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Accuracy of Serum Uric Acid in Predicting Complications of Pre-Eclampsia

Dr. Laila A. Elbeshti

Obstetric And Gynecology Doctor, Aljalla Maternity Hospital Tripoli Libya

ABSTRACT

Background: Pre-eclampsia is one of the largest causes of maternal and fetal mortality and morbidity. Hyper uricemia is often associated with pre-eclampsia.

Objective: to determine the accuracy with which serum uric acid predicts maternal and fetal complications in women with pre-eclampsia.

Patient & Methods: Case series study conducted in Aljalla hospital for obstetrics and gynecology during the year 2009 where 100 pregnant women with pre-eclampsia included and serum uric acid level measured and the maternal and fetal outcome determined to fill in a preformed case sheet, SPSS software was used to analyze the collected data.

Results: The mean serum uric acid was only significantly associated with sever hypertension (P=0. 0004) and insignificant with eclampsia (P=0. 376) and Abruptio placenta (P=0. 724). Maternal death (P=0. 051) was at border line due to small size of study group. And significantly associated with IUGR (P=0. 013) and prematurity (P=0.019).

Conclusion: Serum uric acid could be used as a sensitive indicator of maternal complications in women with preeclampsia (sever hypertension) and fetal complications (IUGR, prematurity).

KEYWORDS: Pre-eclampsia , serum uric acid, Tripoli Libya.

INTRODUCTION

PRE-ECLAMPSIA

Definition: -

Is described: as a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation [7].

It is a condition of hypertension associated with protein urea greater than 0.3 gm/L in a 24 hour urine collection or greater than 1gm/L in a random sample and generalized edema or pitting edema greater than + after 12 hour of rest in bed or weight gain at 5lb or more in one week or both after 20 weeks gestation [9].

Incidence: -

The incidence of pre-eclampsia is commonly cited to be 5 % although rather wide variations are reported. WHO estimates that worldwide over 100,000 women die from pre-eclampsia each year, also it increases the risk of iatrogenic prematurity and carries a significant health care implications in adult life, the offspring of affected pregnancies having an increased risk of hypertension, heart disease and diabetes mellitus [8].

Aetiology: -

The exact nature of the primary event in causing pre-eclampsia is not known. Significant progress has

been made in achieving an understanding of the Aetiology of this condition in recent decades.

The underlying cause appears to be reduced placental perfusion caused by abnormal placentation, leading to an increase fetal demand and the decreased ability of the maternal placental unit to supply the intervillous space. Factors are released into maternal circulation leading to endothelial dysfunction and microangiopatic haemolysis with associated inflammatory mediator release and neutrophil activation [8].

Other aetiological factors: -

Immunological factors: -

There is circumstantial evidence to support the theory that pre-eclampsia is immune mediated beginning in the early second trimester in women destined to develop pre-eclampsia have a significant lower proportion of helper T cell (Th1) compared with that of women who remain normotensive.

This Th1 / Th2 imbalance with Th2 dominance may be mediated by adenosine which is found in higher serum levels in pre-eclampsia compared with normotensive. The helper T lymphocytes secrete specific cytokines that promote implantation and their dysfunction may favor pre-eclampsia. In women with anticardiolipin antibodies placental abnormalities and pre-eclampsia develop more commonly [7].

Genetic factors: -

There is a possibility of polygenic inheritance also a number of single gene mutations have been studied in women with pre-eclampsia. Women homozygous for angiotensinogen gene variant T235 had higher incidence of pre-eclampsia and fetal growth restriction [7.]

Risk factors: -

General risk factors: -

Age: women over the age of 40 years have a double the risk of pre-eclampsia and this increased the risk exists for primiparous and multiparous women [4].

Obesity: increased BMI pre pregnancy or in early pregnancy increases the risk of pre-eclampsia and obesity (BMI≥30) is associated with an approximate doubling of the risk [4].

Genetic risk factors: -

Women whose mothers had pre-eclampsia have a20-25% risk of developing pre-eclampsia. In women with sisters with a history of pre-eclampsia, the risk may be as high as 35-40% [4].

Obstetric risk factors: [4].

- Primiparity (2-3 fold risk)
- Multiple pregnancy (2 fold risk for twins)
- Previous pre-eclampsia (7 fold risk)
- Long birth interval (2-3 fold if 10 years)
- Hydrops with large placenta.
- Hydatidiform mole.
- Triploidy (particularly association with very early onset (before 24 weeks gestation) pre-eclampsia.

Although pre-eclampsia is more common in primiparous women, it is the multiparous women with pre-eclampsia who develop more sever disease and have higher morbidity and mortality rate.

Medical risk factors: [4].

Pre-existing hypertension.

- Renal disease (even without functional renal impairment).
- Diabetes mellitus (pre-existing or gestational).

- Connective tissue disease.
- Inherited thrombophilia.

Pathogenesis: -

Vasospasmin:

Vascular constriction causes resistance and subsequent hypertension. At the same time cell damage causes interstitial leakage through which blood constituents including platelets and fibrinogen are deposited subendothelially. With diminished blood flow because of maldistribution, ischemia of the surrounding tissue would lead to necrosis, haemorrhage and other end-organ disturbances characteristics of the syndrome [7].

Endothelial cell activation:

Endothelial cell activation has become the centerpiece in the contemporary understanding of pathogenesis of pre-eclampsia. Unknown factors, likely from the placenta are secreted into the maternal circulation and provoke activation and dysfunction of the vascular endothelium. The clinical syndrome of pre-eclampsia is thought to result from these wide spread endothelial cell changes [7].

Increased pressor responses:

Normally pregnant women develop refractoriness to infused vasopressors. Women with early pre-eclampsia have increased vascular reactivity to infused nor epinephrine and angiotensin II, more over increased sensitivity to an angiotensin II. Patient who subsequently became hypertensive lost this refractoriness several weeks before the onset of hypertension [7.]

Prostaglandins:

Numbers of prostanoids are central to the pathophysiology of the pre-eclampsia syndrome, for example endothelial prostacyclin (PGI2) production is decreased in pre-eclampsia, at the same time thromboxan A2 secretion by platelets is increased and the prostacyclin: thromboxane A2 ratio decreased. The net result favors increased sensitivity to infused angiotensin II and ultimately vasoconstriction [7].

Nitric oxide:

Endothelial cells synthesize this potent vasodilator; it is also produced by fetal endothelium and is increased in response to pre-eclampsia, Diabetes mellitus and infection. Its production is increased in sever pre-eclampsia possibly as a compensatory mechanism for the increased synthesis and release of vasoconstrictors and platelets aggregating agents. These increased serum concentrations of nitric oxide in women with pre-eclampsia are likely the result of hypertension not the cause [7].

Endothelins (ET-1):

They are 21 amino acid peptides, they are potent vasoconstrictors, the placenta is not the source of increased ET-1 and it likely arises from systemic endothelial activation, it increases in normotensive women but women with pre-eclampsia have even higher levels [7].

Angiogenic factors:

Several glycosylated glycoproteins are selectively mitogenic for endothelial cells; two of these are vascular endothelial growth factor (VEGF) and placental growth factor (PLGF). Their secretion is increased throughout the normal pregnancy. They promote angiogenisis and induce nitric oxide and vasodilatory Prostaglandins. Paradoxically VEGF is increased in serum from women with pre-eclampsia but its bioavailability is decreased [7].

Pathophysiology: -

The entire multisystem clinical picture of pre-eclampsia can be explained in terms of dysfunction of the vascular endothelial cells.

Cardiovascular system:

Increased peripheral resistance leads to generalized vasospasm and hypertension. The intravascular compartment is reduced and endothelial damage leads to increased vascular permeability and oedema, this is accompanied by reduction in central venous and pulmonary wedge pressure [8].

Haematological system:

In the event of endothelial damage platelets adhere to the damaged area, in pre-eclampsia a reduction in the platelet count predates the clinical signs of the disease and may be due to an immunologically mediated consumption. Significant clotting abnormalities are rarely seen in the absence of thrombocytopenia. In terms of regulatory proteins, the level of antithrombin III, protein C and protein S fall in pre-eclampsia reflecting increased consumption [8].

