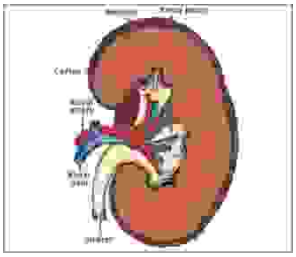
ORIGINAL PROF-782

ASSESSMENT OF RENAL FUNCTIONS DURING 1ST TRIMESTER OF PREGNANCY



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ABSTRACT... shafiqai@yahoo.com **Design:** A Case Control Study. **Purpose:** 1. To obtain basic information about the serum levels of different metabolic nitrogenous end products during pregnancy. 2.To determine the renal function alterations during 1st trimester of normal pregnancy under local conditions. **Study Period:** Study was done at Quaid-e-Azam Medical College, Bahawalpur during the year 1999-2000. **Material & methods:** Subjects in **group-B** having normal pregnancy of 1st trimester was taken. No restriction on diet, fluid intake, socioeconomic status or physical activity was imposed. Pregnant woman having hypertension, renal disease, diabetes & any other complication like toxemia of pregnancy were excluded from this study. Diagnosis was carried out on the basis of history, physical examination and local examination performed by the gynaecologist and on laboratory investigation. In control **group-A** age matched subjects without pregnancy were selected from general population. Most of the controls were selected amongst the students and staff member of QAMC, Bahawalpur. In this group 26 subjects were taken. Renal function was assessed from 24 hours urine collection & morning blood serum samples and the values of creatinine clearance were corrected for body surface area in each case. Data was analysed by SPSS processor. **Results:** In this study total 44 females were included. (group-A (control) 26 Non-pregnant women & group-B (case) 18 pregnant women in their 1st trimester) the rise in GFR (endogenous creatinine clearance) & urinary levels of creatinine was high in case as compared to control group. A small difference in urine specific gravity & urine volume was observed in two groups. A statistically significant change was observed. However the endogenous creatinine clearance (ECC) showed a great variability. **Biochemical Parameters:** Table-III gives the mean value ± SD of serum levels of creatinine, urea, uric acid, glucose and albumin in control (Non-pregnant women) & case (pregnant woman in 1st trimester).Serum level of creatinine, uric acid & albumin was found to decrease in pregnant women. Serum glucose level tends to increase in pregnant women group.

Key Words: Endogenous creatinine clearance, Renal Physiology

INTRODUCTION

Pregnancy (gestation) is the maternal condition of

having a developing embryo or foetus in the body. Normally, human pregnancy lasts 280 days or 40 weeks (9 calendar month or 10 lunar months) from LMP[1].

The physiological, biochemical & anatomical changes occurring during pregnancy are extensive and may be systemic or local. However, most systems return to pre-pregnancy status between the time of delivery and six weeks postpartum[2,3]. The changes that occur in pregnancy also include alteration in renal function and sodium homeostasis[4]. Many changes in renal physiology occur during normal pregnancy. The rate of GFR is increased by about 50% through out most of pregnancy and it falls back to usual non-pregnant level a few days before the onset of labor[5]. In healthy pregnant woman a rise in GFR & small decrease in urine flow was noted. In healthy non-pregnant woman, the daily activity was associated with the rise in GFR and urine flow with the decrease in creatinine index and specific gravity. While during daily activity the GFR and urine flow decrease with an increase in creatinine index & specific gravity as in pregnancy induced hypertension with ankle oedema.[6,7]

GFR is frequently measured by creatinine clearance in dogs & cats but in primates including humans, some creatinine is secreted by the tubules and some may be reabsorbed. In addition, plasma creatinine determination are inaccurate at low creatinine levels because the method for determining creatinine is frequently measures small amount of other plasma constituents.

