	**Mean ± SD**	0.61 ± 0.16	0.79 ± 0.24	5.45 ± 2.03
	Median(IQR)	0.65(0.536 - 0.738)	0.91(0.581 - 0.999)	5.1(4.342 - 6.963)
p value*		0.057	0.107	0.042
Perinatal mortality				
No(n=75)	**Mean ± SD**	0.45 ± 0.19	0.57 ± 0.42	3.34 ± 2.28
	Median(IQR)	0.41(0.305 - 0.541)	0.43(0.274 - 0.921)	2.6(1.594 - 5.120)
Yes(n=2)	**Mean ± SD**	0.65 ± 0.14	1.12 ± 0.12	6.02 ± 2.97
	Median(IQR)	0.65(0.546 - 0.751)	1.12(1.031 - 1.201)	6.02(3.921 - 8.120)
p value*		0.148	0.069	0.106

Note- p value <0.05 considered as statistically significant.

***-Independent t test**

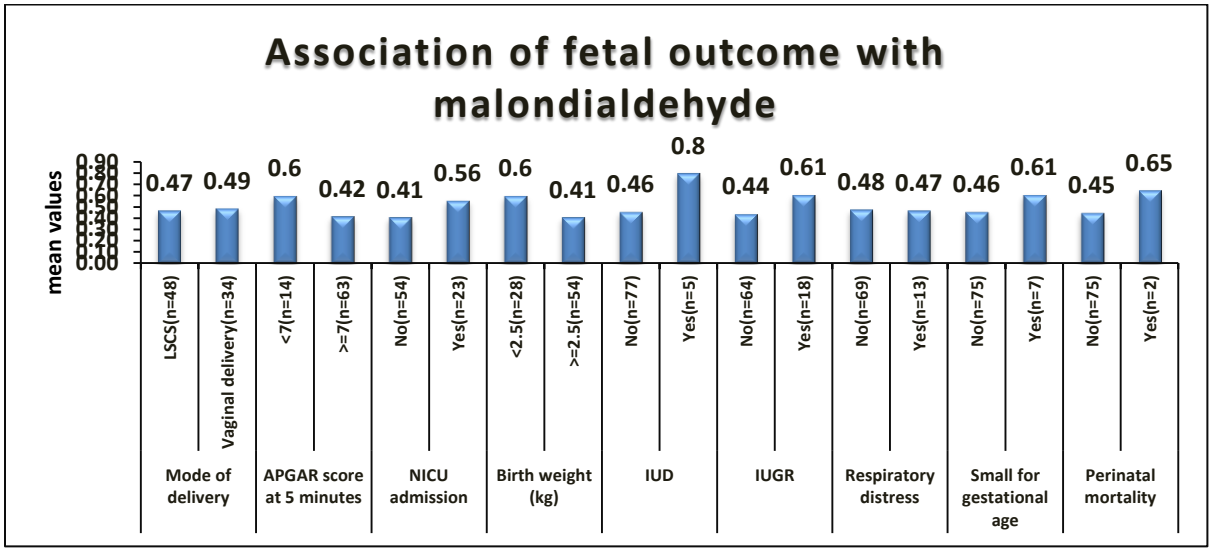


Figure 12(a):- Association of fetal outcome with malondialdehyde.

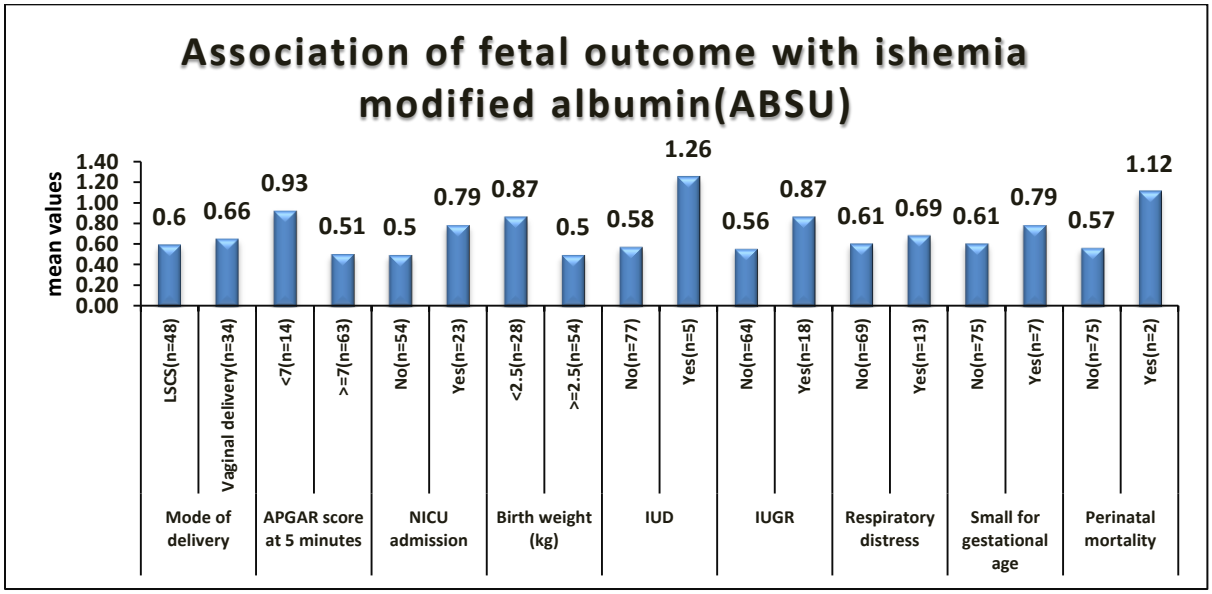


Figure 12(b):- Association of fetal outcome with ishemia modified albumin(ABSU).

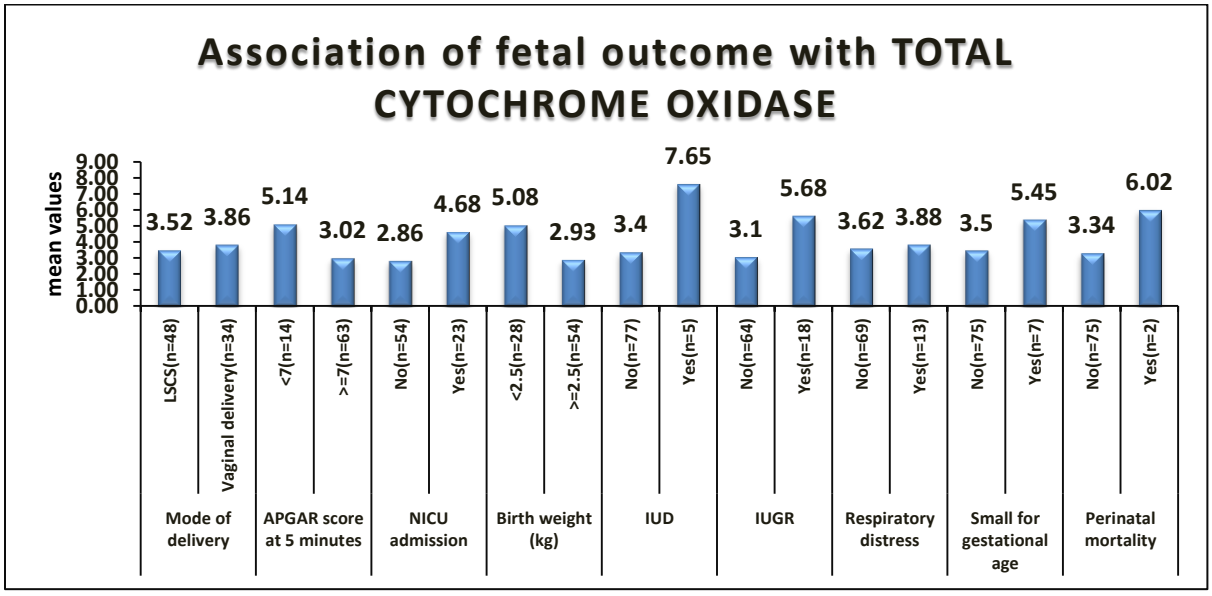


Figure 12(c):- Association of fetal outcome with TOTAL CYTOCHROME OXIDASE.

No significant association was seen between the mode of delivery, respiratory distress and perinatal mortality with MDA, IMA and TOTAL CYTOCHROME OXIDASE. (p value >.05) Mean value of MDA, IMA and TOTAL CYTOCHROME OXIDASE was comparable between LSCS and vaginal delivery and between mother of babies with and without respiratory distress or perinatal mortality without any significant difference between them.

Significant association was seen in the APGAR score at 5 minutes with oxidative and mitochondrial stress markers. (p value <.05) Mother of babies with APGAR score at 5 minutes < 7 had significantly higher levels of oxidative and mitochondrial stress markers as compared to mother of babies with APGAR score at 5 minutes > 7. Mean value of MDA, IMA and TOTAL CYTOCHROME OXIDASE of mother in babies with APGAR score <7 was 0.6 ± 0.21 µmole/liter, 0.93 ± 0.43 ABSU and 5.14 ± 2.15 ng/ml

respectively and in babies with APGAR score >7 was 0.42 ± 0.17 µmole/liter, 0.51 ± 0.38 ABSU and 3.02 ± 2.18 ng/ml respectively.

Significant association was seen in the NICU admission, low birth weight, IUD and IUGR with oxidative and mitochondrial stress markers. (p value <.05) Babies of mother with higher level of MDA, IMA and TOTAL CYTOCHROME OXIDASE had significantly higher chances of low birth weight, requirement of NICU admission, IUD and IUGR.

No significant association was seen between small for gestational age with MDA and IMA. (p value >.05) However mean level of TOTAL CYTOCHROME OXIDASE of mother in small for gestational age babies was significantly higher as compared to without small for gestational age babies (5.45 ± 2.03 ng/ml versus 3.5 ± 2.47 ng/ml). (Table 12, Figure 12(a), (b), (c))

Table 13:- Association of maternal complications with TOTAL CYTOCHROME OXIDASE, ishemia modified albumin (ABSU) and malondialdehyde.

Maternal complications		Malondialdehyde(micro mole/liter)	Ishemia modified albumin(ABSU)	TOTAL CYTOCHROME OXIDASE(ng/ml)
Abruptio placenta				
No(n=74)	**Mean ± SD**	0.45 ± 0.19	0.58 ± 0.41	3.3 ± 2.3
	Median(IQR)	0.41(0.305 - 0.543)	0.43(0.271 - 0.974)	2.58(1.565 - 5.100)
Yes(n=8)	**Mean ± SD**	0.73 ± 0.2	1.06 ± 0.47	7.05 ± 1.45
	Median(IQR)	0.78(0.569 - 0.905)	1(0.715 - 1.466)	6.91(5.948 - 8.441)
p value*		0.0001	0.002	<.0001
Anaemia				
No(n=75)	**Mean ± SD**	0.47 ± 0.2	0.6 ± 0.44	3.52 ± 2.38
	Median(IQR)	0.41(0.306 - 0.546)	0.43(0.274 - 0.994)	2.6(1.744 - 5.530)
Yes(n=7)	**Mean ± SD**	0.54 ± 0.24	0.87 ± 0.46	5.26 ± 3.28
	Median(IQR)	0.54(0.376 - 0.716)	0.92(0.444 - 1.156)	5.15(2.185 - 8.247)
p value*		0.388	0.092	0.21
PRES				
No(n=79)	**Mean ± SD**	0.47 ± 0.2	0.62 ± 0.45	3.51 ± 2.39
	Median(IQR)	0.41(0.306 - 0.546)	0.44(0.285 - 1.003)	2.6(1.689 - 5.278)
Yes(n=3)	**Mean ± SD**	0.69 ± 0.12	0.75 ± 0.28	7.75 ± 1.21
	Median(IQR)	0.75(0.595 - 0.760)	0.91(0.549 - 0.916)	8.28(6.844 - 8.513)
p value*		0.057	0.553	0.013
Maternal mortality				
No(n=82)	**Mean ± SD**	0.48 ± 0.21	0.62 ± 0.44	3.66 ± 2.49
	Median(IQR)	0.42(0.306 - 0.564)	0.45(0.291 - 1.003)	2.88(1.715 - 5.775)
Yes(n=0)	**Mean ± SD**	0 ± 0	0 ± 0	0 ± 0

	Median(IQR)	0(0 - 0)	0(0 - 0)	0(0 - 0)
p value		-	-	-
Antepartum hemorrhage				
No(n=81)	**Mean ± SD**	0.47 ± 0.2	0.61 ± 0.43	3.63 ± 2.48
	Median(IQR)	0.42(0.306 - 0.551)	0.44(0.289 - 1.001)	2.84(1.706 - 5.644)
Yes(n=1)	**Mean ± SD**	0.9 ± 0	1.73 ± 0	6.77 ± 0
	Median(IQR)	0.9(0.904 - 0.904)	1.73(1.731 - 1.731)	6.77(6.770 - 6.770)
p value*		0.134	0.087	0.229
Choriangimoga				
No(n=81)	**Mean ± SD**	0.48 ± 0.21	0.62 ± 0.44	3.68 ± 2.5
	Median(IQR)	0.42(0.306 - 0.576)	0.44(0.289 - 1.001)	2.93(1.706 - 5.784)
Yes(n=1)	**Mean ± SD**	0.42 ± 0	1.02 ± 0	2.6 ± 0
	Median(IQR)	0.42(0.421 - 0.421)	1.02(1.021 - 1.021)	2.6(2.605 - 2.605)
p value*		0.916	0.331	0.916
Oligohydramnios				
No(n=80)	**Mean ± SD**	0.48 ± 0.21	0.62 ± 0.44	3.66 ± 2.51
	Median(IQR)	0.42(0.312 - 0.555)	0.45(0.287 - 1.002)	2.88(1.697 - 5.793)
Yes(n=2)	**Mean ± SD**	0.48 ± 0.24	0.72 ± 0.44	3.76 ± 1.64
	Median(IQR)	0.48(0.306 - 0.647)	0.72(0.411 - 1.031)	3.76(2.605 - 4.920)
p value*		0.964	0.518	0.764
ICU admission				
No(n=77)	**Mean ± SD**	0.46 ± 0.2	0.6 ± 0.43	3.46 ± 2.41
	Median(IQR)	0.41(0.306 - 0.544)	0.43(0.280 - 1.001)	2.6(1.651 - 5.390)
Yes(n=5)	**Mean ± SD**	0.72 ± 0.15	1.03 ± 0.43	6.75 ± 1.62
	Median(IQR)	0.76(0.590 - 0.838)	0.92(0.816 - 1.236)	7.03(5.104 - 8.110)
p value*		0.005	0.035	0.004
PPH				
No(n=73)	**Mean ± SD**	0.46 ± 0.2	0.58 ± 0.42	3.41 ± 2.43
	Median(IQR)	0.41(0.305 - 0.543)	0.43(0.280 - 0.981)	2.6(1.545 - 5.390)