Liver:

Vasoconstriction in the hepatic bed leads to peri-portal fibrin deposition, haemorrhage and hepato-cellular necrosis. This leads to: elevated liver enzyme levels, which may occur as part of haemolysis and low platelet count (HELLP) syndrome. Much more rarely hepatic infarction and rupture of the liver capsule can occur [8].

Kidney:

Renal function deteriorates in two stages; the first stage involves an impairment of tubular function reflected by a reduction in uric acid clearance. Later glomerular filtration becomes impaired and proteinurea of intermediate selectivity occurs. The characteristic renal lesion of pre-eclampsia is glomerular -endotheliosis- involves a combination of swelling of the glomerular endothelial cells and sub-endothelial fibrinoid deposits that encroach on and occlude the capillary lumen [8].

Cerebral effects:

Cerebral vasoconstriction leads to focal ischemia and abnormal electrical activity and thus triggers seizures. The principle post-mortem finding of women dying from or with eclampsia is haemorrhage. Blindness is a rare complication and may be retinal or cortical in origin [8].

Identifying those at risk:

Investigations

Tests to predict pre-eclampsia can be broadly divided into biophysical and biochemical [9].

Biophysical tests:

The most promising biophysical test is that of uterine artery Doppler. This is a relatively quick and inexpensive test that can be performed at a similar time to the anomaly scan. It has the advantage of identifying poor placental perfusion, which is fundamental to the disease process. There is a relatively high resistant circulation with a notch apparent in the uterine artery Doppler. Approximately one in five women who have abnormal Doppler at 20 weeks gestation will develop the eclampsia at 24 weeks gestation the prediction value is greater. Other biophysical tests such as isometric exercise testing and the roll over test have very poor predictive value [9].

Biochemical tests:

They are numerous Haematological and biochemical markers, which have been used to both predict and evaluate pre-eclampsia. Laboratory values are usually unrevealing in cases of mild pre-eclampsia but there are multiple findings in sever forms of the disease. Laboratory changes reflect the effects of the disease on the kidney, liver, feto-placental unit and in some cases the Haematological elements [9].

Full blood count:-

This may demonstrate raised haematocrit (indicating haemo-concentration) and thrombocytopenia (which

is an indicator of sever pre-eclampsia). Thrombocytopenia may also occur as a result of HELLP syndrome [9].

Renal function test: -

Glomerular filtration rate and Creatinine clearance decrease by 25% in women with pre-eclampsia [9].

Uric acid:-

Is a particularly sensitive measure of pre-eclampsia and perinatal outcome but it is only of clinical significance if the levels are increasing or are very high. However there is a high degree of overlap among the values found in normal pregnancy, mild pre-eclampsia, and sever pre-eclampsia [4].

Urine analysis: -

Proteinurea greater than 0.3gm/L in a 24 hour urine collection or greater than 1 gm/L in a random sample 9

Liver function test:

patients show: With mild pre-eclampsia a little or no alteration in hepatic enzyme level , But in sever pre-eclampsia marked increase serum GPT, SGOT and LDH are commonly found [9].

Hypoalbuminaemia.

Increased fibrinogen degradation products.

Fetal assessment: -

Early onset pre-eclampsia is particularly involved with placental insufficiency and more than half of babies born before 34 weeks gestation will be growth restricted (growth below 10th centile for gestational age). This also explains why abruption is more common, occurring in about 1:20 of these early onset cases. Fetal well being should always be carefully considered in all cases of pre-eclampsia and include a symphysio-fundal height assessment. At early gestations an ultrasound scan must be performed to assess fetal growth, and should include amniotic fluid index and umbilical artery Doppler waveforms [9] .

Management: -

Basic management objective for any pregnancy complicated by pre-eclampsia are:

1-termination of pregnancy with the least possible trauma to the mother and fetus.

2-birth of an infant, who subsequently thrives.

3- Complete restoration of health of the mother.

Antepartum hospital management: -

Hospitalization is considered at least initially for women with new onset hypertension specially if there is persistent or worsening hypertension. A systematic evaluation is instituted to include: detailed examination followed by daily scruting for clinical findings such as headache, visual disturbances, epigastric pain, and rapid weight gain- blood pressure readings in the sitting position with an appropriate size cuff every 4 hours except between mid night and morning – measurement of plasma or serum Creatinine, uric acid, haematocrit, platelet, and serum liver enzyme. The frequency to be determined by the severity of hypertension, frequent evaluation of fetal size, and amniotic fluid volume either: clinically or with sonography 7.

Types of pre-eclampsia: [9].

Abnormality	Mild pre-eclampsia	Sever pre-eclampsia
Diastolic BP	≤ 100 mmhg	>100
Proteinurea	Trace to one (+)	Persistent 2+ or more
Headache	Absent	Present
Visual disturbances	Absent	Present

Upper abd. Pain	Absent	Present
Oligurea	Absent	Present
Convulsions	Absent	Present
S. Creatinine	Normal	Raised
Thrombocytopenia	Absent	Present
Liver enzyme elevation	Minimal	Marked
Fetal growth restriction	Absent	Obvious
Pulmonary oedema	Absent	Present

Further management depends on:

1- Severity of pre-eclampsia.

2- Duration of gestation.

3- Condition of cervix.

Mild pre-eclampsia: -

If the patient has a mild pre-eclampsia, an assessment of the gestational age and the lung maturity of the fetus should be done. Management is determined by gestational age. If the pregnancy is 36 weeks or more there is no reason for its prolongation. However, in mild cases there is not the same sense of urgency for delivery as with sever pre-eclampsia.

Patient with mild pre-eclampsia and less than 36 weeks gestation expectant management is the best alternative. For the expectant management to succeed, strict patient selection criteria and meticulous monitoring for signs and symptoms of aggravation of the disease is necessary [7].

Sever pre-eclampsia: -

In severe cases management will consist of:-

1. Prevention of seizures.
2. Control of hypertension.
3. delivery.

1-Prevention of seizures: -

Magnesium sulphate is the most commonly used medication for the treatment or prevention of seizure activity in patients with pre-eclampsia and eclampsia, there is a great deal of controversy over the mechanism of seizure control by magnesium sulphate.

Loading dose: give 4-6 gram of magnesium sulphate diluted in 100 ml of IV fluid administered over 15-20 minutes followed by 1gram per hour, observing for side effects (motor paralysis, absent reflexes, respiratory depression and cardiac arrhythmia). The antidote is 10ml of 10% calcium gluconate given slowly intravenously [9].

2-Control of hypertension: -

The use of antihypertensive drugs in attempt to prolong pregnancy or modify perinatal outcome in pregnancies complicated by various types and severities of hypertensive disorders has been of considerable interest.

Acute treatment of severe hypertension: [8].

In sever pre-eclampsia there are two antihypertensive regimes to choose from,

Labetalol 200mg can be given orally prior to or in the absence of intravenous access, if there is no response within 30 minutes, a second oral dose can be given. If there is no initial response to oral therapy or if it is not tolerated, a bolus of 50mg given intravenously over at least 5 minutes can be administered,

repeated to maximum of 200mg, at 10 minutes interval, following this labetalol infusion can be commenced 5mg/ml at 4ml/hour via a syringe pump,
infusion rate being doubled every 30minutes to maximum of 32ml (1 60mg/hour until blood pressure has dropped and stabilized at an acceptable level). Labetalol is contraindicated in women with asthma and should be used with caution in cardiac disease.
Hydralazine is given by bolus infusion (10-20mg/ over 10-20 minutes, measuring blood pressure every 5 minutes, this may be followed by an infusion (40mg Hydralazine in 40 ml normal saline, which should run at 1-5ml/hour (1-5mg/hour)).
Long term treatment: - [9].
α methyldopa (a centrally acting α adrenergic agonist that inhibits vasoconstricting impulses from the medulla oblongata) has traditionally been the most commonly used agent for the control of blood pressure during pregnancy. Its safety has been well established both in pregnancy and in the long term follow up of the infants. It is given as 1gm load then 1-2gm/day in three divided doses, increasing to a maximum dose of 3gm/day.
Labetalol 300mg in 3 divided doses, increasing to a maximum dose of 1200mg/day.
Hydralazine 100mg/day in 4 divided doses to a maximum of 300mg/day.
Nifedipine is a calcium channel blocker that has in recent years gained popularity in the treatment of chronic hypertension in pregnancy. Data suggest that it is safe, but cumulative evidence is not as extensive as with older drugs such as labetalol and methyldopa.
Angiotensin converting enzyme inhibitors appears to be fetotoxic, and should be avoided in pregnancy.
Diuretics may reduce utero-plcental perfusion and they cause further depletion of a reduced intravascular volume. Their use should be reserved for the treatment of heart failure, pulmonary oedema and idiopathic intracranial hypertension.

