REVIEW OF LITERATURE
REVIEW OF LITERATURE

Folin (1919) and Caldwell, W.E. and Lyle, W.G. (1921) first reported lowered urea nitrogen and non protein nitrogen in pregnancy as compared to normal non pregnant females.

In another study Stander et al (1932) studied various kidney function tests in the differentiation of the toxaemias of pregnancy. They studied various clearance tests and concluded that urea clearance, guanidine and creatinine excretion tests were of real value in differentiating between mild nephritis and mild toxaemia of pregnancy. They recommended the urea clearance and creatinine excretion tests for routine use in all cases of toxaemia of pregnancy, where the diagnosis was not clear. A urea clearance below 80 percent of the mean normal and a creatinine excretion below 155 mg in the first hour are strongly indicative of renal damage.

Stander, H.J. and Cadden, J.F. (1934) studied blood chemistry in pre-eclampsia and eclampsia. They observed that non protein nitrogen content of the blood in eclampsia and pre-eclampsia remains within normal limits, except in certain instances late in the disease when a rise indicates involvement of the kidneys as a result of eclamptic disease. The blood urea nitrogen was low as in normal pregnancy.
The blood uric acid was increased in eclampsia and pre-eclampsia indicating a disturbance in its destruction in liver. The uric acid content in the blood may be regarded as an indicator of severity of disease.

Cadden and Farris (1936) studied non protein nitrogen, urea and rest nitrogen in normal pregnant women at different periods of gestation, during labour and post partum period. They found that non protein nitrogen of blood decreases during first six months of pregnancy and then increased steadily until one week post partum. The urea nitrogen concentration diminished significantly during the first six months and then maintained a constant level until the eighth or ninth month when it begins to rise. The ratio of urea nitrogen to non protein nitrogen is decreased significantly in pregnancy.

Cadden, J.F. and Stander, H.J. studied uric acid metabolism in eclampsia in 1939. They observed that increased blood uric acid in eclampsia can not be explained on the basis of decreased excretion by the kidneys because increase in blood uric acid appears as one of the early signs of the disease whereas kidney manifestations, such as nitrogenous retention as shown by the non protein nitrogen and urea values, appear late in the course of disease. High blood uric acid is probably
due to impaired hepatic destruction of this substance in
the liver. This impairment in hepatic destruction of uric
acid appears early in the disease may perhaps be important
in etiology of eclampsia.

Chesley et al (1941) measured the body water
available for thiocynate distribution i.e. extracellular
water and concluded that patients who are found to have
excessive available water, although apparently normal other-
wise, are prone to develop the classical signs and symptoms
of pre-eclampsia. Preeclampsia very seldom appears in those
patients having normal proportions of available water in late
pregnancy. According to them, measurement of available water
is a more reliable index to the danger of developing toxaeinia
than does weight taking. Patients loose excess available
water by the sixth post partum day.

Lancet, M. and Fisher, I.L. (1956) studied the
value of blood uric acid levels in toxaeinia of pregnancy
and concluded that the level of blood uric acid can serve
as good laboratory indicator in toxaeinia of pregnancy. The
test can serve as diagnostic as well as prognostic guide.
In order to differentiate toxaeinia from primary kidney disease
and hypertensive disease, they suggested routine use of blood
urea estimation as well. High uric acid and normal urea was a
sign of toxaeinia of pregnancy. Both were low in idiopathic
hypertensive disease. When both components were high it suggested primary kidney disease and usual renal function tests were employed.

Von Slyke stated in the same year that blood uric acid is as a rule high in toxaeemia of pregnancy, more so in eclampsia and nephritis.

Easlier Prabhawati, R. (1957) reported elevated uric acid levels in toxaeemia of pregnancy as compared to normal pregnancy. The concluded that it gives a fair indication of the severity of disease.

Danfosen and Hull (1958) suggested that higher concentration of urea in amniotic fluid is due to active transport from the maternal compartment into the amniotic fluid across the chorionicion.