Yes(n=9)	**Mean ± Stdev**	0.64 ± 0.18	0.98 ± 0.45	5.73 ± 2.05
	Median(IQR)	0.61(0.532 - 0.770)	0.92(0.816 - 1.248)	5.13(4.756 - 7.130)
p value*		0.012	0.01	0.008
Eclampsia				
No(n=71)	**Mean ± SD**	0.45 ± 0.2	0.59 ± 0.46	3.34 ± 2.45
	Median(IQR)	0.39(0.304 - 0.540)	0.42(0.231 - 0.994)	2.49(1.505 - 5.278)
Yes(n=11)	**Mean ± SD**	0.62 ± 0.15	0.83 ± 0.23	5.78 ± 1.62
	Median(IQR)	0.61(0.532 - 0.738)	0.92(0.604 - 1.024)	5.04(4.477 - 6.861)
p value*		0.009	0.093	0.002
HELLP				
No(n=78)	**Mean ± SD**	8.27 ± 0.45	5.08 ± 0.07	3.51 ± 2.43
	Median(IQR)	8.27(7.950 - 8.591)	5.08(5.035 - 5.127)	2.6(1.680 - 5.600)
Yes partial(n=2)	**Mean ± SD**	1.31 ± 0.55	0.72 ± 0.29	0.6 ± 0.43
	Median(IQR)	1.31(0.918 - 1.702)	0.72(0.511 - 0.921)	0.43(0.283 - 1.003)
Yes complete(n=2)	**Mean ± SD**	0.79 ± 0.04	0.57 ± 0.06	0.47 ± 0.2
	Median(IQR)	0.79(0.762 - 0.816)	0.57(0.527 - 0.611)	0.41(0.306 - 0.545)
p value#		0.072	0.078	0.018

***-Independent t test**

#-ANOVA

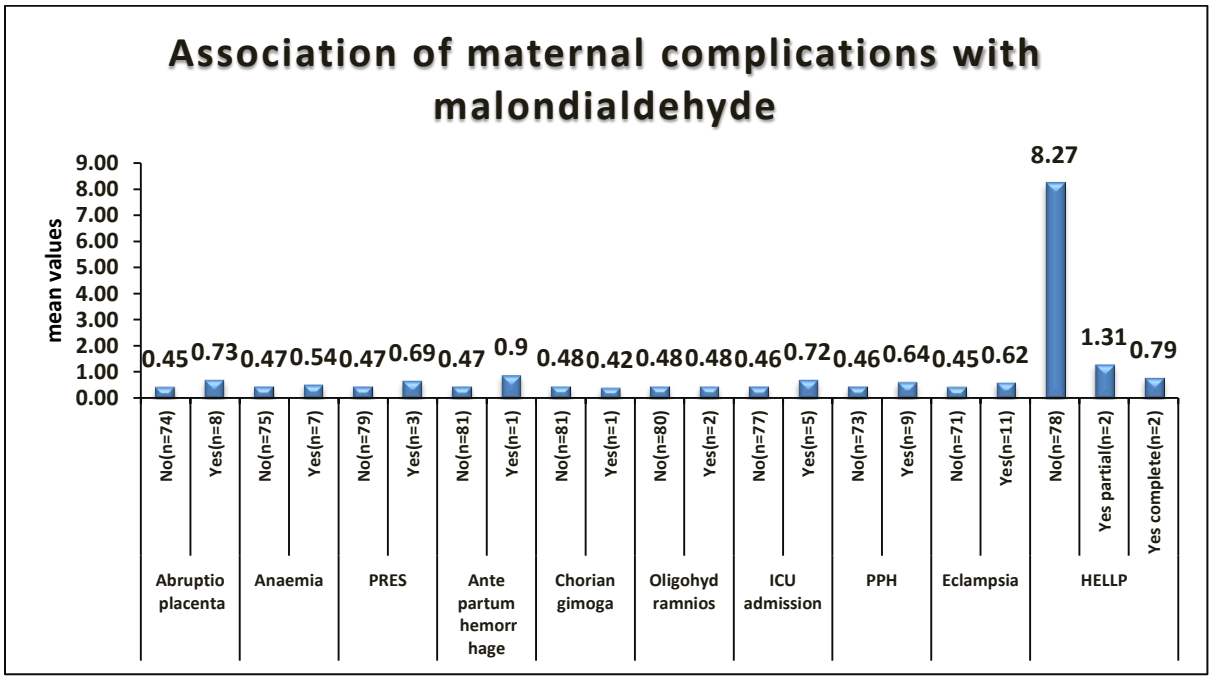


Figure 13(a):- Association of maternal complications with malondialdehyde.

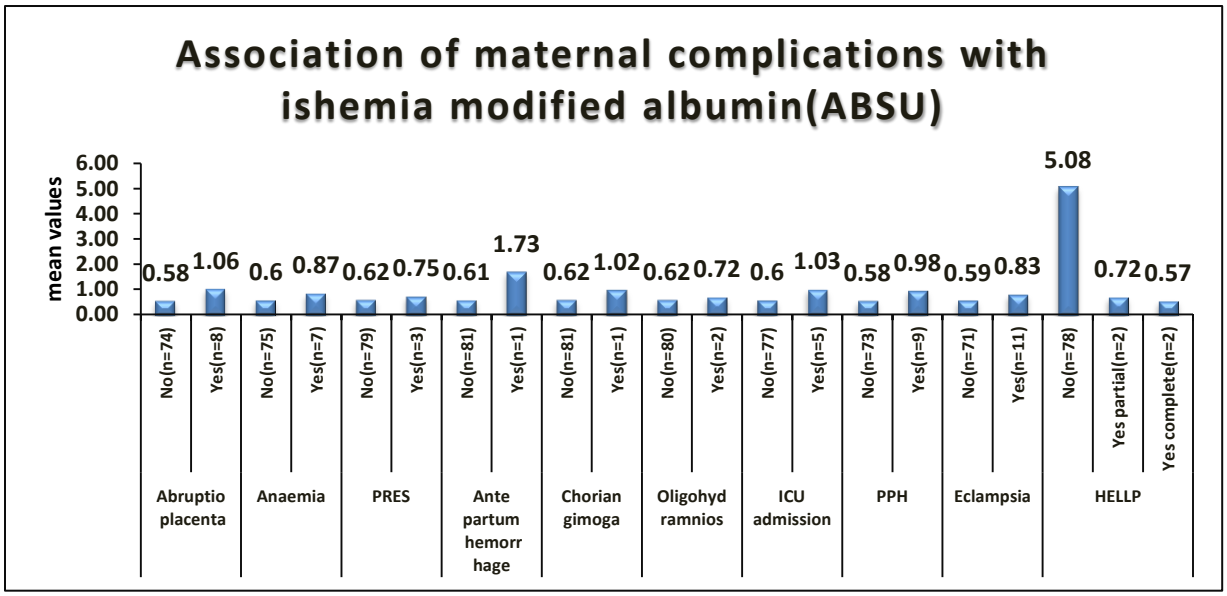


Figure 13(b):- Association of maternal complications with ishemia modified albumin

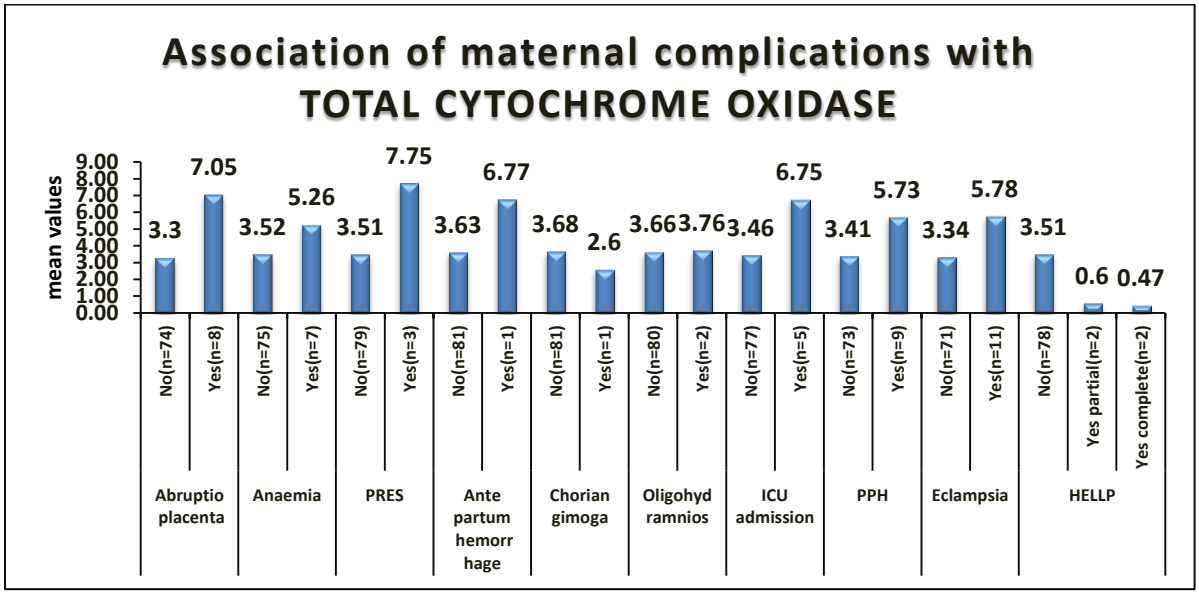


Figure 13(c):- Association of maternal complications with TOTAL CYTOCHROME OXIDASE.

No significant association was seen between anaemia with MDA, IMA and TOTAL CYTOCHROME OXIDASE(p value >.05). Mean value of MDA, IMA and TOTAL CYTOCHROME OXIDASE was comparable mothers with and without anaemia with no significant difference between them. Also due to very small sample size of patients with antepartum hemorrhage, chorioangioma, oligohydramnios and perinatal mortality, no significant association was seen between them with MDA, IMA and TOTAL CYTOCHROME OXIDASE. (p value >.05)

Significant association was seen in abruption placenta, ICU admission and PPH with oxidative and mitochondrial stress markers. (p value <.05) Women with abruption placenta, ICU admission and PPH had significantly higher levels of oxidative and mitochondrial stress markers as compared to women without any such maternal complication. Mean value of MDA, IMA and TOTAL CYTOCHROME OXIDASE of

women with abruption placenta was 0.73 ± 0.2 µmole/liter, 1.06 ± 0.47 ABSU and 7.05 ± 1.45ng/ml respectively, women who required ICU admission was 0.72 ± 0.15 µmole/liter, 1.03 ± 0.43 ABSU and 6.75 ± 1.62 ng/ml respectively and women with PPH was 0.64 ± 0.18 µmole/liter, 0.98 ± 0.45 ABSU and 5.73 ± 2.05 ng/ml respectively.

No significant association was seen between small for gestational age with MDA and IMA. (p value >.05) However mean level of TOTAL CYTOCHROME OXIDASE of women with PRES was significantly higher as compared to without PRES (7.75 ± 1.21 ng/ml versus 3.51 ± 2.39 ng/ml).

No maternal mortality was seen in the present study so no association could be established between maternal mortality with oxidative and mitochondrial stress markers.

No significant association was seen between eclampsia with IMA. (p value >.05) However mean level of MDA and TOTAL CYTOCHROME OXIDASE of women with eclampsia was significantly higher as compared to without eclampsia (p value <.05)

No significant association was seen between HELLP with MDA and IMA. (p value >.05) However mean level of TOTAL CYTOCHROME OXIDASE of women with partial or complete HELLP was significantly higher as compared to without HELLP (5.08 ± 0.07 ng/ml or 8.27 ± 0.45 ng/ml versus 3.51 ± 2.43 ng/ml). (Table 13, Figure 13(a), (b), (c))

Table 14:- Association of maternal outcome with TOTAL CYTOCHROME OXIDASE, ishemia modified albumin (ABSU) and malondialdehyde.