3-Delivery: - [8].

he optimum time of delivery is of crucial importance and remains a balance between the risks of major complications to the mother and intra uterine growth restriction in the fetus against the risks of delivery and prematurity to the fetus.
Criteria for delivering patients with severe pre-eclampsia: -
-Blood pressure persistently 160/110mmhg or greater despite treatment.
-Urine output less than 400ml/24hours.
-Platelet count less than 50,000mm^3.
-Progressive increase in serum Creatinine.
-Lactate dehydrogenase more than 1000IU/L.
-Repetitive late deceleration with poor variability.
-Sever intra uterine growth restriction with oligohydramnios.
-Reversed umbilical artery blood flow.
Mode of delivery: -
It is a balance between caesarian section and vaginal delivery. Labour induction to affect vaginal delivery has traditionally been considered to be in the best interest of the mother.
Several concerns including an unfavorable cervix precluding successful induction of labour, a perceived sense of urgency because of the severity of pre-eclampsia and the need to coordinate neonatal intensive care, have led some practitioners to advocate caesarian delivery [7].
Expectant management of sever pre-eclampsia less than 36 week's gestation: [2].

- Bed rest.
- Daily weight.
- Antihypertensive treatment (methyldopa, labetalol).
- Glucocorticoides to decrease the incidence of respiratory distress and improve fetal survival.
- Liver, renal, Haematologic and D-dimer evaluation daily, or every other day.
- Daily questioning about headaches, visual disturbances, epigastric pain and fetal movement.
- Daily fetal movement counts.
- Fluid volume every week.
- Ultrasound scans for fetal growth every 2 weeks.

Complicated forms of pre-eclampsia: - [9].

Eclampsia: -

It is an extremely severe form of pre-eclampsia, characterized by the onset of generalized tonic clonic seizures in women with pre-eclampsia. It occurs Antepartum in 46.3%, intrapartum in 16.4%, and postpartum in 37.3% of the cases.

Pathogenesis of eclampsia remains unknown. It is possible that sever arterial vasospasm causes rupture of the vascular endothelium and pericapillary haemorrhage with development of foci of abnormal electrical discharges that may generalize and causes convulsions. Eclampsia is associated with elevated maternal and fetal morbidity and mortality. The treatment consists of magnesium sulphate to control convulsions, and should be continued for at least 24 hour after delivery, to avoid postpartum eclampsia, antihypertensive medication to control sever hypertension and delivery.

Acute renal failure: -

Oligurea (urine output less than 80 ml/ 24 hours) is not uncommon in patients with severe pre-eclampsia. In most cases Oligurea resolves after delivery but in few instances it may progress to un urea, acute tubular necrosis, bilateral cortical necrosis, and maternal death.

Renal complications are more common in pre-eclamptic patient with Abruptio placenta.

Abruptio placenta: -

About 7% of all patients with eclampsia will have premature separation of the placenta. Abruption is often unexpected finding at the time of delivery.

Pulmonary oedema: -

It is rather common complications of sever pre-eclampsia and eclampsia. Plasma oncotic pressure decreases appreciably in normal term pregnancy because of decreased serum albumin, and it falls even more with pre-eclampsia because of increased vascular permeability caused by endothelial blood vessel injury. This leads to increase in extra vascular fluid oncotic pressure, and this favors capillary fluid extravasation. Most cases of pulmonary oedema are the result of aggressive use of crystalloid solutions for intravascular volume expansion. It is characterized by profound respiratory distress, sever hypoxemia and diffuse rales on auscultation.

HELLP syndrome: - [17].

is characterized by haemolysis, elevated liver enzymes, and low platelets. The incidence and severity of HELLP syndrome varies with parity, ethnicity, and age. Unlike pre-eclampsia in general, it is more common in those with increasing parity, there is also a trend for older women to be more severely affected. It complicates around 20% of all cases of sever pre-eclampsia. Up to 15% of patients presented in second trimester, 50% presents in third trimester, the remainder presents after delivery, often within a few hours but usually within 48 hours, although it can rarely occur up to 6 days following delivery.

Once diagnosis of HELLP is made management must be centered on the stabilization of the patient condition, control of hypertension, correction of platelet number if it is below 40,000 x 10^3 and correction of coagulopathy with fresh frozen plasma and /or cryoprecipitate [17].

There is a rule of Antepartum corticosteroides in order to stabilize the disease. Dexamethasone given intravenously every 12 hours at a dose of 10 mg until delivery, was found to increase platelet number significantly, and decreases lactate dehydrogenase (LDH), and alanine transaminase (ALT).

Once a woman has been stabilized and steroids given to promote fetal lung maturity, delivery is usually the treatment of choice.

Prophylaxis of pre-eclampsia: -

The key to modern management of pre-eclampsia is close surveillance and timely delivery prior to serious complications.

In ideal words preventing the manifestation of the disease would be far more preferable [8].

Aspirin: - a thromboxane antagonist, inhibits the enzyme cyclooxigenase, which is essential in prostaglandin synthesis. Aspirin selectively inhibits platelet thromboxane release but does not affect the production of prostacyclin in the endothelial cells. It is associated with an improvement in the outcome of sever pre-eclampsia and hence should be initiated early in subsequent pregnancy. The finding from collaborative low dose aspirin study in pregnancy (CLASP) trial do not support routine treatment with low dose aspirin in all women with an increased risk of pre-eclampsia. It may, however, be beneficial in women at risk of early onset pre-eclampsia and may therefore be started prophylactically in the first trimester. Low dose aspirin can reduce the risk of sever recurrent pre-eclampsia by about 15%.

High dose vitamin C and vitamin E: - unfortunately, the recently reported vitamin in pregnancy study failed to demonstrate a protective effect of high dose vitamin C and E in a cohort of women at high risk of developing pre-eclampsia.

PATIENTS AND METHODS

Study design:

Case series study.

Study setting:

Aljalla hospital, for obstetrics and gynecology.

Study period:

This study was carried out between 1/7/2009 to 30/9/2009.

Study population:

100 Pregnant women were admitted to the Aljalla hospital for blood pressure control during the study period and fulfilled the following inclusion criteria: patients with pre- eclampsia, diabetic and non-diabetic, with exclusion of patients with essential hypertension, secondary hypertension, and gestational hypertension

Study measurements:

The serum uric acid level measured twice weekly for each patient and the highest reading was included in the study with a cutoff point of 6 mg/dl.

Statistical analysis:

After collection of data it coded and software of SPSS used for analysis, where mean, SD and percentage used for descriptive statistics and independent T student test used for inferential statistics.

RESULTS

This study include 100 patients with pre-eclampsia, the analysis of their data will be presented as follows:

1. Patient characteristics.
2. Past obstetric history.
3. Clinical profile of present pregnancy.
4. Relation of uric acid level to maternal and fetal complications.

Patient characteristics:

Age distribution;

For the pre-eclamptic cases under this study the age was ranged between 19 and 42 years with mean age = 30.9±6 years, and by using a cutoff point of 35 years, 68% were aged less than 35 years and 32% were aged 35 years or more.

Education level: -

Regarding the education of our patients around half of them (46%) were highly educated (university and above), followed by 40% for secondary level and the remainder were with primary or preparatory level only.

Occupation: -

Regarding the occupation of our patients more than half of them (61%) were house wives, 22% teachers, 16% employees, and about 1% were nurses.

Past obstetric history: -

Regarding the parity of the patients under this study it was ranged from 0 to 8 children, where P.G. made 56% and multipara (2-4) and grand multipara (>4), made 27% and 17% respectively.