In spite of this, the clearance of endogenous creatinine is frequently measured in patients. The values correlate quite well with the GFR values measured with inulin because, although the value for U_{cr} V is high as a result of tubular secretion the value for P_{cr} is also high as a result of nonspecific chromogens, and the error thus tend to cancel. In clinical practice 24 hours creatinine clearance is commonly used to assess GFR, but reports of change in 24 hours pregnancy are conflicting. Serum albumin can be seen to fall through out pregnancy, with the expectant rise in 6 weeks postpartum. In seeking evidence that glomerular permeability to albumin increases during pregnancy, it is important to consider two other variables which influence the rate at which albumin passes through the glomerular filterate, namely serum albumin concentration & the glomerular filtration rate. As both of these vary in pregnancy, it is necessary to measure them and incorporate them with the urinary albumin concentration to calculate an albumin/creatinine clearance ratio. The rise in albumin/creatinine clearance ratio in each trimester suggests that glomerular permeability is increased steadily during pregnancy.

Since pregnancy is associated with high GFR & may lead to glomerular damage & excretion of albumin is a well-established marker of that[28]. It is essentially important to know & ascertain the timing and degree of change in increase maternal renal function, as it may be an early sign of pregnancy-induced hypertension (PIH, Gestational HTN). The conditions associated with PIH include:

A low calcium/creatinine ratio[9].
Increased blood urea & uric acid[10]
Decreased maternal albumin, IgG levels &
Decreased GFR with retention of Salt & water[11]

Similarly altered GFR could affect the excretion of various drugs especially those which are potentially toxic or which have low binding capacity to plasma proteins and predominantly drugs with renal excretion requiring their dose to be adjusted accordingly.

This aspect of obstetrical therapeutics obviously requires further investigation[12]. In addition the estimate of renal function will enable the clinician to prescribe fluids, electrolytes and many therapeutics with greater safety than would otherwise be possible[13]. According to workers in Pakistan, blood urea nitrogen, creatinine and uric acid in apparently healthy subjects were lower than those reported from West[14].

MATERIAL & METHOD

This was a case control study which was conducted at Quaid-e-Azam Medical College, Bahawalpur during the year 1999-2000.

Subjects (Case) in group-B having normal pregnancy during 1st trimester were selected from antenatal Gynaecology outpatient department & Gynaecology ward-I & ward-II of Bahawal Victoria. Hospital, Bahawalpur. Diagnosis was carried out on the basis of history, physical examination and local examination performed by the gynaecologist and on laboratory investigation. In control group-A age matched subjects without pregnancy were selected from general population. Most of the controls were selected amongst the students and staff member of QAMC, Bahawalpur. In this group 26 subjects were taken.

Inclusion criteria: Subjects having normal pregnancy of 1st trimester were taken. No restriction on diet, fluid intake, socioeconomic status or physical activity was imposed.

Exclusion criteria: Pregnant woman having hypertension, renal disease, diabetes & any other complication like toxemia of pregnancy were excluded from this study.

Sampling Technique: Renal function was assessed from 24 hours urine collection & morning blood serum samples and the values of creatinine clearance were corrected for body surface area in each case. About 10 ml of blood was collected and serum was separated from clotted blood by centrifugation. Serum was cooled down till analysis. To collect 24 hours urine sample, patients were instructed accordingly. Volume of 24 hours urine was noted; 10ml of aliquote urine was drawn for analysis & remaining was discarded. Performa was filled from antenatal card and by history taking from the subjects at the time of sampling. Weight and height was measured. Pulse and temperature was noted. Blood pressure was also measured. Following parameters were measured:

Creatinine Clearance was measured by formula

$C = UV/P \times 1.73/A = ml/min/m^2$

While A (body surface area) meter^2 was calculated by nomogram[15].

Biochemical parameters measured were Creatinine (serum & urine), Serum urea, Uric acid, Albumin & Glucose were analyzed by commercially available kits.

Statistical Analysis: Complete data of all subjects (case & control) along with biochemical parameter were measured and compared. For Data collection and processing of both groups computer program SPSS was used. Mean, mode, medium, standard deviation, standard error mean and other statistical variables were collected through SPSS processor.