Maternal outcome		Malondialdehyde(micro mole/liter)	Ishemia modified albumin(ABSU)	TOTAL CYTOCHROME OXIDASE(ng/ml)
Antihypretensive				
No(n=48)	**Mean ± SD**	0.38 ± 0.16	0.39 ± 0.33	2.31 ± 1.8
	Median(IQR)	0.34(0.290 - 0.420)	0.31(0.204 - 0.430)	1.97(1.106 - 2.723)
Yes(n=34)	**Mean ± SD**	0.62 ± 0.19	0.95 ± 0.37	5.58 ± 2.03
	Median(IQR)	0.56(0.456 - 0.762)	1.01(0.603 - 1.053)	5.69(4.150 - 7.162)
p value*		<.0001	<.0001	<.0001
Need of blood product				
No(n=68)	**Mean ± SD**	0.45 ± 0.2	0.57 ± 0.41	3.31 ± 2.32
	Median(IQR)	0.41(0.305 - 0.543)	0.42(0.244 - 0.955)	2.58(1.623 - 5.123)
Yes(n=14)	**Mean ± SD**	0.58 ± 0.22	0.91 ± 0.47	5.37 ± 2.66
	Median(IQR)	0.54(0.418 - 0.762)	0.92(0.491 - 1.201)	5.14(3.921 - 8.120)
p value*		0.031	0.007	0.004

***-Independent t test**

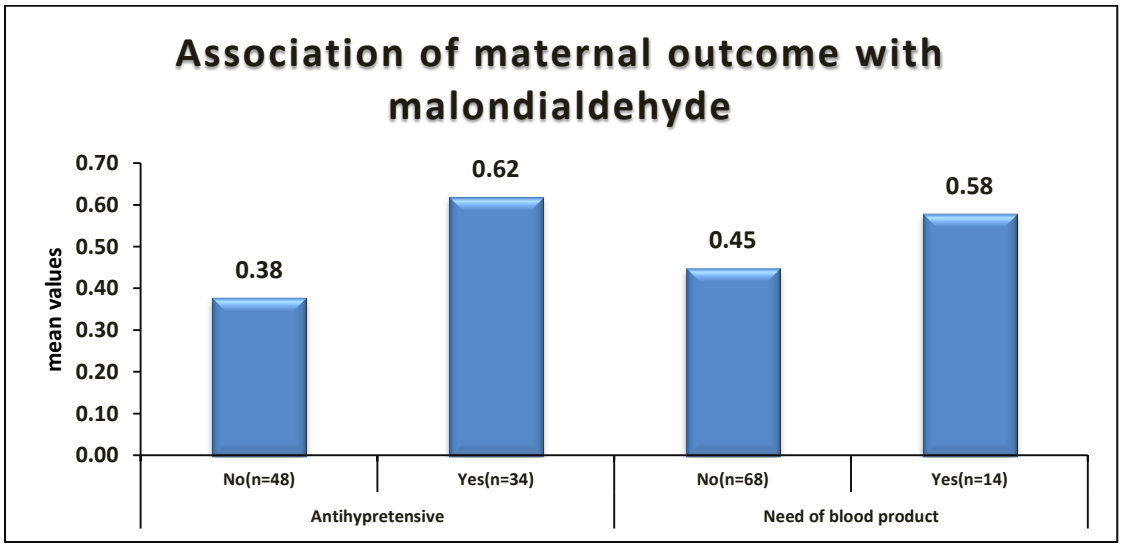


Figure 14(a):- Association of maternal outcome with malondialdehyde.

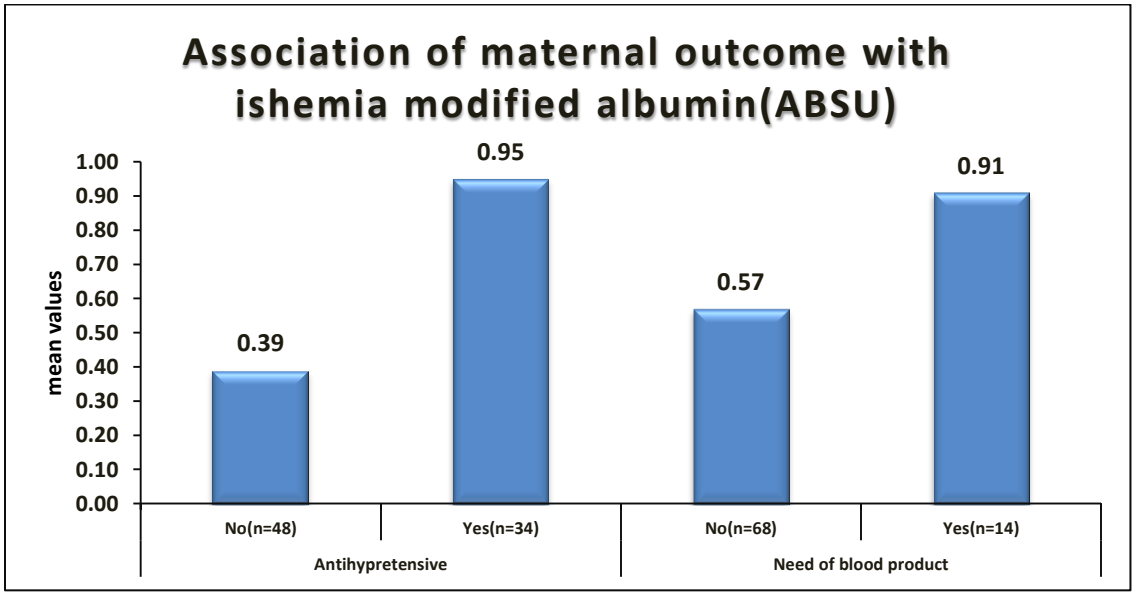


Figure 14(b):- Association of maternal outcome with ishemia modified albumin (ABSU).

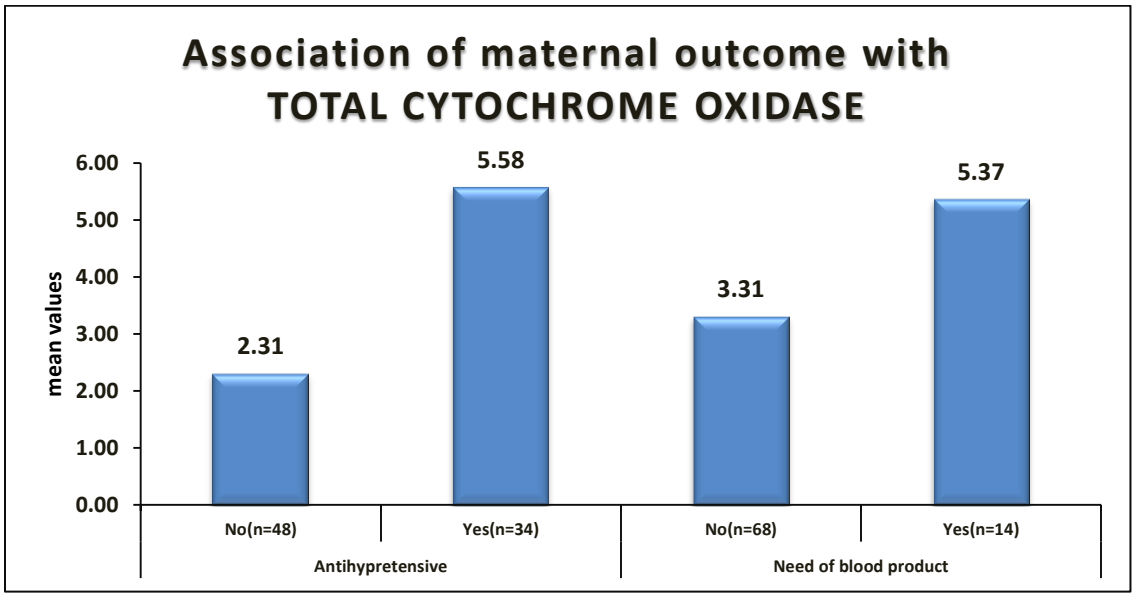


Figure 14(c):- Association of maternal outcome with TOTAL CYTOCHROME OXIDASE.

Significant association was seen in antihypertensive and need of blood product with oxidative and mitochondrial stress markers. (p value <.05) Women who required blood product or antihypertensive had significantly higher levels of oxidative and mitochondrial stress markers as compared to women who did not require them. Mean value of MDA, IMA and TOTAL CYTOCHROME OXIDASE of women who required blood product was 0.58 ± 0.22 µmole/liter, 0.91 ± 0.47 ABSU and 5.37 ± 2.66 ng/ml respectively and women who required antihypertensive was 0.62 ± 0.19 µmole/liter, 0.95 ± 0.37 ABSU and 5.58 ± 2.03 ng/ml respectively. (Table 14, Figure 14(a), (b), (c))

Table 15:-Correlation of TOTAL CYTOCHROME OXIDASE, ishemia modified albumin (ABSU) and malondialdehyde with birth weight and number of days of NICU admission.

Correlation matrix		Malondialdehyde(micro mole/liter)	Ishemia modified albumin(ABSU)	TOTAL CYTOCHROME OXIDASE(ng/ml)
Birth weight(kg)	Correlation Coefficient	-0.375	-0.349	-0.389
	P value*	0.0006	0.0014	0.0003
Number of days of NICU admission	Correlation Coefficient	0.301	0.437	0.322
	P value*	0.1631	0.0373	0.1335

Note- p value <0.05 considered as statistically significant.

***-Pearson correlation coefficient**

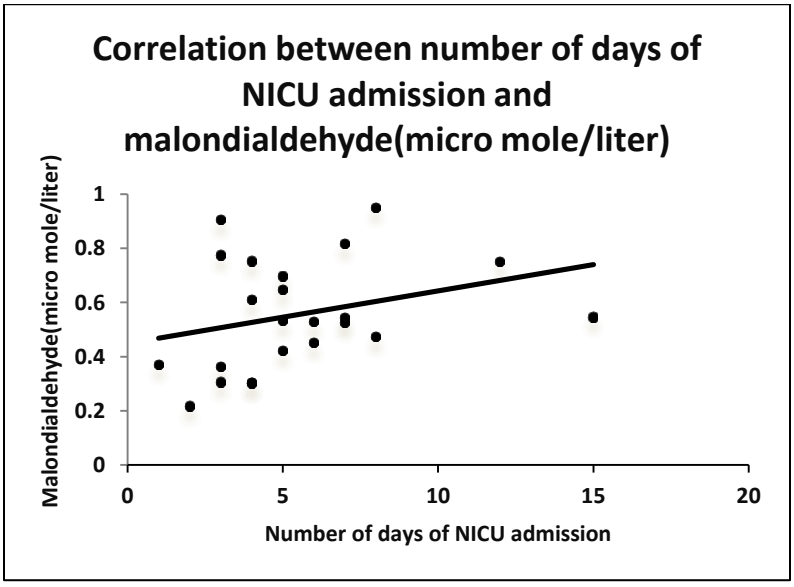


Figure 15(a):-Correlation of malondialdehyde with number of days of NICU admission.

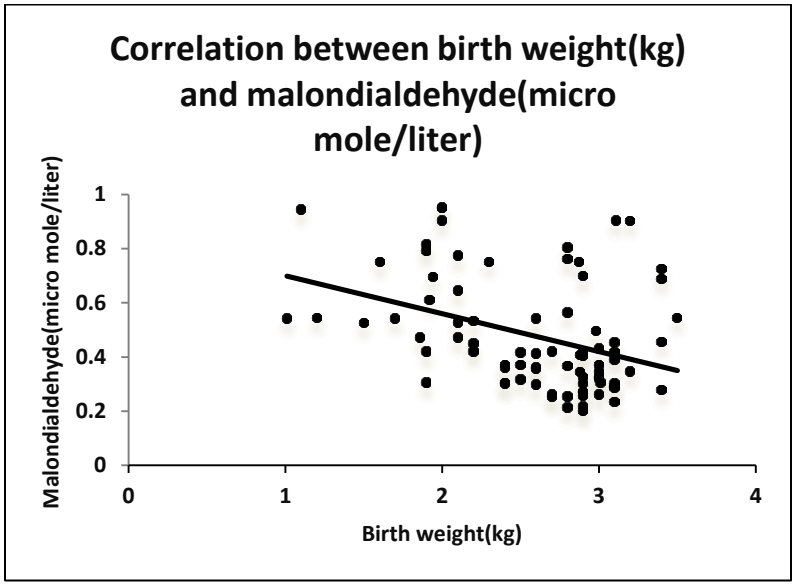


Figure 15(b):-Correlation of malondialdehyde with number of birth weight.

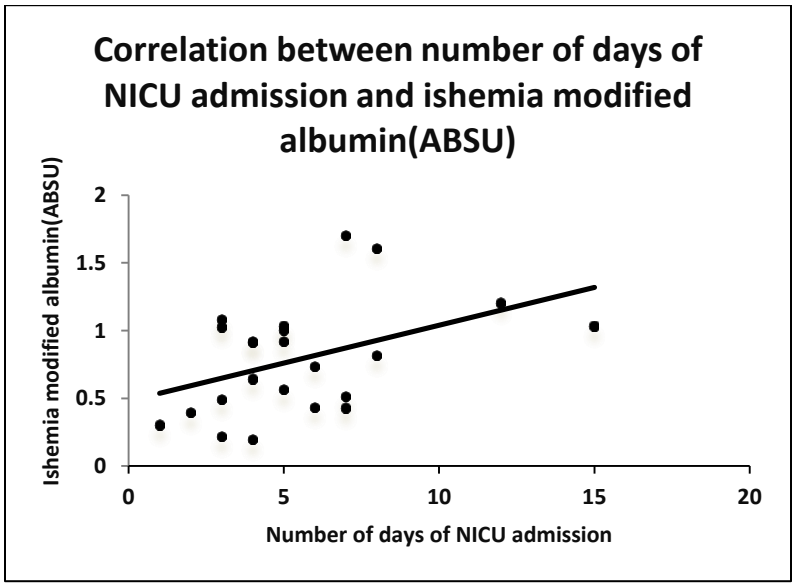


Figure 15(c):-Correlation of ischemia modified albumin(ABSU) with number of days of NICU admission.