About the number of previous abortions it was ranged from no abortion (82%), to history of one abortion in 9%, and history of more than one abortion in 9%.

Clinical profile of present pregnancy:-

Gestational age at diagnosis: -

The GA at time of PE diagnosis ranged between 24 to 41 weeks with mean GA =35±3.8 weeks, all of them diagnosed in the third trimester except of 2 cases; one diagnosed in 24 weeks and the other diagnosed at 26 weeks.

Associated diseases: -

The only disease associated with PE found in this study was DM making a percentage of 7%.

Severity of preeclampsia: -

Regarding the severity of preeclampsia in cases under this study, 39% of cases had sever pre-eclampsia, 36% of cases were mild, 18% of cases were imminent and 7% of cases complicated with Eclamptic fit.

Treatment of pre-eclampsia: -

Treatment ranged from no treatment (19%), single antihypertensive drug with Aldomet, Labetalol, or Apresoline (32%, 5%, 3% respectively), and combined antihypertensive drugs, Aldomet +Apresoline, Aldomet + Apresoline+ labetalol, and Aldomet +Apresoline + Mg sulphate (12%, 5%, 24% respectively).

Table 1: - distribution of types of treatment in pre-eclamptic patients under study (Aljalla maternity hospital 2009).

treatment of PE

		Frequency	Percent
Valid	no ttt	19	19.0
	aldomet	32	32.0
	labetalol	5	5.0
	aprosoline	3	3.0
	aldomet+apresoline	12	12.0
	aldomet+labetalol+ apresoline	5	5.0
	aldomet+apresoline +MgSulphate	24	24.0
	Total	100	100.0

Maternal complications: -

In this study, there were only 4 complications: 60 cases complicated with sever hypertension, 11 patients cases complicated with eclampsia, 7 cases complicated with Abruptio, and only one maternal death; the dead patient was Nigerian with no regular antenatal follow up and the direct cause of maternal death was intracranial haemorrhage.

Fetal assessment: -

Regarding fetal growth pattern it was normal in 57% 0f cases and 43% of the fetuses were growth retarded

Fetal complications: -

In this study, 50% of fetuses were normal; the other 50% were complicated by IUGR, IUFD, prematurity, RDS, or combination of 2 or more of these complications as shown in table 2.

Table 2: - distribution of fetal complications in pre-eclamptic patients under study (Aljalla maternity hospital 2009).

Fetal complication

	Frequency	Percent
Normal	50	50.0
IUGR	27	27.0
IUFD	3	3.0
Prematurity	2	2.0
IUGR and prematurity	8	8.0
IUGR prematurity and RDS	4	4.0
IUGR AND IUFD	6	6.0
Total	100	100.0

Gestational age at delivery: -

Regarding gestational age at time of delivery 52% 0f fetuses were delivered at term and 48% of the fetuses were prematurely delivered.

Mode of delivery: -

Regarding mode of delivery 51% 0f foetuses were vaginally delivered and 49% of the foetuses were delivered by Caesarean section.

Birth weight: -

Regarding the birth weight the result showed that weight ranged between 710 and 5200 grams with the mean birth wt = 2519±964grams.

Table: -3 distribution of birth weight in pre-eclamptic patients under study (Aljalla maternity hospital 2009).

birth eight distribution

		Frequency	Percent
Valid	normal	52	52,0
	low birth weight	33	33,0
	very low birth weight	8	8,0
	extrem low birth weight	7	7,0
	Total	100	100,0

Serum uric acid level and it's relation with maternal and fetal complications: -

Serum uric acid level for our cases ranged between 2 to 9.5 mg/dl with mean value= 5.7±1.8mg/dl, by using a cutoff point of 6mg there were 46% with high uric acid level, and 54% were normal.

Relation with maternal complication: -

The mean s.uric acid, of the mothers without maternal comp. =5.0mg/dl and the mean s.uric acid for the mothers with any type of maternal comp. =6.2mg/dl and by using T student test to compare these two means we found that the difference was statistically significant (p=0.000).

Table 4: -Relation between mean s.uric acid and occurrence of maternal complication: - (Independent-samples T test)

Complication	I. Mean Serum uric acid	P value
A. Sever hypertension		
YES	6.2 mg/dl	0.0004
NO	4.9 mg/dl	
Maternal mortality		
YES	9.2 mg/dl	0.051
NO	5.7 mg/dl	
Eclamptic fit		
YES	6.1 mg/dl	0.376
NO	5.9 mg/dl	
Abruptio placenta		
YES	5.5 mg/dl	0.724
NO	5.7 mg/dl	

Relation with fetal complication: -

The mean s.uric acid, of the mothers with no fetal comp. =5.0mg/dl and the mean s.uric acid for the mothers with any type of fetal comp. =6.2mg/dl and by using T student test to compare these two means we found that the difference was statistically significant (p=0.002).

By further studying of each type of fetal complications we found that the serum uric acid level was high with each type fetal complication as shown in the next table , but it was statistically significant only with IUGR and prematurity and not with IUFD.

Table: - 5 the relation between fetal complications and the mean uric acid level

Fetal Complication	II. Mean Serum uric acid	P value
A. IUGR		
YES		0.013
NO	6.2 mg/dl	
	5.3 mg/dl	
B. Prematurity		
YES		0.019
NO	6.1 mg/dl	
	5.3 mg/dl	
IUFD		
YES	6.4 mg/dl	0.272
NO	5.6 mg/dl	

DISCUSSION

In this study we considered tow complications, maternal and fetal. The occurrence of maternal complications was defined as sever hypertension, eclampsia, HELLP, Abruptio, renal failure, pulmonary oedema and maternal death. The fetal complications were defined as intrauterine growth restriction, prematurity and intrauterine fetal death.

Mean serum uric acid in all patients was 5.7 -/+1.8 mg/dl.

Serum uric acid (SUA) level is one of the parameter used in early diagnosis of PIH. It has been reported that Hyperuricemia correlated with the severity of hypertension and distinguishes reliably between PIH and chronic hypertension.14 Hyperuricemia in PIH is a result primarily of decreased renal clearance of uric acid, a decrease that exceeds the reduction in glomerular filtration rate and Creatinine clearance [5].

Voto LS et al; the maximum serum uric acid (SUA) levels during the third trimester of pregnancy were selected in 215 hypertensive pregnant women, The increase in SUA levels was statistically significant in women with severe PE (6.22 +/- 1.30 mg%) [18].

Ranjan Mustaphi et al found that all the women with severe PIH and 45% of women with mild PIH had levels more than 5.5 mg%[14].

Redman and Varma also reported similar findings. [15], [16].

Lim et al. Found that serum uric acid levels were significantly elevated in pre-eclamptic patients (6.6mg/dl) comparing with 5.7mg/dl in our study [11].

Williams KP, Galerneau; in a study found that Preeclamptic women with HELLP syndrome also demonstrated elevated uric acid levels ($p < .05$) [20].

In our study group the mean SUA was 6.2mg/dl in patients with severe hypertension and it was statistically significant with P value of 0.0004, and there were no cases of HELLP syndrome.

C.M.coopmans et al showed that Evidence on the accuracy of SUA in the prediction of HELLP syndrome is limited [6].