Russel, R. and Gloria, E. et al (1958) reported a series of renal clearances in normal pregnancy and found a significant decrease in clearances due to elevated glomerular filtration rate which began in first trimester of early in second trimester and persisted through the remainder of pregnancy. When normal pregnancy is compared with toxaeemia of pregnancy and when mild degrees of toxaeemia are compared with severe pre eclampsia and eclampsia, a direct relationship existed between severity of toxaeemia and the depression in glomerular filtration.
MacGaughey et al (1959) investigated the equilibration of urea between the amniotic fluid, maternal and cord blood and concluded that diffusion of urea takes place through chorioamniotic surface and is not limited to maternal exchange through placenta.

Pollak, V.E. and Nettles, J.B. (1960) studied renal biopsies and observed the relations of histologic observations in relation to clinical and biochemical findings. Combination of hypertension, proteinuria and edema was found in sixty percent of patients with preeclampsia. In the patients with histologic evidence of preeclampsia, the values of serum urea nitrogen, non protein nitrogen and uric acid were elevated significantly above those in healthy pregnancy. The preeclamptic renal lesions were divided into three groups on the basis of the severity of the glomerular involvement. The levels of urea nitrogen non protein nitrogen and uric acid in the serum increased with increasing severity of glomerular involvement. In those patients with mild glomerular lesions, the serum uric acid was significantly elevated, whereas the urea nitrogen and non protein nitrogen levels were significantly elevated only in the presence of more severe renal lesions. Thus serum uric acid level is an excellent guide post to the diagnosis of preeclampsia and to the severity of the underlying renal lesion in preeclampsia.
Sosanski (1961) also reported higher urea content of the amniotic fluid in late toxæmia of pregnancy and stated that in toxæmia the urea content was highest in the urine of newborn obtained immediately after birth. He further stated that in toxæmia of pregnancy, the foetus is often in a state of asphyxia, so that the "Intruterine reflex retention of urination" may be disturbed in the foetus. In these circumstances a large amount of urea may get into amniotic fluid, resulting in a rise of the urea content of amniotic fluid.

Hutchison et al (1962) investigated the distribution and metabolism of carbon labelled urea in pregnant primates and concluded that there was rapid exchange of urea between maternal and foetal bloods but the transfer to the amniotic fluid was slower.

Gupta, F.; Kothari, L.K. and Gupta, S.N. (1963) estimated blood urea and uric acid levels in normal non pregnant and pregnant groups. In pregnancy complicated by toxæmia, urea was moderately high in 70 percent of cases while uric acid was conspicuously raised in all cases. The precise mechanism which leads to accumulation of uric acid in blood is still uncertain, although impaired renal excretion, diminished destruction by the liver and excessive formation associated with muscular exertion during convulsions have all been suggested as likely possibilities.
Reidel (1963) in a study showed that blood urea of mother rises with severity of toxaemia. He did not take into account the possible influence of gestation, age or parity on urea concentration.

Juvaie and Gokhale (1964) studied the urea clearance test in normal pregnancy and toxaemia and they failed to detect any difference.

Mc Kay, E. and Kilpatrick, S.J. (1964) showed that the urea concentration in the umbilical venous plasma of non-toxaemic pregnancies was raised when the birth weight was below average for the gestation period i.e. in infants showing IUGR. When the effect of gestation period was removed, a significant negative correlation was found between urea concentration and birth weight, the urea concentration being higher in low birth weight.

Increase in blood urea in dysmaturity was caused either by placental insufficiency which prevented the foetus from excreting its NEP (non protein nitrogen) through placenta or by increase in tissue destruction or by both mechanisms.

Later on, in 1965, Kilpatrick and Mc Kay studied umbilical cord urea concentration in toxaemic pregnancies and their relationships with birth weight and gestational age. They divided the cases into three groups namely 'Normotensives', 'Toxemic' and 'Other hypertensives'. They found
that under weight infants of normotensives have a significantly higher mean urea than their fellows of normal weight. However, in toxæmic mothers, there appeared to be a reversal of the effect of birth weight on cord urea i.e. under weight had a lower mean urea concentration. Both hypertensive groups had higher urea concentration than normal pregnancies. These differences were independent of birth weight and gestation period. Toxaemic group had a significantly lower birth weight than normotensive group. Their studies suggested that the level of maternal blood pressure is more important in determining cord urea concentration than is gestation age or birth weight.