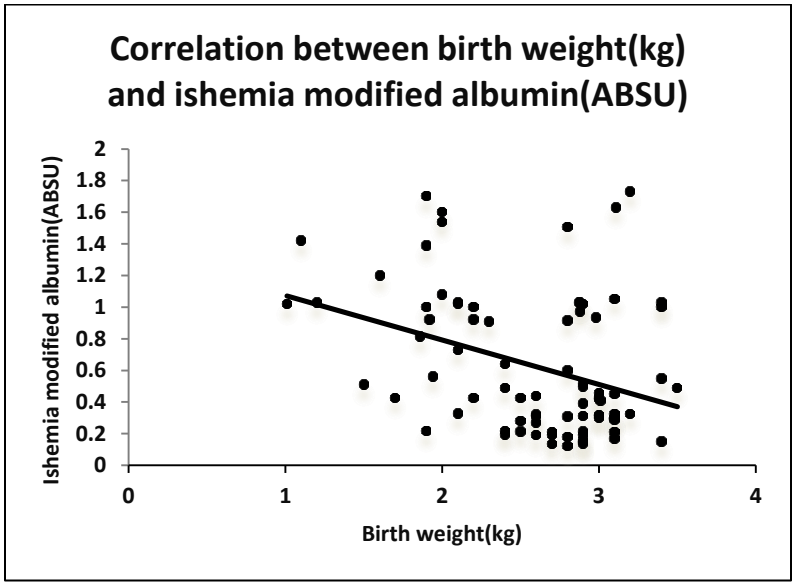


Figure 15(d):-Correlation of ischemia modified albumin(ABSU) with birth weight.

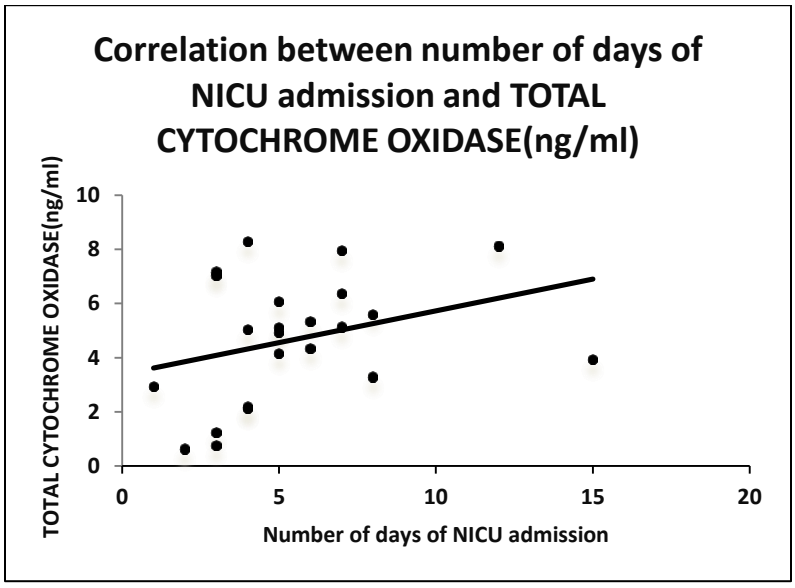


Figure 15(e):-Correlation of TOTAL CYTOCHROME OXIDASE with number of days of NICU admission.

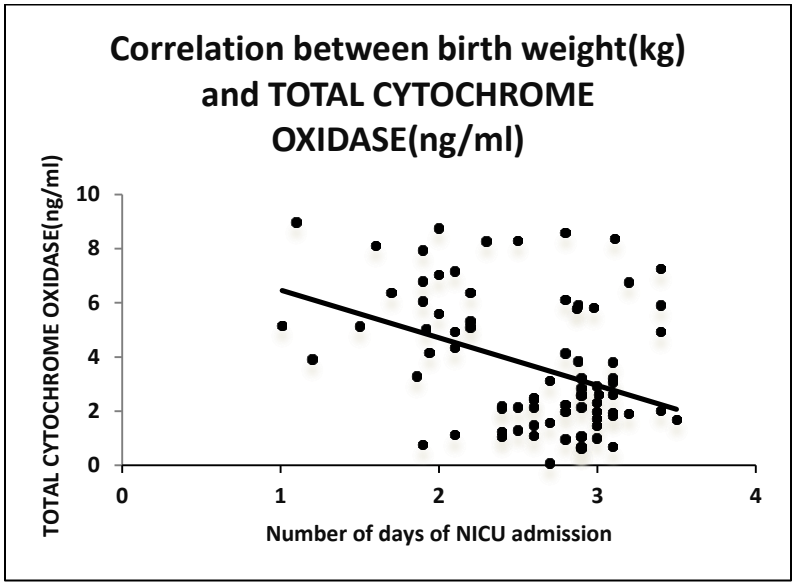


Figure 15(f):-Correlation of TOTAL CYTOCHROME OXIDASE with birth weight.

Significant negative moderate correlation was seen between birth weight with oxidative and mitochondrial stress markers. (p value <.05) Correlation coefficient of birth weight with MDA was -0.375, with IMA was -0.349 and with TOTAL CYTOCHROME OXIDASE was -0.389. So it can be concluded that with the decrease in value of oxidative and mitochondrial stress markers , birth weight significantly increases. Significant moderate positive correlation was seen between number of days of NICU admission with IMA with r=0.437. Non-significant positive correlation was seen between number of days of NICU admission with MDA and TOTAL CYTOCHROME OXIDASE with r=0.301 and 0.322 respectively. (Table 15, Figure (a), (b), (c), (d), (e), (f)

DISCUSSION

DISSUSSION

Our study is a comparative observational study conducted in R L Jalappa Hospital, attached to Sri Devaraj Urs Medical college, Tamaka, kolar with study population of 82 singleton pregnancies between 20-40 weeks of gestation. Among them 41 are normotensive pregnancies and 41 are Preeclampsia cases are studied from January 2018-December 2018**.**

During healthy pregnancy there is an increased but stable oxidative environment. But in cases of preeclampsia there will be increased oxidative stress and systemic inflammatory response due to release of free radicles and reactive oxygen species. OS induced in the ischemic placenta causes a systemic inflammatory response and activates maternal endothelial cells.

MATERNAL AGE

STUDIES ON MDA(AGE)	GROUP A(NORMAL) (Mean Age±SD)	GROUP B(PE) (Mean Age±SD)	P VALUE
ELISA LLURBA et al	31.12±5.6	29.4±5.8	>0.05
Niyazi Tug et al	26±2	25±2	>0.05
R. MADAZLI et al	31·3±1·5	29·6±6·1	0·223
OUR STUDY	25.88 ± 4.11	24.71 ± 3.7	0.179

In our study, no significant difference was seen in age distribution between normal and preeclampsia group. (p value >.05). Majority of the women in both the groups belonged to 21 to 25 years of age group; 39.02% in normal group and 48.78% of patients in preeclampsia group.

STUDIES ON MDA(MDA LEVELS)	GROUP A(NORMAL) (Mean ±SD)	GROUP B(PE) (Mean ±SD)	P VALUE
Niyazi Tug et al	(nmol/ml) 1.9 ± 0.2	0.84 ± 0.2	<0.05*
R. MADAZLI et al	(nmol/ml)4·49±0·71	6·06±0·94	< 0·001
OUR STUDY	0.35 ± 0.1	0.61 ± 0.2	<0.001

Several studies were done on MDA levels in preeclampsia, they have concluded that there will be increased levels of Plasma malondialdehyde thus indicating the high levels of oxidative stress compared to normal pregnancy .

MDA LEVELS

In a study by Necip Ilhan et al observed that, in the preeclamptic group malondialdehyde, Cu levels were significantly increased, while Zn and SOD levels were significantly decreased compared to normal control group and healthy pregnant women. These findings give support that radical scavenging SOD is consumed by the increased lipid peroxidation in preeclampsia. This observation may indicate an involvement of free radicals in the pathophysiology of preeclampsia. This study suggests a relationship

between increased MDA, Cu levels and decreased SOD, Zn levels in pregnancy and preeclampsia.

A study by Gohil J. T et al was carried out on 3 group of women ie; Non-pregnant normotensive—50 patients, Pregnant women without preeclampsia, and third group being pregnant women with preeclampsia. Malondialdehyde, an indicator of lipid peroxidation and oxidative stress, was calculated in all the subjects and mean calculated. It was found to be highly significantly increased in normal pregnancy(mean-6.91) compared to nonpregnant females(mean-5.19). The levels further showed a highly significant increase in preeclampsia (mean-8.1)than normal pregnancy. Concentration in preeclampsia was found to be almost less than the double in non pregnant women[53]. Post partum the level was found to be decreasing again [3.]

IMA LEVELS

STUDIES ON IMA (IMA LEVELS)	GROUP A (NORMAL) (Mean ±SD)	GROUP B(PE) (Mean ±SD)	P VALUE
Kar Kaushik et al	31.55± 1.15 U/ML	45.66±1.6 UNIT/ML.	p<0.0001
C D Dayanand et al	1.0171 ABSU	0.328ABSU	< 0·02
OUR STUDY	0.29 ± 0.12ABSU	0.96 ± 0.39ABSU	<.0001

Kar Kaushik et al done a study on Placental ischemia modified albumin may be a marker of oxidative stress in preeclampsia. They have found that Mean IMA in controls was 31.55± 1.15 U/ML in controls whereas the same in cases are 45.66±1.6 UNIT/ML. there was a significant difference of mean IMA between preeclampsia cases and normal pregnants ($p<0.0001$)[10].

In a study by C D Dayanand et al, Ischemia Modified Albumin (IMA) was measured in thirty normal pregnant and thirty preeclampsia women before and after the delivery within 48 hours, that were compared to 30 non–pregnant women as controls. The Median IMA level in the preeclampsia group before delivery 1.0171 ABSU and the same within 48hrs after delivery 1.013ABSU was significantly higher ($p<0.02$) than in normal pregnant group before

delivery 0.328 ABSU and the same within 48hrs after delivery 0.570ABSU [22].

LIPING HE et all has conducted a study in china on TOTAL CYTOCHROME OXIDASE subunit I messenger RNA in placentas from pregnancies complicated by preeclampsia and they concluded that the In conclusion, our study has shown that the amount of total cytochrome oxidase subunit I mRNA in placental villous syncytiotrophoblasts was statistically lower in the patients with preeclampsia than in the control patients[54].

Studies on TOTAL CYTOCHROME OXIDASE are limited. In our study along with the oxidative stress measurement, mitochondrial stress was measured in terms of total cytochrome oxidase. The results were correlated with the maternal and fetal outcome.

Significant difference was seen in the blood pressure between the normal and preeclampsia patients. (p value <.05) Median(IQR) value of systolic and diastolic blood pressure in normal women was 120(110 - 120) mmHg and 76(70 - 80) mmHg respectively and in women with preeclampsia was 160(150 - 170) mmHg and 100(100 - 110) mmHg respectively.

Significant difference was seen in the mean levels of MDA, IMA and TOTAL CYTOCHROME OXIDASE. (p value <.05) Mean values of MDA, IMA and TOTAL CYTOCHROME OXIDASE in normal women was 0.35 ± 0.1 µmole/liter, 0.29 ± 0.12 ABSU and 1.78 ± 1.05 ng/ml respectively and in preeclampsia women was 0.61 ± 0.2 µmole/liter, 0.96 ± 0.39 ABSU and 5.55 ± 2.04 ng/ml respectively. So it was evident that the mean values of MDA, IMA and TOTAL CYTOCHROME OXIDASE was significantly higher in preeclampsia group as compared to the normal group. (Table 6, Figure 6)

In our study significant difference was seen in the APGAR score at 5 minutes, NICU admission, birth weight, IUGR and small for gestational age between normal and preeclampsia group (p value <.05) APGAR score at 5 minutes <7 was found in 33.33% of the babies in preeclampsia group as compared to only 4.88% of babies in normal group. Also the proportion of the babies who required NICU admission was significantly higher in preeclampsia group as compared to the normal group (47.22% versus 14.63%) with significantly higher mean value of days of NICU admission. Low birth weight was also seen in preeclampsia group significantly more as compared to the normal group (53.66% versus 14.63%) with mean value of birth weight in preeclampsia group as 2.39 ± 0.66 kg and in normal group as 2.8 ± 0.33 kg. Around 41% of the babies in preeclampsia

group were IUGR as compared to only 2.44% of the babies in normal group. Small for gestational age was also significantly higher in preeclampsia group as compared to normal group (17.07% versus 0%). (Table 9, Figure 9(a), (b))

On comparing maternal complications between normal and preeclampsia group, no significant difference was seen in the distribution of anaemia, PRES, maternal mortality, antepartum haemorrhage, chorioangioma, oligohydramnios, ICU admission and HELLP syndrome between the two groups. (p value >.05) Significant difference was seen in the distribution of abruption placenta, PPH, and eclampsia between the two groups. 19.51% of the patients in preeclampsia group had abruptio placenta as compared to 0% in normal group. Also incidence of PPH and eclampsia was significantly higher in the preeclampsia group as compared to the normal group. (Table 10, Figure 10)

Significant association was seen in the APGAR score at 5 minutes with oxidative and mitochondrial stress markers. (p value <.05) Mother of babies with APGAR score at 5 minutes < 7 had significantly higher levels of oxidative and mitochondrial stress markers as compared to mother of babies with APGAR score at 5 minutes > 7.

Significant association was seen in the NICU admission, low birth weight, IUD and IUGR with oxidative and mitochondrial stress markers. (p value <.05) Babies of mother with higher level of MDA, IMA and TOTAL CYTOCHROME OXIDASE had significantly higher chances of low birth weight, requirement of NICU admission, IUD and IUGR.