Univariante analysis revealed statistical significance for SUA concentration of more than 8.1mg/dl as a risk factor for eclampsia [1]. Elevated uric acid has been related to eclamptic seizures 18. In our study we found a mean SUA of 6.1mg/dl in eclamptic patients which is statistically insignificant (P=0.376).
Williams KP, Galerneau found that in Women with PIH with SUA >5.5mg, had a higher incidences of IUGR (55%) [20].
In our study: the incidence of IUGR (43%), with mean serum uric acid of 6.2mg/dl.
Thankam R. Varma suggests that serum urate is a reliable index of fetal welfare when pregnancy is complicated by pre-eclampsia 16. Hosna1 A et al; in a study of 100 patients found that measurement of serum uric acid is a better indicator of the fetal consequences of preeclampsia than the measurement of blood pressure itself [3].
M. Fakhri et al in their Results showed that the sensitivity of uric acid levels in diagnosis of preeclampsia is moderate and measuring uric acid can be used in determining the severity of preeclampsia, maternal and especially fetal outcomes (preterm, IUGR,) [12].
Norvald Sagen et al found in severe pre-eclampsia significantly higher levels of serum uric acid prior to parturition in cases of growth retardation and perinatal distress[13].
James M. Roberts et al found that In the presence of hypertension with or without proteinuria, the incidence of preterm delivery increased as uric acid increased 10. in our study: the incidence of preterm (48%), with mean serum uric acid of 6.1mg/dl.
Redman 25 years ago demonstrated an increased risk of fetal death in preeclampsia with elevated uric acid15. In our study: the incidence of IUFD (7%), with mean serum uric acid of 6.4mg/dl P =0.019
In our study patients who have mean serum uric acid more than 6.2mg/dl are associated with fetal complication, IUGR (46%) with P =0.019 and prematurity (14%)with P =0.013.

CONCLUSION

This study indicated that in pregnant women with hypertension, measurement of serum uric acid is a good indicator of the fetal consequences of preeclampsia (IUGR P value 0.013 and prematurity P value 0.019)
Low values indicate a good prognosis for the fetus, rising or high values indicate high-risk cases. The estimation of serum uric acid levels does help to identify those fetuses at risk of developing IUGR and also helps to identify the severity of the hypertensive disease (P value 0.0004).
Serum uric acid measurement is an inexpensive and simple test and its use in the management of preeclampsia is useful to predict maternal and fetal and complications improves the maternal and fetal outcome.

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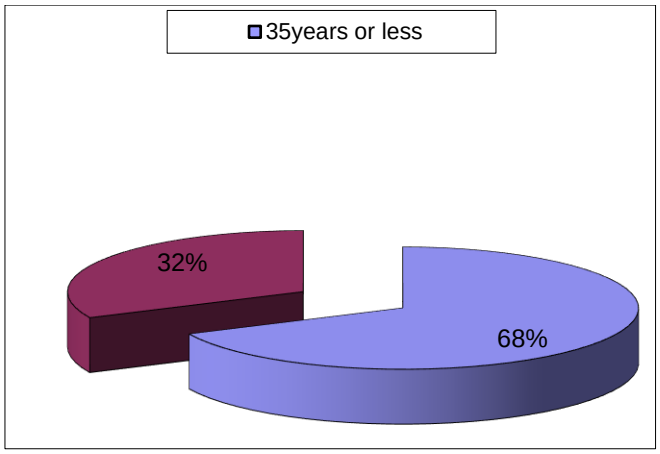

Figure 1: age distribution of pre-Eclamptic patients under study (Aljalla maternity hospital 2009).

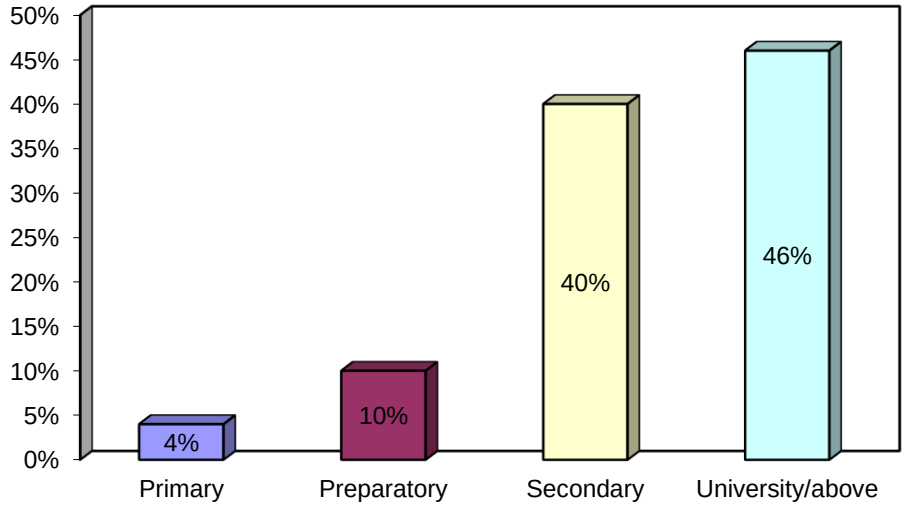

Figure 2: distribution of pre-Eclamptic patients under study (Aljalla maternity hospital 2009) by educational level.

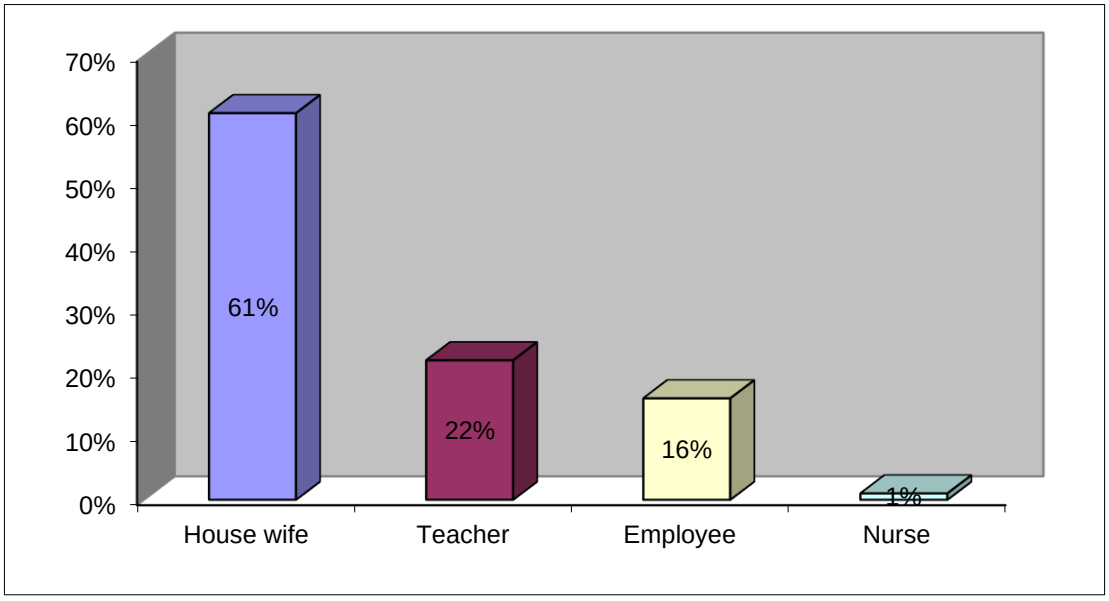

Figure 3: distribution of pre-Eclamptic patients under study (Aljalla maternity hospital 2009) according to occupation

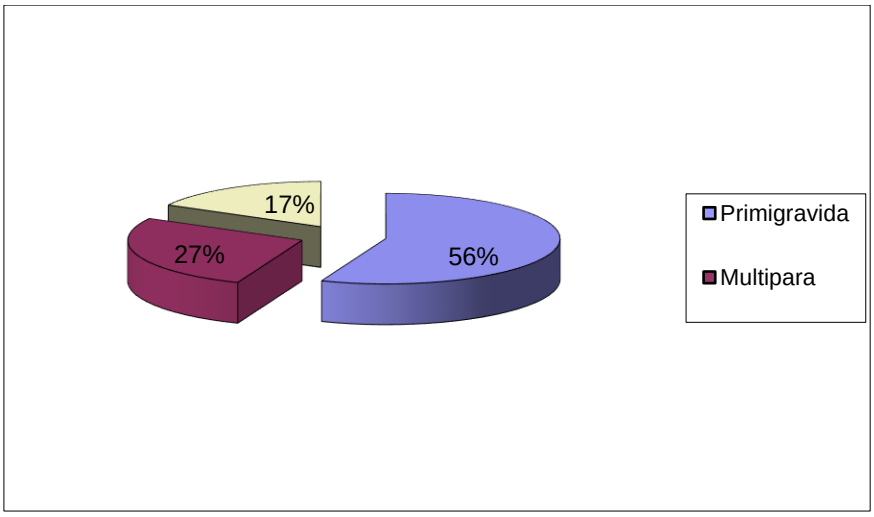

Figure 4: distribution of parity of pre-Eclamptic patients under study (Aljalla maternity hospital 2009