Test of Significance: As in this study we have calculated the numerical variables for comparison of two groups (case & control), Paired Student t- test was most appropriate for two groups. P- Value was equal to or less than 0.05, results were found to be Statistically Significance and null hypothesis was proved to be wrong. (In case the p- value was less than 0.001 the results were highly significant statistically).

RESULTS

In this study total 44 females were included. In group-A (control) 26 Non-pregnant women & group-B (case) 18 pregnant women in their 1st trimester were selected for the study. Physiological and clinical status of both groups was recorded and given in Table-I, which include number of cases, age, gestation, parity, height, weight, blood pressure & pulse. The values are expressed as mean $\pm$ SD Gestation is represented in weeks.

GFR & Urine Analysis:

Table-II shows urine analysis, urinary levels of creatinine & GFR (endogenous creatinine clearance). A small difference in urine specific gravity was noted between group-A & group-B. A negligible variability in urine volume was observed in two groups. A statistically significant change was observed in urinary levels of creatinine. However the endogenous

creatinine clearance (ECC) showed a great variability. So the rise in GFR was high in case subjects as compared to control group.

Biochemical Parameters:

Table-III gives the mean value ± SD of serum levels of creatinine, urea, uric acid, glucose and albumin in control (Non-pregnant women) & case (pregnant woman in 1st trimester).Serum level of creatinine was found to decrease in pregnant women as compared to control group. Serum uric acid & albumin also showed a decrease. Serum glucose level tends to increase in pregnant women group.

Table-I Physiological & Clinical Status of Control & Case Subject(Values are expressed as mean ± SEM)

Physiological & Clinical Parameters		Control group	Case group
No. of cases		26	18
Age (in Years)		26.77 ± 0.91	25.00 ± 1.09
Period of Gestation (in weeks)		-	12.50 ± 0.33
No. Of previous pregnancies		2.38 ± 0.38	1.50 ± 0.35
Height (in centimeter)		153.65 ± 1.06	152.52 ± 1.37
Weight (in Kg.)		54.59 ± 2.21	54.22 ± 2.22
Blood pressure	Systolic	111.38 ± 1.70	106.38 ± 2.73
(In mm. Of Hg.)	Diastolic	71.54 ± 1.54	70.00 ± 2.21
Pulse per minute		75.19 ± 0.81	80.50 ± 1.38

Table-II GFR & URINE ANALYSIS OF CONTROL & CASE SUBJECT (Values are expressed as mean ± SEM)

Urine analyses parameter & GFR	Control group	Case group
No. of cases	26	18
Urine pH	6.29 ± 0.13	6.39 ± 0.10 (NS)
Urine Specific gravity	1.006 ± 0.001	1.009 ± 0.001(NS)
Urine volume (in ml/ 24 hours)	1415.12 ± 40.16	1423.89 ± 62.52(NS)
Urinary Creatinine	88.15 ± 1.60	101.49 ± 3.99(SS)
GFR (ml/ min/ b.s.a.)	119.12 ± 3.28	152.47 ± 4.61(HSS)

NS = Results not statistically significant (P > 0.5)
SS = Results statistically significant (P < 0.05)
HSS = Results highly statistically significant (P <0.001)

Test of significance:

As it is shown in Table-II & Table-III, the values are expressed in mean of observed values ± standard error mean. As the data is numerical in two groups Paired Student t- test was applied. The urinary pH, specific gravity and volume difference found was not

statistically significant (P> 0.05). The urinary creatinine level changes were found to be statistically significant (P< 0.05); while the increase in endogenous creatinine clearance was found to be highly statistically significant (P< 0.001).

Biochemical parameter showed that serum creatinine was low but results found were not statistically significant. Serum urea & serum albumin was low and results were statistically significant (P< 0.05). Decrease in serum uric acid in group-B was highly statistically significant (P< 0.001).