No significant association was seen between small for gestational age with MDA and IMA. (p value >.05) However mean level of TOTAL CYTOCHROME OXIDASE of

mother in small for gestational age babies was significantly higher as compared to without small for gestational age babies (5.45 ± 2.03 ng/ml versus 3.5 ± 2.47 ng/ml). (Table 12, Figure 12(a), (b), (c))

Significant association was seen in abruption placenta, ICU admission and PPH with oxidative and mitochondrial stress markers. (p value <.05) Women with abruption placenta, ICU admission and PPH had significantly higher levels of oxidative and mitochondrial stress markers as compared to women without any such maternal complication. Mean value of MDA, IMA and TOTAL CYTOCHROME OXIDASE of women with abruption placenta was 0.73 ± 0.2 µmole/liter, 1.06 ± 0.47 ABSU and 7.05 ± 1.45ng/ml respectively, women who required ICU admission was 0.72 ± 0.15 µmole/liter, 1.03 ± 0.43 ABSU and 6.75 ± 1.62 ng/ml respectively and women with PPH was 0.64 ± 0.18 µmole/liter, 0.98 ± 0.45 ABSU and 5.73 ± 2.05 ng/ml respectively.

SUMMARY

SUMMARY

- It is a comparative observational study done in the department of OBTETRICS AND GYNECOLOGY & admitting to labour room of R L JALAPPA Hospital and Research Center, of SRI DEVARAJ URS MEDICAL COLLEGE Tamaka, Kolar, from January 2018-December 2018**.** After applying inclusion/exclusion criteria and taking informed consent, 41 normal pregnant women taken as controls and 41 severe preeclamptic women taken as cases in whom hypertension was developed after 20 weeks of gestation. Detailed history regarding age, parity, gestational age, menstrual history, obstetric history and any complications in present pregnancy is taken. General clinical examination, complete obstetric examination and necessary investigations are done. Five ml of venous blood is taken for the analysis of serum MDA, IMA and TOTAL CYTOCHROME OXIDASE. Each women is followed up until delivary and the foetal and maternal outcome is noted and parameters involved with increased oxidative & mitochondrial stress are noted. MDA is measured by TBARS method.IMA is measured by turbidometric method.TOTAL CYTOCHROME OXIDASE is measured by ELISA method. Following results and observations are made in the study.
- Majority of the women in both the groups belonged to 21 to 25 years of age group; 39.02% in normal group and 48.78% of patients in preeclampsia group. Age was comparable between both the groups

- Proportion of referred patients were significantly higher in preeclampsia group as compared to normal group (92.68%).
- The gestational age was significantly less(preterm) in women with preeclampsia as compared to normal women indicating higher proportion of preterm birth in preeclampsia.
- Both systolic and diastolic blood pressure was significantly higher in preeclampsia women as compared to normal women.
- The mean values of MDA, IMA and TOTAL CYTOCHROME OXIDASE was significantly higher in preeclampsia group as compared to the normal group (p value <0.05).
- On comparing the fetal outcome between normal and preeclampsia women no significant difference was seen in the distribution of the mode of delivery, respiratory distress, perinatal mortality and causes of perinatal mortality between the two groups (p value >.05). However, significant difference was seen in the APGAR score at 5 minutes, NICU admission, birth weight, IUGR and small for gestational age between normal and preeclampsia group (p value <.05)
- Incidence of abruption placenta, PPH and eclampsia was significantly higher in the preeclampsia group as compared to the normal group.
- Significant difference was seen in the maternal outcome between normal and preeclampsia group. (p value <.05) as the patients in preeclampsia group required more blood products and antihypertensives as compared to the normal group. So we can say that the maternal outcome was significantly better in normal group as compared to the preeclampsia group. Women who required blood product or

antihypertensive had significantly higher levels of oxidative and mitochondrial stress markers as compared to women who did not require them.

- Significant association was seen in the APGAR score at 5 minutes with oxidative and mitochondrial stress markers. (p value <.05) Mother of babies with APGAR score at 5 minutes < 7 had significantly higher levels of oxidative and mitochondrial stress markers as compared to mother of babies with APGAR score at 5 minutes > 7. Major association was seen in the NICU admission, low birth weight, IUD and IUGR with oxidative and mitochondrial stress markers. (p value <.05) Babies of mother with higher level of MDA, IMA and TOTAL CYTOCHROME OXIDASE had significantly higher chances of low birth weight, requirement of NICU admission, IUD and IUGR.
- No significant association was seen between small for gestational age with MDA and IMA. (p value >.05) However mean level of TOTAL CYTOCHROME OXIDASE of mother in small for gestational age babies was significantly higher as compared to without small for gestational age babies.
- In terms of maternal complications, significant association was seen in abruption placenta, ICU admission and PPH with oxidative and mitochondrial stress markers. (p value <.05) Women with abruption placenta, ICU admission and PPH had significantly higher levels of oxidative and mitochondrial stress markers as compared to women without any such maternal complication.
- Mean level of TOTAL CYTOCHROME OXIDASE of women with PRES was significantly higher as compared to without PRES. Mean level of MDA and TOTAL CYTOCHROME OXIDASE of women with eclampsia was significantly higher by

six fold as compared to without eclampsia (p value <.05)

- There was no correlation seen between HELLP with MDA and IMA. (p value >.05) However mean level of TOTAL CYTOCHROME OXIDASE of women with partial or complete HELLP was significantly higher as compared to without HELLP.
- Significant negative moderate correlation was seen between birth weight with oxidative and mitochondrial stress markers. (p value <.05). It can be concluded that with the decrease in value of oxidative and mitochondrial stress markers , birth weight significantly increases. Significant moderate positive correlation was seen between number of days of NICU admission with IMA and non-significant positive correlation was seen between number of days of NICU admission with MDA and TOTAL CYTOCHROME OXIDASE

Strengths of the study

Preeclampsia is the most common obstetric complication characterized by maternal and perinatal morbidity and mortality. Even though, several factors directly links to preeclampsia, the exact cause for onset of preeclampsia is poorly understood and unclear and has become the challenge for health care delivery system. Identification of any newer marker for early assessment of later onset on preeclampsia during pregnancy condition is most prerequisite criteria in the management of preeclampsia. Several research reports indicated oxidative stress as one of the condition under hypoxic environment there by determination of Oxidative stress served as essential, since oxidative stress implicated in damage of cell and cellular components.

However information is not available on the influence of oxidative stress and its intensity on mitochondria in pregnancy condition. This research gap of finding MDA, IMA along with human TOTAL CYTOCHROME OXIDASE has become the basis of the current study. Oxidative stress was measured in terms of MDA and the same was potentiated by measurement of IMA together.

- Mitochondrial stress marker was measured in terms of TOTAL CYTOCHROME OXIDASE in serum of preeclamptic women, it is the initial (first) study in the literature studied among the preeclamptics cases in serum.
- Previous studies done were evaluated the oxidative stress markers, but the correlation of the markers to the maternal and fetal outcome was not elaborated well. In our study

correlation of the oxidative and mitochondrial stress markers with maternal and fetal outcome was recorded.

- Study results propose for use of human TOTAL CYTOCHROME OXIDASE with oxidative stress markers in the early assessment of preeclampsia cases for the benefit of effective management of the mother and the fetus.
- The measured study parameters are in direct correlation with maternal and fetal outcome, hence these parameters can be used as diagnostic and prognostic tool in pregnancy complications.
- There is no Maternal mortality observed during the study period.

Limitations of the study

- The current study has a limitation with respect to Sample size, the choosen parameters in the study needs to be evaluated in the larger population in all the trimisters during pregnancy follow up. However the study also require to rule out contribution to serum TCO in non pregnants.

CONCLUSION

CONCLUSION

The study concludes that oxidative stress markers MDA and IMA along with mitochondrial stress marker, TOTAL CYTOCHROME OXIDASE elevated in preeclampsia in comparison with normotensive pregnants.

These markers evinced positive correlation with respect to degree of severity of maternal and fetal outcomes.

Multifarious increase of TOTAL CYTOCHROME OXIDASE observed in PE cases, who developed eclampsia during the course of the study where as moderate increase noticed in preeclampsia cases who has not developed eclampsia compared to normal pregnants.

High levels of oxidative stress markers and mitochondrial stress markers cause the cellular damage and cause adverse fetal and maternal outcome.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Bell M. J. A Historical Overview of Preeclampsia-Eclampsia. Journal of Obstetric, Gynecologic & Neonatal Nursing; 2010:39(5).
2. Vousden, N, Lawley, E., Seed, P. T, Gidiri, M. F, Goudar S, Sandall J. Incidence of eclampsia and related complications across 10 low- and middle-resource geographical regions: Secondary analysis of a cluster randomised controlled trial. PLOS Medicine;2019: 16(3).
3. Aouache R, Biquard L, Vaiman D, Miralles F. Oxidative Stress in Preeclampsia and Placental Diseases. International Journal of Molecular Sciences;2018: 19(5),
4. Raijmakers, M. T. M, Dechend, R, Poston L. Oxidative Stress and Preeclampsia: Rationale for Antioxidant Clinical Trials. Hypertension;2004: 44(4).
5. Lucca1 L D, Pancich Gallarreta F M, Gonçalves T D. Oxidative Stress Markers in Pregnant Women with Preeclampsia .*American Journal of Medical and Biological Research; 2015:3(68-73)*
6. MN Gowda V, AR A, L Krishna. Studies on oxidative stress in preeclampsia. Allied academies. July 12 2009.
7. Shete SA, Gupta R. The study of oxidative stress in normal pregnancy and preeclampsia. Acta Biomedica Scientica.2014;1(4):185-188.

8. J.TGohil, P.K Patel, Priyanka G. Evaluation of Oxidative Stress and Antioxidant Defence in Subjects of Preeclampsia. The journal of obstetrics &gynecology of India. Nov-Dec 2011;61(6):638-640.

9. LLURBA E, GRATACOS E, MARTIN-GALLAN P, CABERO L, DOMINGUEZ C. A Comprehensive Study Of Oxidative Stress And Antioxidant Status In Preeclampsia And Normal Pregnancy. Free Radical Biology & Medicine. 2004;37(4):557–570.

10. Koushik K, Satwika S, Placental ischemia modified albumin may be a marker of oxidative stress in preeclampsia. Scholars journal of applied medical sciences. 2016;4(1A):52-56.

11. Dikensoy E, Balat O, Pence S, Balat A, Cekman M, Yurekli M. The Changes of Plasma Malondialdehyde, Nitric Oxide, and Adrenomedullin Levels in Patients with Preeclampsia. Hypertension in Pregnancy. 2009;28:383–389.

12. Tug N, Celik H, Cikim G, Ozcelik O, Ayar A. The correlation between plasma homocysteine and malondialdehyde levels in preeclampsia. Neuroendocrinology. Dec 2003;24(6).

13. Necip I, Nevin I, Simsek M. The changes of trace elements, malondialdehyde levels and superoxide dismutase activities in pregnancy with or without preeclampsia. Clinical Biochemistry. 2002;35:393–397.

14. . Madazil A, Benian A, Aydin S, Uzun H, Tolun N. The plasma and placental levels of malondialdehyde, glutathione and superoxide dismutase in pre-eclampsia. Journal of Obstetrics and Gynaecology. 2002;22(5):477–480.

15. Gupta S, Agarwal A, Sharma RK. The Role of Placental Oxidative Stress and Lipid Peroxidation in Preeclampsia. Obstetrical and gynecological survey. 2005;60(12).

16. Shilpa AV, Zubaida PA, Rajalekshmi G. Changes in homocysteine levels during normal pregnancy and preeclampsia and its relation with oxidative stress. International Journal of Research in Medical Sciences. Jan 2017;5(1):330-334.
17. Atamer Y, Kocyigit Y, Yokus B, Atamer A, Erden CA. Lipid peroxidation, antioxidant defense, status of trace metals and leptin levels in preeclampsia. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2005;119:60–66.
18. . Madazli R, Benian A, Aydin S, Uzun H, Tolun N. The plasma and lacental levels of malondialdehyde, glutathione and superoxide dismutase in pre-eclampsia. Journal of Obstetrics and Gynaecology. 2002;22(5):477–480.
19. Hung T, Burton JG. Hypoxia and reoxygenation: a possible mechanism for placental oxidative stress in preeclampsia. Taiwanese J Obstet Gynecol. Sep 2006;45(3).
20. Mert I, Oruc SA, Yuksel S, Cakar SE, Buyukkagnıcı U, Karaer A, Danisman N. Role of oxidative stress in preeclampsia and intrauterine growth restriction. Journal of Obstetrics and Gynaecology Research. April 2012;38(4):658–664.
21. Vyakaranam1S, Bhongir1 A V, Patlolla1 D, and Chintapally2 R, Maternal serum ischemia modified albumin as a marker for hypertensive disorders of pregnancy: a pilot study .Int J Reprod Contracept ObstetGynecol. June 2015;4(3):611-616.
22. Dayanand C D,Bambrana V, Sivaraj N, Rani Inala M S. Is ischemia Modified Albumin is a Marker in Preeclampsia? A Case Control Study in Kolar Population-a South West of India. American journal of pharmacy and health research;2016:3(6).