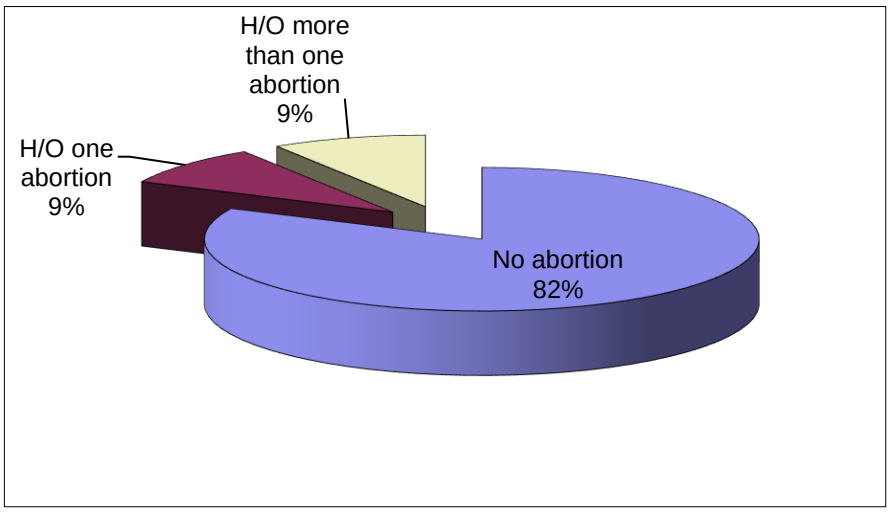

Figure 5: distribution of number of abortion of pre-Eclamptic patients under study (Aljalla maternity hospital 2009).

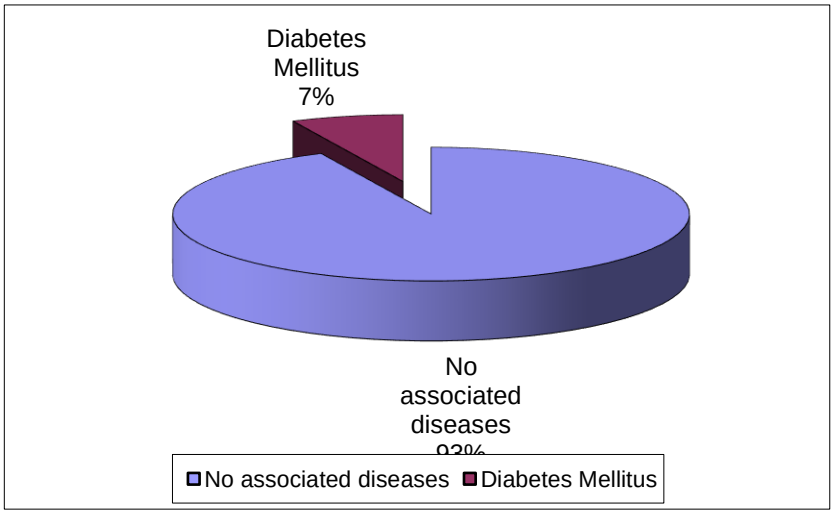

Figure 6: distribution of diseases associated with pre-Eclamptic patients under study (Aljalla maternity hospital 2009).

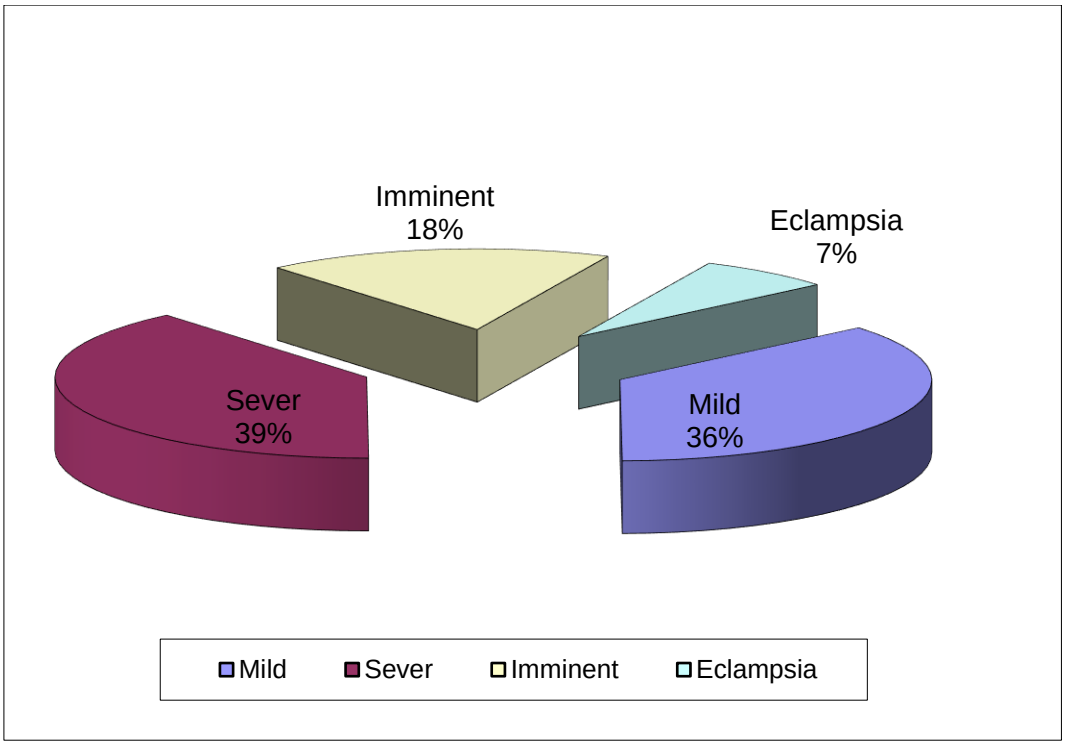

Figure 7: distribution of severity of diseases in pre-Eclamptic patients under study (Aljalla maternity hospital 2009).

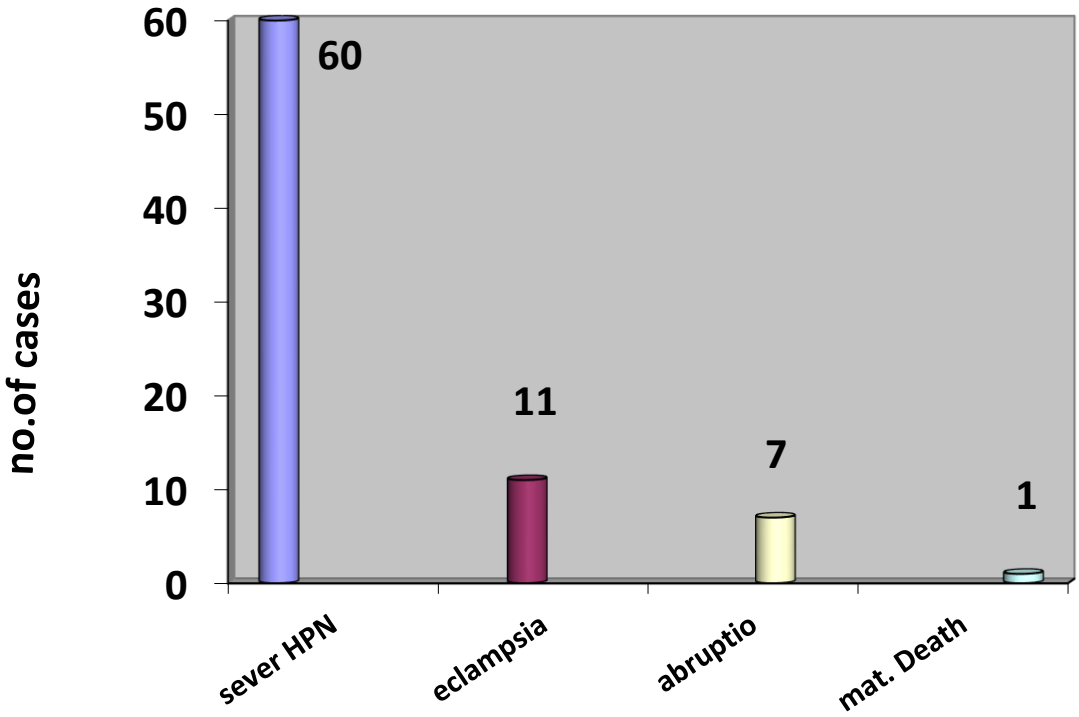

Figure 8: distribution of maternal complications associated with pre-eclampsia in patients under study (Aljalla maternity hospital 2009).