Table-III BIOCHEMICAL PARAMETERS OF CONTROL & CASE SUBJECT (Values are expressed as mean ± SEM)

Biochemical Parameters	Control group	Case group
No. of cases	26	18
Serum creatinine (mg/ dl)	0.81 ± 0.02	0.74 ± 0.04$^{(NS)}$
Serum urea (mg/ dl)	19.08 ± 0.90	16.08 ± 0.90$^{(SS)}$
Serum uric acid (mg/ dl)	5.12 ± 0.04	3.54 ± 0.13$^{(HSS)}$
Serum glucose (mg/ dl)	76.65 ± 1.78	87.16 ± 1.60$^{(SS)}$
Serum Albumin (mg/ dl)	4.80 ± 0.54	4.04 ± 0.06$^{(SS)}$

NS = Results not statistically significant (P > 0.5)
SS = Results statistically significant (P < 0.05)
HSS = Results highly statistically significant (P < 0.001)

DISCUSSION

Pregnancy has been reported to induce marked and widely varying circulatory and biochemical changes in women. These physiological adaptations to the pregnant state are further exaggerated or altered by the effect of climate or other environmental conditions & genetic factors[16]. Thus, renal function with in the bounds of normal in a given population may be considered abnormal in another, even though both the populations are healthy[17]. Indeed, the individual variations in these changes during pregnancy are so widespread that full appreciation of the pattern of changes, may only be achieved through serial investigation[16]. Serial investigation of the subjects in this study was difficult because in Pakistan women rarely seek advice during early pregnancy.

GFR being the best overall index of renal function is assessed by endogenous creatinine clearance in this study, which is widely used in the measurement of GFR in many conditions[18,19,20,21]. In another study it was found that the results of GFR with ECC and inulin clearance are in good agreement[22].

Changes and variations in ECC during pregnancy closely parallel those of the inuline clearance[23]. In our study it was found that there is a tendency of an apparent increase in creatinine clearance in 1st trimester. Results are highly significant. The results are in agreement with the study of Assali et al[6,24,25]. They found GFR (Inuline Clearance) to increase significantly in 1st trimester. Workers in another serial study on pregnant women by ECC found the same results[8,23,26]. Although same results were found in above mentioned study but difference in percentage was in excellent agreement with the results of Blants et al & Ploth et al who found about 30% increase in GFR[27].

The actual mechanism is unknown. It is postulated that it may be due to the secretion of ovarian & placental hormones through their effect on maternal Aldosterone metabolism as well as plasma protein synthesis, which influence plasma volume, renal plasma flow & in turn, GFR[6, 8,23,28].

In the present study Serum Creatinine & urinary creatinine were also measured as ECC mainly depends on both these parameters. Serum creatinine has been found to be lower during pregnancy in 1st trimester but the decrease was not statistically significant. In comparison Davison found a statistically significant decrease in first trimester[24]. The different levels may be due to different method adopted. Urinary creatinine was decreased significantly in 1st trimester as in above-mentioned study.

Decline in serum urea was significant in our study which is in accordance with the study of Sims & Krantz, Davison & Noble[23,24]. Serum uric acid levels showed a highly statistically decrease in 1st trimester results which are also in accordance with Eguatu & many other workers[16,23,29,30,31]. The increase is due to haemodilution & increase plasma volume. The decrease in serum albumin (Table III) is in according with the study of Wright et al[8,] this is probably due to progressive rise in mean glomerular permeability to albumin. Nevertheless the rise in albumin/ creatinine clearance ratio in 1st trimester shows that glomerular permeability increased steadily during pregnancy[8,32]. The increase pulse rate as found in our study is also mentioned by Goodlin due to maternal hypovolaemia with declined maternal haemocrit.

CONCLUSION

The measurement of renal function during pregnancy is of marked interest in clinical nephrology. Especially, for the evaluation of suspected renal disease, to follow the course of disease & to calculate the dosage of potentially toxic drugs mainly excreted by the kidney with low binding capacity to plasma proteins.

This study has provided a baseline data for clinician to adjust doses of therapeutic agents and electrolyte during pregnancy. The values above or below the data provided may indicate abnormal renal function.

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