23. . Liping H, Zehua W, Yongyu S. Reduced amount of TOTAL CYTOCHROME OXIDASE subunit I messenger RNA in placentas from pregnancies complicated by preeclampsia. Acta Obstet Gynecol Scand. 2004;83:144–148.
24. Many A, Hubel AC, Fisher JS, Roberts MJ, Zhou Y. Invasive Cytotrophoblasts Manifest Evidence of Oxidative Stress in Preeclampsia. American Journal of Pathology. Jan 2000;156(1).
25. Silver HM, Seebeck M, Carlson R. Comparison of total blood volume in normal, preeclamptic and non-proteinuric gestational hypertensive pregnancy by simultaneous measurement of red blood cell and plasma volumes. Am J Obstet Gynecol. 1998; 179:87.
26. Villar K, Say L, Gu¨lmezoglu AM, Merialdi M, Lindheimer MD, Betran AP, Piaggio G. Eclampsia and pre-eclampsia: a health problem for 2000 years. In: Critchley H, MacLean AB, Poston L, Walker JJ, eds. Preeclampsia.London: RCOG Press; 2003;189–207.
27. Brown MA, Lindheimer MD, de Swiet M, van Assche A, Moutquin JM.The classification and diagnosis of the hypertensive disorders of pregnancy:statement from the International Society for the Study of Hypertension in Pregnancy (ISSHP). Hypertens Pregnancy. 2001;20:IX-XIV.
28. Curtin WM, Weinstein L. A review of HELLP syndrome. J Perinatol. 1999;19:138–143.
29. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: Current concepts. Am J Obstet Gynecol 1998 ; 179:1359-1375.
30. P Baker, Broughton P. Screeing tests for PIH. Progress in obstetrics and

gynecology John Studd. 2012; 10:69-86.

31. Mohammad S, Mohamoud S. The clinical value of microtranferrinuria and microalbuminuria in the prediction of Preeclampsia. Clinical Chemistry and Laboratory medicine; 39(1):29-34.
32. Hypertension in pregnancy: diagnosis and management. NICE guidelines, June 2019.
33. Kristin H, Coopage, Sibai BM. Managment of preeclampsia remote from term. Postgradute Obstetrics and Gynaecology 2003; 23(14).
34. Roberts JM, Redman CWG. Pre-eclampsia: more than pregnancy induced hypertension. Lancet 1993;341:1447–51.
35. Dekker GA. Etiology and pathophysiology of preeclampsia. Zentralbl Gynakol 1994;116:57–60.
36. Roberts JM, Cooper DW. Pathogenesis and genetics of preeclampsia. Lancet 2001; 357:53–56.
37. Kauma S, Takacs P, Scordalakes C, Walsh S. Increased endothelial monocyte chemoattractant protein-1 and interleukin-8 in preeclampsia. Obstet Gynecol 2002; 100:706–714.
38. Serdar Z, Gur E, Develioglu O, Colakogullari M. Placental and desidual lipid peroxidation and antioxidant defenses in preeclampsia lipid peroxidation in preecclampsia. Pathophysiology 2002; 9:21–25.
39. Kumar CA, Das UN. Lipid peroxides, antioxidants and nitric oxide in patients with preeclampsia and essential hypertension. Med Sci Monit 2000; 6:901–907.
40. Sikkema JM, Van Rijn BB, Franx A, et al. Placental superoxide is increased in

preeclampsia. Placenta 2001; 22:304–308.

41. Anwaruddin S, Januzzi JL, Baggish AL et al. Ischemia modified albumin improves the usefulness of standard cardiac biomarkers for the diagnosis of myocardial ischemia in the emergency department setting. Am J ClinPathol 2005; 123:140-15.
42. Roy D, Quiles J, Gaze DC et al. Role of reactive oxygen species on the formation of the novel diagnostic marker ischemia modified albumin. Heart 2006; 92:113-14.
43. Gidenne S, Ceppa F, Fontan E et al. Analytical performance of the albumin cobalt binding (ACB) test on the cobas MIRA Plus analyzer. ClinChem Lab Med 2004; 42:455-61.
44. Bar-Or, D, Lau E, Winkler JV. A novel assay for cobalt-albumin binding and its potential as a marker for myocardial ischemia-a preliminary report. J Emerg MED. 2000; 19(4): 311-15.
45. Vatish M, Harpal SR, Grammatopoulos KD. Hormonal regulation of placental nitric oxide and pathogenesis of preeclampsia. Trends Mol Med 2006; 12:223–233.
46. Kilicdag EB, Ay G, Çelik A, Ustundag B. Oxidant–antioxidant system changes relative to placental-umbilical pathology in patients with preeclampsia. Hypertens Preg 2005; 24:147–157.
47. Forest, J.C., Masse, J., Moutquin, J.M., and Radouco-Thomas, M., 1989, Preeclampsia:physiopathology and prospects for early detection, Clin Biochem , 22, 483-489.
48. Hubel, C.A., 1999, Oxidative stress in the pathogenesis of preeclampsia, Proc Soc Exp Biol Med, 222, 222-235.American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy.

Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122: 1122–1131.

49. Buchbinder A, Sibai BM, Caritis S et al. Adverse perinatal outcomes are significantly higher in severe gestational hypertension than in mild preeclampsia. Am J Obstet Gynecol 2002; 186: 66–71.
50. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol 2003; 102: 181–192.
51. Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. Am J Obstet Gynecol 2009; 200: 481. e1–481. e7.
52. Aoki S, Toma R, Kurasawa K, Okuda M, Takahashi T, Hirahara F. Expectant management of severe preeclampsia with severe fetal growth restriction in the second trimester. Pregnancy Hypertens 2014; 4: 81–86.
53. Cicero AF, Degli Esposti D, Immordino V et al. Independent determinants of maternal and fetal outcomes in a sample of pregnant outpatients with normal blood pressure, chronic hypertension, gestational hypertension, and preeclampsia.J Clin Hypertens 2015; 17: 777–782.

ANNEXURES

ANNEXURES

CASE PROFORMA

Name- UHID NO :

Age- IP NO :

Address

Occupation Husband's name :

Education Occupation :

Socioeconomic status Education :

HISTORY

H/O Amenorrhea yes/no

CHIEF COMPLAINTS

H/o bleeding /PV spotting yes/no

H/o pain abdomen yes/no

H/o increased BP readings yes/no

HISTORY OF PRESENT PREGNANCY

BOOKED/UNBOOKED

TRIMESTER1

TRIMESTER2

TRIMESTER3

OBSTETRIC HISTORY

Married life CM/NCM

G P L D A

OUT COME OF PREVIOUS PREGNANCY

LAST DELIVERY

MENSTRUAL HISTORY

Age of menarche

Past menstrual cycles: regular/irregular

duration of flow heavy/mod/less

Dysmenorrhea :

Last menstrual period :

Expected date of delivery :

Gestational age

PAST HISTORY

Previous history of placenta previa : yes/no

H/o Hypertension : yes/no

H/o Diabetes : yes/no

Past history of medical illness/blood transfusion/ thyroid disorders/ cardiac disorders/ surgeries/bleeding disorders

FAMILY HISTORY

PERSONAL HISTORY

Habits: smoking: alcohol: others:

RISK FACTORS

AGE

PARITY

INFECTIONS

MULTIFETAL GESTATION

PREVIOUS LSCS

PREVIOUS PLACENTA PREVIA

PRIOR CURATTAGE/SPONTANEOUS ABORTION/MTP

INTRA UTERINE SURGERIES

HABITS -SMOKING/COCAINE/ALCOHOL

SOCIOECONOMIC STATUS

PHYSICAL EXAMINATION

Concious or not :

Height :

Weight :

BMI :

Temperature :

Pulse

Rate :

volume :

Blood pressure :

Pallor +/-

Icterus +/-

Edema +/-

B/L Breast,spine,thyroid :

R/S: CVS:

P/A:

Uterine height :

Uterine contraction :

Uterus,tense &tenderness :

Presentation :

Position :

Engaged or unengaged :

P/S:

ANTENATAL COMPLICATIONS

PROVISIONAL DIAGNOSIS :

Hb: PCV:

Blood grouping &RH typing :

Urine -albumin :

Sugar :

microscopy :

Other investigations :

Obstetric Ultrasonography :

Obstetric Doppler study :

Non Stress Test :

TREATMENT:

Mode of delivery: Vaginal/Caesarean section

Retroplacental clot : +/-

Placental pathology

Maternal outcome:

Postpartum haemorrhage: yes/no

Need for blood or blood components transfusion: Yes /no

Disseminated intravascular coagulopathy : yes/no

Renal failure : yes/no

ICU admission :yes/no

Puerperal complications

Death : yes/no

Fetal outcome:Preterm/term/IUGR

Congenital anomolies

Live born/still born/macerated

Sex :

Birth weight :

Apgar score :

If live born

mother side

NICU care

Stay in NICU

Mother side

Condition on discharge:

Complications

ANTENATAL

INTRANATAL

POSTNATAL

PATIENT INFORMATION SHEET

Study title: CORRELATION OF OXIDATIVE AND MITOCHONDRIAL STRESS MARKERS IN NORMAL PREGNANCY AND IN PREECLAPMSIA AND WITH ITS FOETAL AND MATERNAL OUTCOME.

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Details- Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or from a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

Patients who are of clinically proven preeclampsia cases admitted to OBG department of R L Jalappa hospital attached to Sri Devaraj Urs medical college are recruited in the study after obtaining patient information consent.

Similarly, the normotensive pregnant women at third trimester visiting OBG department will also be included in the study after obtaining the patient information consent.

5 ml of venous blood is collected from the study subjects for MDA, IMA & TOTAL CYTOCHROME OXIDASE levels estimation

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact patient's signature/thumb impression

Dr.Supriya.H.M

Post graduate, Department of obstetrics and Gynaecology

R L Jalappa hospital, Kolar .Phone no: 9986563307. Witness signature/thumb impression

ರೋಗಿಯ ಮಾಹಿತಿ ಪತ್ರ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ:-

ಕೋರಿ ಲೇಷನ್ ಆಕ್ಸಿಡೇಟಿವ್ ಅಂಡ್ ಮೈಟೋಕಾಂಡ್ರಿಯಲ್ ಸ್ಟೆಸ್ ಮಾರ್ಕರ್ಸ್ ಪ್ರಿಎಕ್ಲಾಂಷಿಯ ಅಂಡ್ ಇನ್ ನಾರ್ಮಲ್ ಪ್ರಗ್ನೆನ್ಸಿ ವಿತ್ ಫೀಟಲ್ ಅಂಡ್ ಮೆಟರ್‌ನಲ್ ಔಟ್‌ಕಮ್

ಸಂಸ್ಥೆ ಹೆಸರು: ಶ್ರೀ ದೇವರಾಜ್‌ಅರಸ್ ವೈದ್ಯಕೀಯ ಮಹಾವಿದ್ಯಾಲಯ, ಆರ್,ಎಲ್, ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಟಮಕ, ಕೋಲಾರ

ಶ್ರೀ/ಶ್ರೀಮತಿ ಆದ ನಾನು ಈ ಮೇಲಿನ ಸಂಶೋಧನ ವಿಷಯದ ಬಗ್ಗೆ ನನಗೆ ಅರ್ಥವಾಗುವ'ರೀತಿಯಲ್ಲಿ ನನ್ನದೇ ಭಾಷೆಯಲ್ಲಿ ತಿಳಿಸಿರುತ್ತಾರೆ. ಈ ಸಂಶೋಧನಾ ವಿಷಯದಲ್ಲಿ ನಾನು ಒಬ್ಬ ವಿಷಯಿಯಾಗಿ ಭಾಗವಹಿಸಲು ನನ್ನ ಸಂಪೂರ್ಣವಾಗಿ ಒಪ್ಪಿಗ'ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ಉದ್ದೇಶವನ್ನು ಪೂರ್ಣವಾಗಿ ಅರಿತಿರುತ್ತೇನೆ. ಈ ಸಂಶೋಧನೆಗೆ ನನ್ನಿಂದ ಯಾವುದೇ ಆರ್ಥಿಕತೆಯ ಅವಶ್ಯಕತೆ ಇರುವುದಿಲ್ಲ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಸಹಕಾರವನ್ನು ಹಿಂಪಡೆದು ಈ ಸಂಶೋಧನೆಯಿಂದ ಹೊರಹೋಗುವ ಹಕ್ಕನ್ನು ಹೊಂದಿರುತ್ತೇನೆ. ಇದರಿಂದ ನನ್ನ ಚಿಕಿತ್ಸೆಗೆ ಯಾವುದೇ ರೀತಿಯ ತೊಂದರೆಯಾಗುವುದಿಲ್ಲ. ಮುಖ್ಯವಾಗಿ ನನ್ನಿಂದ ಪಡೆದ ಈ ಮಾಹಿತಿಯು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಸೀಮಿತವಾಗಿರುತ್ತದೆ. ಮತ್ತು ಈ ಮಾಹಿತಿಯು ಎಲ್ಲೂ ಸೋರಿಕೆಯಾಗದಂತೆ ಎಚ್ಚರಿಕೆ ವಹಿಸುವುದಾಗಿ ತಿಳಿವಳಿಕೆ ನೀಡಿರುತ್ತಾರೆಂದು ನಾನು ದೃಡಪಡಿಸಿಕೊಂಡು ಒಪ್ಪಿಗೆ ನೀಡಿರುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ/ ಸಾಕ್ಷಿ ಸಹಿ. ಸಂಶೋಧಕನ ಸಹಿ

ಬೆರಳಚ್ಚು.

PATIENT CONSENT FORM

CORRELATION OF OXIDATIVE AND MITOCHONDRIAL STRESS MARKERS IN NORMAL PREGNANCY AND IN PREECLAPMSIA WITH THE FOETAL & MATERNAL OUTCOME.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I have understood that I have the right to refuse consent or withdraw it at any time during the study and this will not affect my treatment in any way.
I consent voluntarily to participate in this study

Name of Participant_____

Signature/ thumb print of Participant _____

Date _____

Statement by the researcher/person taking consent:

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 that the following will be done: 5 ml venous blood sample taken for measureme:nt of **MDA(malondialdehyde)**, **IMA(ischemia modified albumin)** & **TOTAL CYTOCHROME OXIDASE** levels**.**

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 correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Name of Researcher/person taking the consent: Dr. Supriya.H.M

Signature of Researcher /person taking the consent_____

Date _____

Name and Address of Principal Investigator:

Dr.SUPRIYA.H.M

R.L Jalappa Hospital

Tamaka, Kolar.