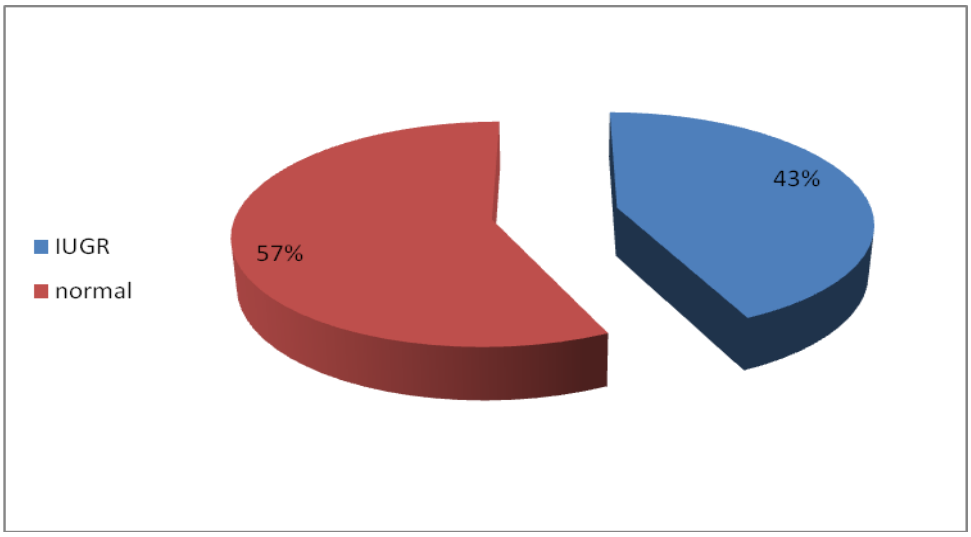

Figure 9: distribution of fetal growth pattern in pre-eclamptic patients under study (Aljalla maternity hospital 2009).

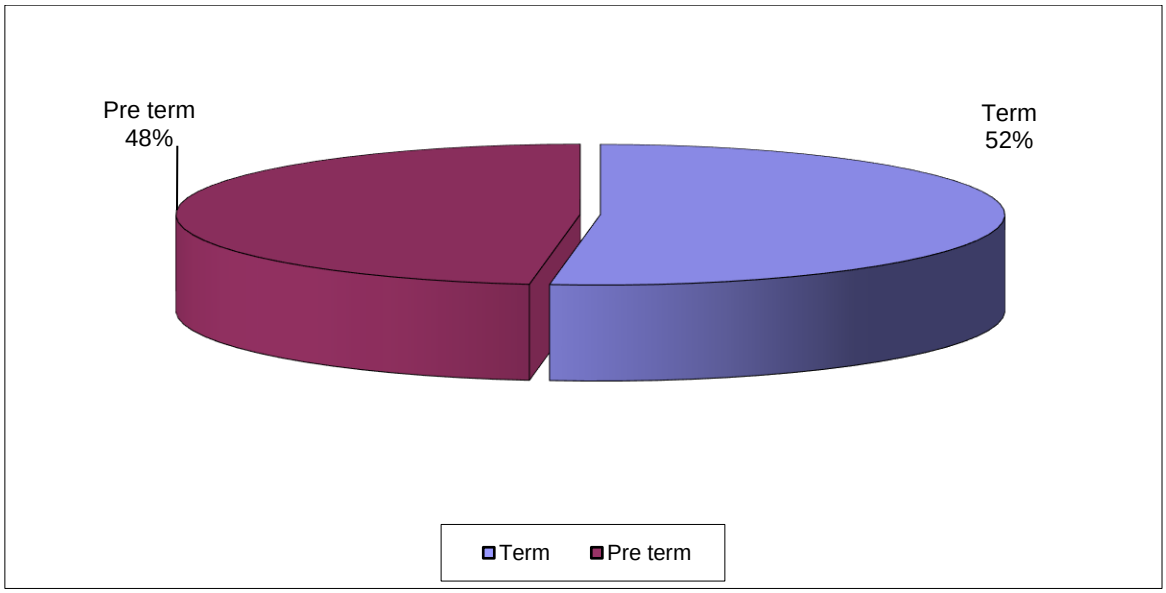

Figure 10: distribution of gestational age at time of delivery in pre-eclamptic patients under study (Aljalla maternity hospital 2009

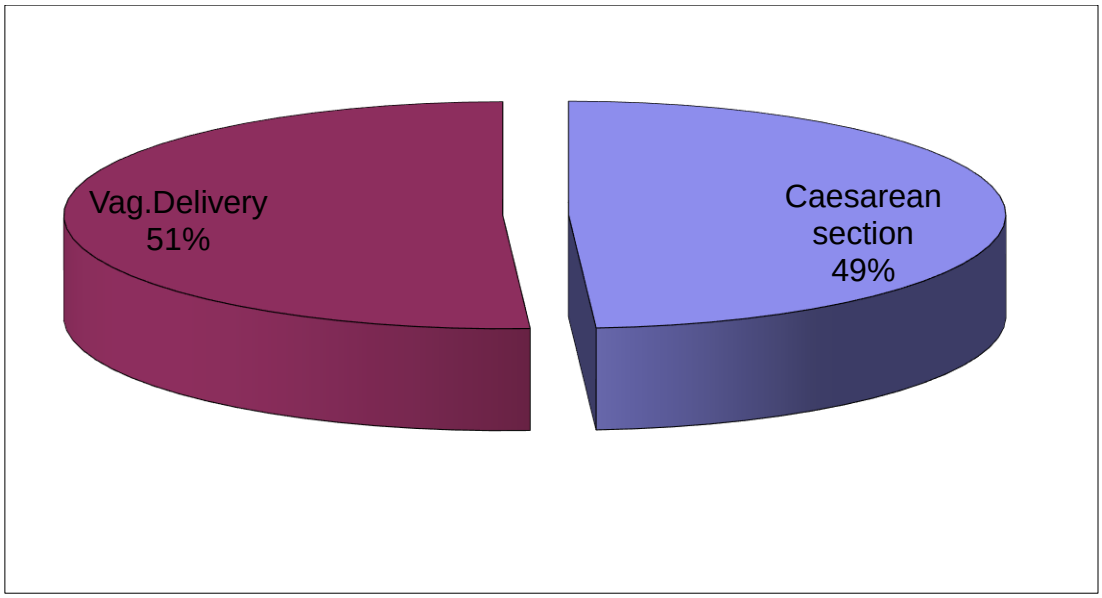

Figure 11: distribution of mode of delivery in pre-eclamptic patients under study (Aljalla maternity hospital 2009