Kishore, N. and Tandon, S. (1965) studied blood urea, non protein nitrogen and serum uric acid and ophthalmoscopic findings in normal non pregnant females, healthy pregnant women and in pregnancy with toxæmia. Toxaemia cases were divided in four groups, mild and severe preeclampsia, eclampsia and pregnancy with essential hypertension. They concluded that the level of blood uric acid can serve as an important diagnostic criterion in toxæmias. Prognosis can be told and future line of treatment can be decided by the levels of blood uric acid. Blood non protein nitrogen was not changed significantly in cases of toxæmias of pregnancy.
Blood urea decreased in normal pregnancy, increased in toxæmia and came to normal on about 6th to 10th post partum day. Most common fundal change was found retinal spasm.

Chesley, L.C. (1966) studied sodium retention in preeclampsia and made serial estimations of exchangeable sodium and peurperial sodium loss and concluded that oedematous toxæmic women loose large amount of salt in the puerperium and that the salt loss is related to the degree of oedema and its regression. The rational explanation is that in the puerperium, there is a reversal of changes that occurred in pregnancy, the salt loss has been retained during pregnancy.

Eastmann and Hilman (1967) also reported a significantly reduced urea clearance in toxæmia of pregnancy when compared to normal pregnancy.

Hytten Leitch (1971) showed the lower levels of serum urea and creatinine in normal pregnant woman compared with non pregnant subjects. It reflects the increased glomerular filtration rate in normal gestation and increased renal clearance. They also showed normal serum uric acid in normal pregnancy.
Saxena, C. and Kharoliwal, S. (1971) estimated urea concentration in the amniotic fluid and blood in normal pregnancy and toxaemia of pregnancy. They concluded that there was a rise in mean blood urea levels with the increase in severity of toxaemia and highest blood urea level was in eclampsia. There was definite increase in urea level of amniotic fluid with the increase in severity of toxaemia. Amniotic fluid urea was higher than the blood urea in both normal as well as toxaemic cases. The ratio of average maternal blood urea to average amniotic fluid urea was more. Therefore, though the increase in amniotic fluid urea is more in comparison to maternal blood urea.

Sinha, H.B. and Mukherjee, A.K. (1973) observed the urea content of amniotic fluid, maternal and foetal blood in normal pregnancy, preeclamptic toxaemia and eclampsia. Investigations were carried out between 38 and 41 weeks of gestation and cases were of the following types. They found that urea content of the amniotic fluid was found to rise with increasing severity of toxaemia and the highest mean value was observed in eclampsia. The rise in amniotic fluid urea content may be caused by diminished urea clearance by the foetus through the placenta, due to reduced circulation in chorodecidual space in toxaemia of pregnancy and increased excretion of urea through the foetal urine which under normal conditions would have been excreted through the placenta.
Parallel rise of maternal and cord blood urea was found in toxaemic cases compared with normal pregnancy. Rise in cord blood urea can be due to rise in amniotic fluid and maternal blood urea levels. Increased breakdown of proteins in foetal system may also contribute towards increase in cord blood urea because in their study the mean birth weight of the babies born to toxaemic mothers was significantly lower than the mean birth weight of normal babies. Positive correlation of the amniotic fluid urea level with that in maternal and cord blood in normal and toxaemic pregnancies suggests that free diffusion of urea takes place between the three fluids.

Rohtagi, P. and Tewari, K. et al (1973) evaluated a relationship of liquor urea with placental and foetal weight. They showed that there was rise in both blood urea and liquor urea in toxaemia cases, but liquor urea increased more as compared to blood urea. The mean birth weight of babies showed a significant fall in moderate, severe P.E.T. group and eclampsia group. Placental weight was lowered significantly in all groups of toxaemia.