ರೋಗಿಯ ಒಪ್ಪಿಗೆ / ಸಮ್ಮತಿ ಪತ್ರ

ಸಂಸ್ಥೆ ಹೆಸರು: ಶ್ರೀ ದೇವರಾಜ್‌ಅರಸ್ ವೈದ್ಯಕೀಯ ಮಹಾವಿದ್ಯಾಲಯ, ಆರ್,ಎಲ್, ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಟಮಕ, ಕೋಲಾರ

ಸಂಶೋಧಕರ / ಅಧ್ಯಯನ ಮಾಡುವವರ ಹೆಸರು – ಡಾ. ಸುಪ್ರಿಯ.ಎಚ್.ಎಮ್

ಮಾರ್ಗದರ್ಶಿಯ ಹೆಸರು: ಡಾ. ಶೀಲಾ.ಎಸ್.ಆರ್

ಅಧ್ಯಯನದ ಶೀಷೀಕೆ / ಸಂಶೋಧನೆಯ ಹೆಸರು: ಕೋರಿ ಲೇಷನ್ ಆಕ್ಸಿಡೇಟಿವ್ ಅಂಡ್ ಮೈಟೋಕಾಂಡ್ರಿಯಲ್ ಸ್ಟ್ರೆಸ್ ಮಾರ್ಕರ್ಸ್ ಪ್ರಿಎಕ್ಲಾಂಷಿಯ ಅಂಡ್ ಇನ್ ನಾರ್ಮಲ್ ಪ್ರಗ್ನೆನ್ಸಿ ವಿತ್ ಫೀಟಲ್ ಅಂಡ್ ಮೆಟರ್‌ನಲ್ ಔಟ್‌ಕಮ್

ಭಾಗವಹಿಸುವವರ ಹೆಸರು /ತೀರ್ಮಾನ ತೆಗೆದುಕೊಳ್ಳುವವರ ಹೆಸರು:_____

ಮೇಲೆ ಕಾಣಿಸಿದ ಸಂಶೋಧಕರುತಾವು ನಡೆಸುವಅಧ್ಯಯನ/ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೋಳ್ಳುವಂತೆ/ ಭಾಗವಹಿಸುವಂತೆ ನನ್ನನ್ನು ಆಹ್ವಾನಿಸಿದ್ದಾರೆ. ನನಗೆ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ಚಿಕಿತ್ಸೆಯ ಕ್ರಮ, ಮಾಡಬೇಕಾದ ಪರೀಕ್ಷೆಗಳು, ಪಡೆಯಬೇಕಾದ ರಕ್ತ ಮುಂತಾದ ವಿವರಗಳನ್ನು ಮನಮುಟ್ಟುವಂತೆ ತಿಳಿಸಿದ್ದಾರೆ. ಇದರಿಂದ ಅಡ್ಡ ಪರಿಣಾಮಗಳು ಆಗುವುದಿಲ್ಲವೆಂದೂ ಯಾವುದೇ ಪರೀಕ್ಷೆಗೆ ಯಾವ ರೀತಿಯ ವೆಚ್ಚವೂ ಆಗುವುದಿಲ್ಲವೆಂದೂ ತಿಳಿಸಿದ್ದಾರೆ.

ಈ ಮಾಹಿತಿಯನ್ನು ಓದಿ / ತಿಳಿದು ಮತ್ತು ಹಲವಾರು ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಿ ಸಮಂಜಸ ಉತ್ತರ ಪಡೆದಿದ್ದೇನೆ ಹಾಗೂ ನಾನು ಈ ಅಧ್ಯಯನದಿಂದ ಯಾವಾಗ ಬೇಕಾದರೂ ನಿರ್ಗಮಿಸಬಹುದೆಂದು, ಹಿಂತೆಗೆಯ ಬಹುದೆಂದೂ ಸಂಶೋಧಕರು ನನಗೆ ವಿವರಿಸಿದ್ದಾರೆ.

ಆದ್ದರಿಂದ ಈ ಕೆಳಗೆ ಸಹಿ ಮಾಡಿರುವ ನಾನು ಈ ಅಧ್ಯಯನ / ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಸ್ವಇಚ್ಚೆಯಿಂದ ಒಪ್ಪಿರುತ್ತೇನೆ ಮತ್ತು ನನ್ನ ಸ್ವಂತ ವಿವರಗಳನ್ನು ಸಂಗ್ರಹಿಸಲು ಹಾಗೂ ಬೇಕಾದ್ದಕ್ಕೆ ಬಳಸಿಕೊಳ್ಳಲು ಅನುಮತಿ ನೀಡಿರುತ್ತೇನೆ. ನೀವು ತಿಳಿಸಿದಂತೆ ನನ್ನ ಮಾಹಿತಿ ಗೋಪ್ಯವಾಗಿರಬೇಕೆಂದೂ ತಿಳಿಸಲು ಬಯಸುತ್ತೇನೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವ ನನಗೆ ಯಾವುದೆರೀತಿ ಹಣ ನೀಡಲಾಗುವುದಿಲ್ಲ ಎಂಬುದನ್ನು ಅರಿತಿದ್ದೇನೆ.

ಭಾಗವಹಿಸುವವರ ಹೆಸರು/ಸಹಿ/ಹೆಬ್ಬೆಟ್ಟು

ಸಾಕ್ಷಿಯ ಹೆಸರು

ದಿನಾಂಕ:

KEY TO MASTER CHART

INDICATIONS FOR LSCS

1. FETAL DISTRESS
2. OLIGOHYDRAMNIOS
3. MATERNAL DESIRE
4. PREVIOUS LSCS
5. IUGR WITH DOPPLER CHANGES
6. IUGR WITHOUT DOPPLER CHANGES
7. FAILED INDUCTION
8. OLIGOHYDRAMNIOS
9. ANTEPARTUM ECLAMPSIA WITH UNFAVOURABLE CERVIX
10. CONTRACTED PELVIS
11. CEPHALOPELVIC DISPROPORTION
12. BREECH PRESENTATION
13. IMMINENT ECLAMPSIA
14. ABRUPTIO PLACENTA

NICU (ADMISSION CONCERNS)

1. RESPIRATORY DISTRESS
2. PREMATURITY
3. SMALL FOR GESTATIONAL AGE

APGAR SCORE

1. 1" 7/10, 5" 9/10
2. ABNORMAL APGAR

CAUSE OF PNM

1. RESPIRATORY FAILURE- SECONDARY TO PREMATURITY
2. ABRUPTIO PLACENTA
3. SEPSIS

IUGR

1. PRESENT
2. ABSENT

DOPPLER CHANGES

1. PRESENT
2. ABSENT

ABBREVATIONS

B/R

B-BOOKED

R- REFERRED

VAGINAL DELIVERY

Y- YES

LSCS

Y-YES

FETAL OUTCOME

IUD- INTRA UTERINE FETAL DEMISE

AGA- AVERAGE FOR GESTATIONAL AGE

SGA- SMALL FOR GESTATIONAL AGE(IUGR)

MOTHER SIDE

1. YES
2. NO

PERINATAL MORTALITY

Y- YES

N- NO

CAUSE OF PNM

1. RESPIRATORY FAILURE- SECONDARY TO PREMATURITY
2. ABRUPTIO PLACENTA
3. SEPSIS

MATERNAL OUTCOME

N- NORMAL

PPH(POST PARTUM HEMORRHAGE)

Y- YES

N- NO

NEED OF BLOOD PRODUCTS

Y- YES

N- NO

ICU ADMISSION

Y- YES

N- NO

ABRUPTIO

PLACENTA

Y- YES

N- NO

HELLP SYNDROME

Y- YES (PARTIAL)

N- NO

ECLAMPSIA

Y- YES

N- NO

ANTIHYPERTENSIVES(REQUIREMENT)