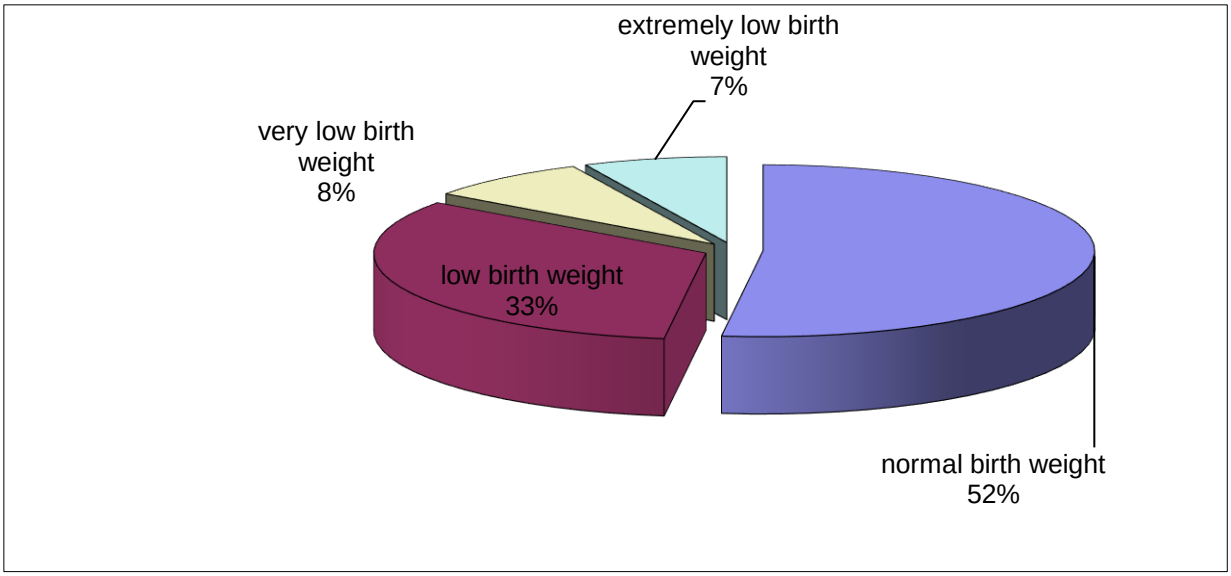

Figure 12: distribution of birth weight in pre-eclamptic patients under study (Aljalla maternity hospital 2009).

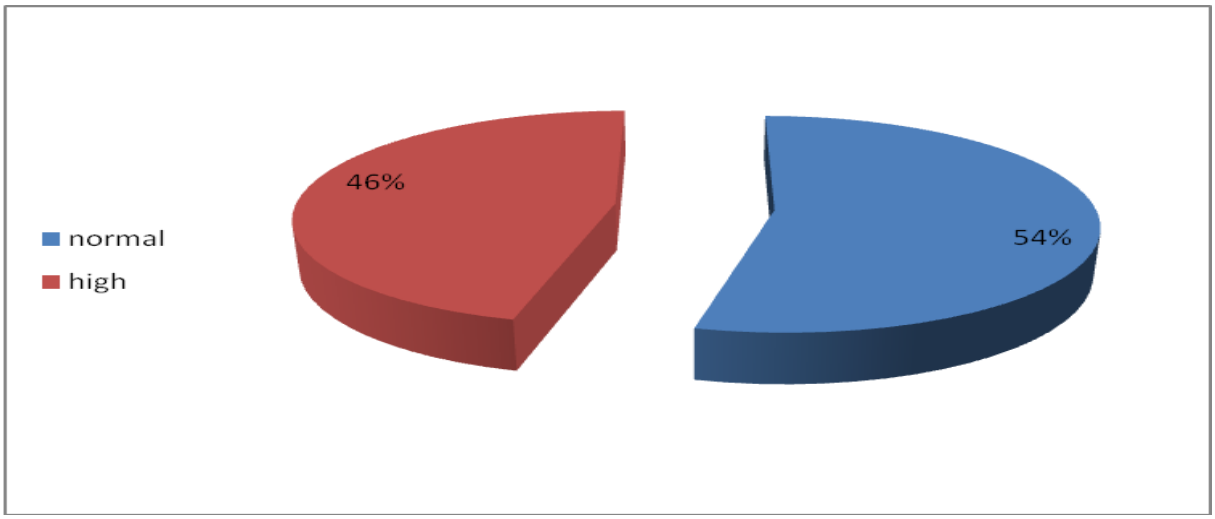

Figure 13: distribution of maternal and foetal complications in pre-eclamptic patients under study (Aljalla maternity hospital 2009)

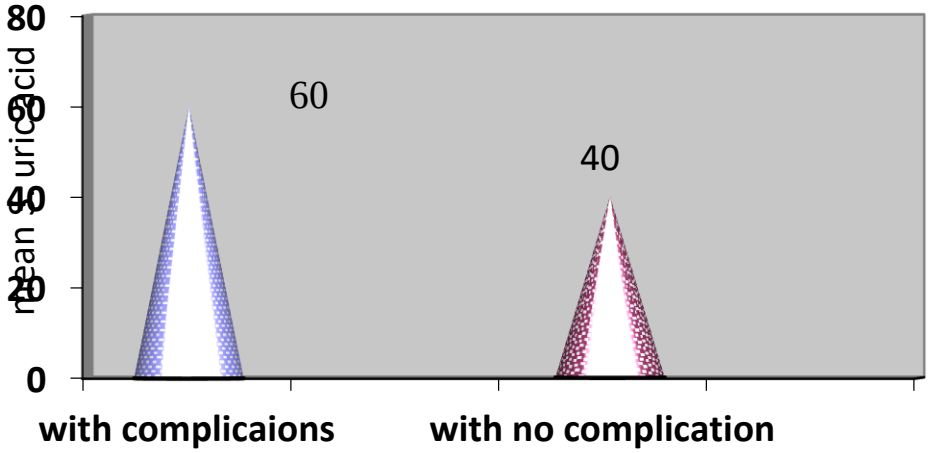

Figure:-14 mean serum uric acid level in relation to maternal complication presence among pre-eclamptic patients under study (Aljalla maternity hospital 2009) By further studying of each type of maternal complications we found that the serum uric acid level was high with each type of maternal complication, except for Abruptio placenta where the mean serum uric acid is slightly higher among patients not complicated with Abruptio (5.7mg/dl) than for patients with Abruptio (5.5mg/dl), but by using T student test for independent samples, the difference between all the means was statistically insignificant except for sever hypertension. For the maternal mortality in this study of 100 women only one mother died, the P value was 0.051(at the border line due to small sample size, 100cases).in this study there were no cases complicated with pulmonary oedema, nor HELLP syndrome or renal failure.

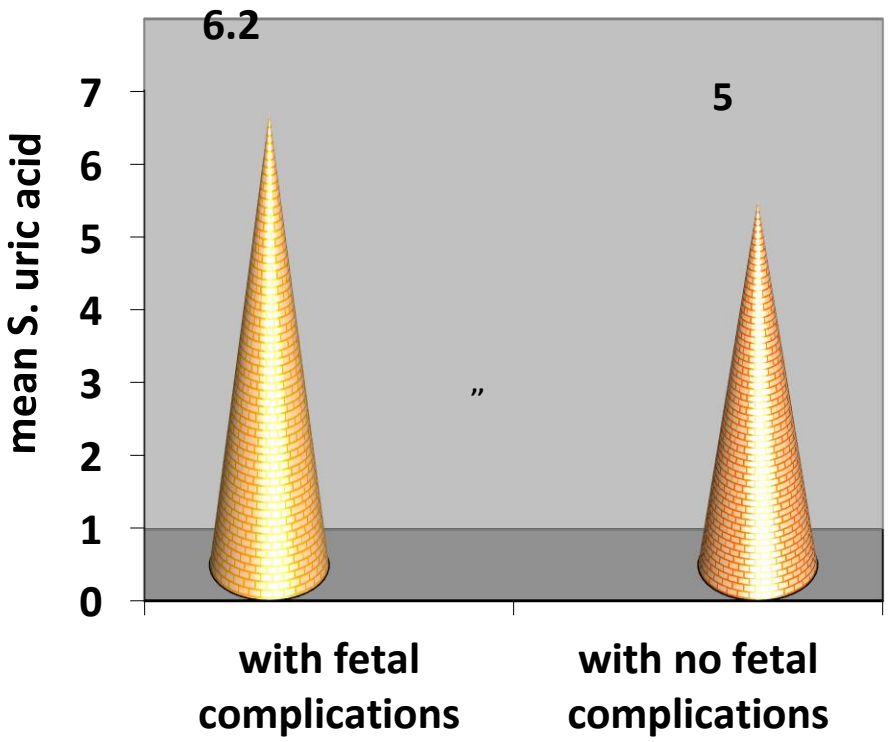

Figure:-15 mean serum uric acid level in relation to fetal complication presence among pre-eclamptic patients under study (Aljalla maternity hospital 2009).