Increase of liquor urea was negatively correlated to placental and foetal weight in all the groups of toxaemia which was highly significant in eclampsia. They concluded that rise of liquor urea is indicative of placental damage and due to placental damage there might be lowering of foetal weight as well.
Semple et al (1974) studied changes in uric acid concentration in a longitudinal study. This study suggested that serum uric acid concentration fell markedly in early pregnancy; thereafter there was a gradual rise throughout the pregnancy; but values after 30 weeks gestation were still significantly lower than those obtained after the puerperium. In addition renal clearance of uric acid rose through pregnancy, but this appeared to occur in parallel with increase in glomerular filtration rate, thus implying that no change occurred in specific renal handling of uric acid. The changes in uric acid concentration reflected 'dilution' in early pregnancy followed by a gradual increase in the maternal uric acid due to foetal uric acid production.

Dunlop, W. and Davison, J.M. (1977) studied the effect of normal pregnancy upon the renal handling of uric acid and discussed with reference to that in preeclampsia. Plasma uric acid concentration appeared to be inversely related to uric acid clearance. When a comparison between non pregnant values and those obtained during pregnancy was done, the plasma uric acid concentration decreased and uric acid clearance increased. An increase in fractional uric acid clearance was also demonstrated, indicating that the proportional reabsorption of uric acid was reduced.

Ojha, J. and Sarin, C.N. (1979) also studied the significance of maternal and cord blood urea in the toxemia
of pregnancy and foetal outcome. They found higher urea levels in maternal and cord blood of toxaemic mothers and the rise was parallel with rise of blood pressure. Low birth weight and high cord blood urea levels were directly related to the severity of toxaemia.

Brazy and associates (1982) studied neonatal manifestations of severe maternal hypertension and they also reported that symmetrical intrauterine growth retardation and neonatal complications were frequent in infants of eclamptic mothers. Similarly Lopez Llora and associates and Weinstein et al (1982) also reported growth retardation and a syndrome of haemolysis, elevated liver enzymes and low platelet count as a consequence of severe hypertension in pregnancy.

Von Slyke stated that blood uric acid is as a rule high in toxaemia of pregnancy, more so in eclampsia or nephritis.

Saxena, S.K., Maewal, S., Khare, S. et al (1982) studied the comparison of amniotic fluid urea and blood urea in normal pregnancy and preeclamptic toxaemia. In normal pregnancy, in spite of the greatly increased demands for protein involved in the mother for foetus, the body is able to maintain the lower limits of normal blood urea. Amniotic fluid urea levels show a small rise over maternal serum urea levels in early weeks of pregnancy, but rises considerably in the later weeks of pregnancy, i.e. it was negatively correlated
in early pregnancy and in labour patient while positively in later weeks of pregnancy. There was definite rise in levels of blood urea and amniotic fluid urea with the increasing severity of toxaemia when compared with normal pregnancy. High urea concentration in amniotic fluid has definite correlation with the degree of toxaemia.

Despite the persistent efforts to decrease the incidence and improve the management of eclampsia, this obstetric complication continues to be a major causes of perinatal death world wide. Sibai, B.M. et al (1982) studied neonatal outcome, growth and development in eclampsia and found that infants of eclamptic mothers are at increased risk for prematurity, intrauterine growth retardation and perinatal asphyxia. Most of the immediate neonatal complications were related to prematurity and growth retardation.

Razdan, S., Sharma, M. and Mishra, K. et al (1984) studied the comparison of urea content in maternal blood, cord blood, and amniotic fluid in normal and toxamic pregnancies and its significant in relation to foetal outcome. Cord blood urea level increased with increase in the degree of toxaemia and mean birth weight decreased with increase in mean cord blood urea level. Maternal blood, cord blood urea in severe P.E.T. group and eclampsia were significantly higher than mild and moderate P.E.T. group. Therefore estimation of maternal blood urea concentration may serve as a guide to severity of disease.