Y- YES

N- NO

MATERNAL MORTALITY

Y- YES

N- NO

SL NO	UHID NO	NAME	Group	AGE	A/R	OBSTETRIC INDEX	GESTATIONAL AGE	SBP	DBP	IUGR	DOPPLER CHANGES	URINE ALBUMIN	VAGINAL DELIVERY	LSCS	INDICATION FOR LSCS	FETAL OUTCOME	APGAR SCORE	NICU ADMISSION (NO OF DAYS)	BIRTH WEIGHT(KG)	NICU(REASON)	MOTHER SIDE	PERINATAL MORTALITY	CAUSE OF PNM	MATERNAL OUTCOME	PPH	NEED OF BLOOD PRODUCTS	ICU ADMISSION	ABRUPTIO PLACENTA	HELLP SYNDROME	ECLAMPSIA	ECLAMPSIA	ANTIHYPERTENSIVES	MATERNAL MORTALITY	OTHERS	MDA	IMA	CYTOCHROME OXIDASE
1	700597	MEENAKSHI	PE	22	R	G2P1L1	32WK+4	140	90			2+	Y			LIVE			2																	0.952	1.541	8.755
2	693481	SHILPA. N	PE	23	R	PRIMI	38WK+1D	140	100			TRACES		Y	1	TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N							0.421	1.021	2.605
3	680303	REENA KOUSER	PE	23	R	PRIMI	39WK+2D	170	100			2+		Y	2	TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N							0.412	1.053	3.212
4	612261	LAKSHMIDEVAMMA	PE	30	R	PRIMI	35WK+3D	180	110			3+	Y			PRETERM	5*6/10	7	1.9	Y- 1,2	N	N	N	N	N	N	Y	N	N	Y(COMPLETE)	N					0.816	1.702	7.95
5	593470	NAVYA.	PE	25	R	G2P1L1	28WK+1D	160	100			2+	Y			PRETERM	5*5/10	15	1.2	Y-1,2	N	Y			Y	N	N	N	N	N	Y	POST PARTUM ECLAMPSIA	Y	N		0.546	1.031	3.921
6	602227	JAMUNA	PE	27	R	PRIMI	38WK	150	98			1+		Y	3	TERM AGA	5*9/10		2.88		Y	N	N	N	N	N	N	N	N	N						0.345	0.974	3.836
7	650990	ARUNA	PE	22	R	PRIMI	38WK+4D	150	90	1		2+		Y	2	TERM SCA	5*7/10	5	2.1	Y-3	N	N	N	N	N	N	N	N	N	Y	POST PARTUM ECLAMPSIA	Y	N	OLIGOHYDRAMNIOS	0.647	1.031	4.92
8	615913	SUSHEELA	PE	26	R	G2P1L1	40WK	140	100			2+		Y	4	TERM AGA	5*9/10		3.2		Y	N	N	N	N	N	Y	N	N	Y					APH	0.904	1.731	6.77
9	617917	LATHA	PE	27	R	G2P1L1	35WK+2D	150	110	1		1 2+		Y	6	PRETERM	5*6/10	8	2	Y-2	N	N	N	N	N	N	N	N	N	N						0.955	1.604	5.6
10	613184	UMA	PE	24	R	G2P1L1	38WK+4D	140	98	1		1 2+	Y			TERM SGA	5*8/10	4	2.4	Y- 1,3	N	N	N	N	N	N	N	N	N	N						0.302	0.642	2.17
11	626126	GAYITHRI	PE	21	R	PRIMI	37WK+3D	150	100			1+	Y			TERM AGA	5*9/10		2.8		Y	N	N	N	N	N	N	N	N	N						0.806	1.506	6.121
12	536397	ARUNA	PE	24	R	G1P1L1A1	38WK+3D	160	100			1+		Y	4	TERM AGA	5*9/10		2.87		Y	N	N	N	N	N	N	N	N	N						0.751	1.031	5.775
13	698357	LAKSHMIDEVI	PE	28	R	G3P1L1A1	36WK+2D	170	110	1		2+		Y	4, 13	IUGR	5*7/10	5	1.94	Y-2,3	N	N	N	N	N	N	N	N	N	Y	IMMINENT ECLAMPSIA	Y	N		0.697	0.561	4.15
14	649941	CHETANA	PE	28	R	PRIMI	38WK+3D	150	100			1+		Y	7	TERM AGA	5*8/10		2.88		Y	N	N	N	N	N	N	N	N	N						0.408	1.031	5.91
15	698885	NASEEMA TAJ	PE	24	R	G3P2L2	32WK+2D	130	90	1		2+	Y			IUD			1.9		Y				Y	Y	N	N	N						0.792	1.395	6.8
16	615933	SHAHEEDA	PE	24	R	PRIMI	37WK+6D	140	100			1+	Y			TERM AGA	5*8/10		2.98		Y	N	N	N	N	N	N	N	N	N						0.496	0.936	5.81
17	617137	SUJATHAMMA	PE	20	R	PRIMI	40WK	180	110			2+	Y			TERM AGA	5*8/10		3.11		Y	N	N	N	N	N	N	N	N	N	H(ANEMIA)	N	N	N	ANEMIA	0.605	1.631	8.365
18	621614	NAGINA	PE	25	R	G2A1	29WK+5D	144	104			2+	Y			IUD			1.1																	0.945	1.421	8.961
19	685920	SAVITHA	PE	31	R	G2P1L1	38WK+6	150	100			1+		Y	4	TERM AGA	5*9/10		3		Y	N	N	N	N	N	N	N	N	N						0.263	0.318	0.99
20	662863	SHABREEN BEGUM	PE	31	R	PRIMI	38WK+6D	160	100			1+		Y	8	TERM AGA	5*9/10		3.01		N	N	N	N	N	N	N	N	N	N					OLIGOHYDRAMNIOS	0.306	0.411	2.605
21	701639	KURESHI SALMA	PE	26	R	G3P2L2	27WK+1	170	100			1+	Y			IUD			1.01						Y	N	N	N	N	N					ANEMIA	0.542	1.021	5.154
22	694215	REENA	PE	21	R	PRIMI	35WK	140	90	1		1 2+		Y	5	IUGR	5*6/10		2.2		Y	N	N	N	N	N	N	N	N	N						0.422	1.003	6.375
23	670643	SUVARNA	PE	26	R	PRIMI	39WK+6	170	110			3+		Y	9	PRETERM	5*7/10	5	1.9	Y-2	N	N	N	N	N	N	N	N	N	Y	ANTEPARTUM ECLAMPSIA	Y	N		0.421	1.003	6.06
24	655768	SWETHA	PE	22	R	PRIMI	39WK	170	110			1 2+		Y	6	TERM SGA	5*7/10	4	2.3	Y-3	N	N	N	N	N	N	N	N	N	Y	INTRAPARTUM ECLAMPSIA	Y	N	PRES	0.752	0.911	8.281
25	655753	AYESHA	PE	22	R	PRIMI	35WK+1D	170	110	1		3+		Y	6	IUGR	5*7/10	7	1.72	Y-3	N	N	N	N	N	N	N	N	N	Y	IMMINENT ECLAMPSIA	Y	N	PRES	0.543	0.428	6.365
26	653365	SHOBHA	PE	30	R	PRIMI	37WK+6D	150	100			2+		Y	10	TERM AGA	5*9/10		2.8		Y	N	N	N	N	N	N	N	N	N						0.564	0.603	4.127
27	666629	SWARNA	PE	27	R	G2P1L1	39WK+4D	160	100			1+		Y	4	TERM AGA	5*9/10		3.4		Y	N	N	N	N	N	N	N	N	N						0.725	1.003	5.91
28	558587	VASANTHAMMA	PE	25	R	PRIMI	37WK+5D	150	100	1		1 2+		Y	3	TERM SGA	5*6/10	3	2.1	Y-3	N	N	N	N	N	N	N	N	N	N						0.775	1.025	7.162
29	655768	SHWETHA	PE	22	R	PRIMI	39WK	160	110	1		1 3+		Y	5	TERM SGA	5*6/10	5	2.2	Y-1,3	N	N	N	N	Y	Y	N	N	N	N						0.534	0.921	5.1
30	655793	YALLAMMA	PE	22	R	G2P1L1	40WK	150	100			1+	Y			TERM AGA	5*8/10		3.4		Y	N	N	N	N	N	N	N	N	N						0.689	1.029	7.25
31	621614	NAZEEMA	PE	24	R	PRIMI	38WK	130	110	1		1 3+	Y			PRETERM	5*8/10	12	1.6	Y-1,2	N	Y	1,3	N	N	Y	Y	N	N	N				ANEMIA	0.753	1.201	8.12
32	248479	SHARADAMMA	PE	34	R	G4P3L3	36WK+1D	170	104			2+	Y			PRETERM	5*6/10	4	1.92	Y-1,2	N	N	N	N	Y	Y	Y	Y	Y	Y(PARTIAL)	Y				ANEMIA	0.611	0.921	5.035
33	629542	PAVITHRA	PE	31	R	G2P1L1	35WK	170	110	1		1 3+		Y	4	PRETERM	5*6/10	8	1.86	Y-2	N	N	N	N	N	N	N	N	N	N						0.474	0.817	3.281
34	598823	LAKSHMI	PE	19	R	PRIMI	36WK	160	100	1		3+		Y	1	PRETERM	5*6/10	3	2	Y-2	N	N	N	N	N	N	Y	N	N	Y	ANTEPARTUM ECLAMPSIA	Y	N		0.905	1.081	7.026
35	602575	PRIYANKA	PE	20	R	PRIMI	30WK	170	110	1		1 2+	Y			IUD	IUD		2.8		N	N	N	N	Y	Y	Y	Y	Y	Y(COMPLETE)	Y	ANTEPARTUM ECLAMPSIA	Y	N	PRES	0.762	0.918	8.591
36	680521	SUREKHA	PE	27	R	G2P1L1	39WK+4D	160	100			2+	Y			TERM AGA	5*8/10	7	3.1		Y	N	N	N	N	N	N	N	N	N						0.419	0.301	3.065
37	679822	PAVITHRA	PE	21	R	PRIMI	37WK+2D	130	100	1		1+		Y	14	TERM AGA	5*9/10		2.5		Y	N	N	N	N	N	N	Y	N	N				ANEMIA	0.418	0.428	8.29
38	657460	SUMAYA SULTANA	PE	19	R	PRIMI	40WK	160	114			2+		Y	13	TERM AGA	5*9/10		3.4		Y	N	N	N	N	N	N	N	N	N	IMMINENT ECLAMPSIA	Y	N		0.456	0.549	4.926
39	624225	PREMA	PE	25	R	PRIMI	32WK+1D	180	120	1		1 2+		Y	1	PRETERM	5*6/10	7	1.5	Y-1,2	N	N	N	N	Y	Y	Y	Y	Y	Y(PARTIAL)	N					0.527	0.511	5.127
40	685250	PAVANI	PE	19	R	PRIMI	36WK+1D	160	110	1		2+		Y	5,13	PRETERM	5*6/10	6	2.1	Y-2	N	N	N	N	N	N	N	N	N	N	IMMINENT ECLAMPSIA	Y	N		0.528	0.731	4.329
41	701972	BHAVYASHREE	PE	26	R	PRIMI	40WK	150	110			2+		Y	1	TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N						0.391	0.453	2.605
42	700304	LATHA.	N	30	R	G2P1L1	34WK	120	80			NIL	Y			TERM AGA	5*9/10		3.2		Y	N	N	N	N	N	N	N	N	N						0.347	0.328	3.906
43	622104	PALLAVI.N	N	20	R	PRIMI	40WK	110	70			NIL	Y			TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N						0.288	0.288	1.83
44	657123	KAVITHA	N	23	R	PRIMI	40WK	110	70			NIL		Y	1	TERM AGA	5*9/10		3		Y	N	N	N	N	N	N	N	N	N						0.321	0.459	1.972
45	629986	ANITHA.	N	26	R	G2P1L1	39WK+2D	120	84	1		NIL		Y	5	TERM SGA	5*9/10	2	2.9	Y-1	N	N	N	N	Y	Y	Y	Y	Y	N				ANEMIA	0.217	0.391	0.625
46	698943	ASHWINI	N	26	R	PRIMI	36WK+3D	110	80			NIL		Y	3	PRETERM	5*9/10	3	2.4	Y-1	N	N	N	N	Y	N	N	N	N	N				ANEMIA	0.362	0.491	1.235
47	659962	RAMYA	N	28	R	G2P1L0	39+6D	120	80			NIL		Y	3	TERM AGA	5*9/10		2.7		Y	N	N	N	N	N	N	N	N	N						0.254	0.136	1.565
48	695015	JYOTHI PRIYA	N	31	R	PRIMI	38WK+5D	110	80			NIL	Y			TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.257	0.191	1.053
49	683060	REKHA	N	28	R	G4P1L1A2	37WK+2D	120	70			NIL		Y	4	TERM AGA	5*9/10		2.6		Y	N	N	N	N	N	N	N	N	N						0.543	0.321	2.415
50	683333	SUSHEELA	N	32	R	G3P1L1A1	39WK+1D	120	70			NIL		Y	4	TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.699	0.501	3.216
51	649595	MAMATHA	N	30	R	G2P1L1	37WK+5D	110	70			NIL		Y	4	TERM AGA	5*9/10		2.5		Y	N	N	N	N	N	N	N	N	N						0.318	0.283	2.149
52	678765	SOWMYA	N	28	R	G3A2	39WK+2D	120	70			NIL	Y			TERM AGA	5*9/10		2.8		Y	N	N	N	N	N	N	N	N	N						0.213	0.125	2.225
53	631443	SAJIDA KHANUM	N	28	R	PRIMI	40WK	120	70			NIL		Y	10	TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N				PROM	0.453	0.291	3.815
54	701626	SUMITHRA	N	20	R	PRIMI	39WK+3D	120	70			NIL		Y	1	TERM AGA	5*9/10		2.6		Y	N	N	N	N	N	N	N	N	N						0.299	0.191	1.485
55	622123	ASMA	N	25	R	PRIMI	40WK	120	80			NIL		Y	1,11	TERM AGA	5*9/10		3.5		Y	N	N	N	N	N	N	N	N	N						0.545	0.491	1.68
56	651393	ASHWINI	N	26	R	PRIMI	40WK	130	80			NIL		Y	11	TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N						0.235	0.328	-0.635
57	693546	GEETHA	N	25	R	PRIMI	39WK+5D	110	80			NIL	Y			TERM AGA	5*9/10		3		Y	N	N	N	N	N	N	N	N	N						0.432	0.431	2.31
58	594345	VENKATA LAKSHMI	N	29	R	G2P1L1	38WK+5D	110	70			NIL		Y	12	TERM AGA	5*9/10		2.7		Y	N	N	N	N	N	N	N	N	N						0.421	0.212	3.115
59	643123	SWATHI	N	19	R	PRIMI	40WK	120	80			NIL		Y	11	TERM AGA	5*9/10		3		Y	N	N	N	N	N	N	N	N	N						0.327	0.312	1.715
60	682970	SHILPA	N	20	R	PRIMI	40WK	120	80			NIL		Y	12	TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.327	0.149	2.145
61	562222	USHA	N	25	R	G3P1L1A1	39WK	120	80			NIL		N		TERM AGA	5*9/10		2.6		Y	N	N	N	N	N	N	N	N	N						0.358	0.271	2.49
62	629980	SANYA KUMARI	N	19	R	PRIMI	39WK+5D	110	80			NIL	Y			TERM AGA	5*9/10		2.8		Y	N	N	N	N	N	N	N	N	N						0.255	0.182	0.97
63	602903	BHARATHI	N	27	R	PRIMI	40WK	120	70			NIL		Y	1	TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.303	0.312	2.565
64	682212	LAVANYA	N	25	R	PRIMI	37WK+3D	110	70			NIL	Y			TERM AGA	5*9/10	1	3	Y(1)	N	N	N	N	N	N	N	N	N	N						0.371	0.301	2.93
65	631053	VASANTAMMA	N	31	R	PRIMI	39WK+5D	110	80			NIL	Y			TERM AGA	5*9/10		2.8		Y	N	N	N	N	N	N	N	N	N						0.367	0.311	1.974
66	685484	NOOR AHAMADI	N	27	R	G2P1L1	40WK	120	70			NIL	Y			TERM AGA	5*9/10		2.6		Y	N	N	N	N	N	N	N	N	N						0.413	0.438	2.138
67	611975	ROOPA	N	24	R	PRIMI	38WK+4D	120	70			NIL		Y	1	TERM AGA	5*9/10		2.7		Y	N	N	N	N	N	N	N	N	N						0.262	0.194	0.0749
68	604817	INDRAA	N	24	R	G2A1	39WK	130	70			NIL	Y			TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.271	0.158	0.665
69	618293	RAMYA	N	34	R	G3P2L2	39WK	120	70			NIL		Y	4	TERM AGA	5*9/10		2.4		Y	N	N	N	N	N	N	N	N	N						0.371	0.217	1.058
70	657890	VASANTHA KUMARI	N	34	R	G2P1L1	37WK+5D	110	70			NIL		Y	4	TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.405	0.519	2.84
71	657654	SANDHAYINI	N	22	R	G2P1L1	38WK+5D	111	70			NIL		Y	2	TERM AGA	5*9/10		3		Y	N	N	N	N	N	N	N	N	N						0.347	0.421	1.46
72	683742	RAMYA	N	21	R	PRIMI	40WK	120	80			NIL		Y	11	TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N						0.302	0.211	0.685
73	605628	VANITHA	N	29	R	G3P2L2	38W+5D	110	80			NIL	Y			TERM AGA	5*9/10		3.4		Y	N	N	N	N	N	N	N	N	N						0.278	0.154	2.012
74	600103	NETHRAVATHI	N	38	R	G3P1L1A1	40WK	120	80			NIL		Y	2	TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N						0.293	0.172	1.943
75	656619	AMARAVATHI	N	22	R	PRIMI	40WK	110	80			NIL	Y			TERM AGA	5*5/10	4	2.4	Y-1	N	N	N	N	Y	Y	N	N	N	N						0.305	0.196	2.109
76	699710	ASMA	N	23	R	G2P1L1	40WK	120	80			NIL	Y			TERM AGA	5*9/10		2.9		Y	N	N	N	N	N	N	N	N	N						0.271	0.215	1.075
77	610234	VAKALASHMI	N	22	R	G1P1L1A1	39WK+2D	110	80			NIL	Y			PRETERM	5*7/10	6	2.2	Y-1,2	N	N	N	N	N	N	N	N	N	N						0.453	0.429	-5.32
78	685469	VASANTHA KUMARI	N	34	R	G2P1L1	39WK+2D	120	70			NIL		Y	4	TERM AGA	5*9/10		2.6		Y	N	N	N	N	N	N	N	N	N						0.362	0.312	1.091
79	617089	GAYITHRI	N	24	R	G2A1	39WK+1D	120	70			NIL	Y			TERM AGA	5*9/10		2.5		Y	N	N	N	N	N	N	N	N	N						0.372	0.215	1.298
80	621764	SHILPA	N	23	R	G3P2L2	40WK	120	70			NIL	Y			TERM AGA	5*9/10		2.1		Y	N	N	N	N	N	N	N	N	N						0.472	0.329	1.121
81	692120	KALPANA	N	25	R	PRIMI	35WK+1D	110	80			NIL		Y	2	PRETERM	5*6/10	3	1.9	Y-1,2	N	N	N	N	N	N	N	N	N	N				PPROM	0.306	0.217	0.761
82	537946	USHA	N	24	R	G2P1L1	40WK	120	70			NIL	Y			TERM AGA	5*9/10		3.1		Y	N	N	N	N	N	N	N	N	N						0.202	0.139	0.665