

SERUM CREATININE AND CREATININE CLEARANCE STUDIES IN NORMAL PREGNANCY AND TOXAEMIA

by

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During pregnancy the normal creatinine metabolism is disturbed. There is fall in plasma creatinine level in normal pregnancy. This may be explained by hormonal effect on renal tubules in which creatine excretion is selectively increased (Kuhlback and Widholm 1966) which results in lowered plasma and urinary creatinine values.

There is considerable change in the renal function in cases with pre-eclampsia and eclampsia. The most obvious causes are alteration in renal haemodynamics due to vascular spasm and in advance stages of the condition due to haemo-concentration. As a result, the glomerular filtration is reduced which causes a lowering of creatinine clearance. Creatinine clearance test is a good diagnostic and prognostic aid in toxæmia of pregnancy.

Material and Method

Following groups of patients were studied:

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Group I: 15 non-pregnant females having no renal disease and with normal blood pressure.

Group II: Ninety-five pregnant patients without any features of toxæmia and were divided into three sub-groups.

(a) Fifteen cases of gestation less than 12 weeks.

(b) Thirty cases with period of gestation between 13-28 weeks.

(c) Fifty cases of gestation between 29-40 weeks.

Group III: Toxæmia group: Divided into following sub-groups:

(a) Pre-eclamptic toxæmia. a. Mild—40 cases. b. Severe—16 cases.

(b) Eclampsia—10 cases.

(c) Pregnancy with essential hypertension—12 cases.

(d) Hypertension with superimposed toxæmia—12 cases.

Serum creatinine and creatinine clearance rates were estimated by Brod and Sirota's method.

Observations and Discussion

Serum creatinine value fell slightly in first and second trimesters but again went up in third trimester. However, the variations were not statistically significant. (Table I). Serum creatinine

TABLE I
Serum Creatinine Values in Controls and Normal Pregnancy

Groups	No. of cases	Range mg%	Mean mg%	S.D.	't' value	'P' value
Controls	15	0.6-1.0	0.80	0.14	—	—
1st trimester	15	0.6-1.1	0.77	0.13	0.60	>0.50
2nd trimester	30	0.5-1.1	0.79	0.50	0.21	>0.70
3rd trimester	50	0.5-1.2	0.85	0.15	1.05	>0.30
Normal pregnancy (as a whole)	95	0.5-1.2	0.82	0.14	0.51	>0.50

1st trimester vs 2nd trimester 't'—0.49 'P' >0.60

1st trimester vs 3rd trimester 't'—1.74 'P' >0.05

2nd trimester vs 3rd trimester 't'—1.51 'P' >0.30

levels were increased significantly in all the groups of toxæmia of pregnancy including hypertension. The increase was more in severe pre-eclampsia than in mild pre-eclampsia and serum creatinine level was maximum in cases of eclampsia. (Table II).

cal significance when compared with that of control.

93.3% in the control group had value between 81 to 121 ml/minute and only 1 case had a creatinine clearance rate of 123.8 ml/minute. On the other hand, in the first trimester 73.3% had values be-

TABLE II
Serum Creatinine Values in Toxæmias of Pregnancy

Groups	No. of cases	Range mg%	Mean mg%	S.D.	't' value	'P' value
Normal pregnancy third trimester	50	0.5-1.2	0.85	0.15	—	—
Mild pre-eclampsia	40	0.7-1.4	0.99	0.35	4.7	<0.001
Severe pre-eclampsia	16	0.6-1.6	1.11	0.22	5.3	<0.001
Eclampsia	10	1.0-1.4	1.27	0.16	8.1	<0.001
Hypertension	12	0.7-1.5	0.97	0.20	2.3	<0.05
Hypertension with super-imposed toxæmia	12	0.8-1.3	1.00	0.18	3.1	<0.01

It is seen from Table III that creatinine clearance rate was increased in early pregnancy followed by a subsequent reduction. The difference in the creatinine clearance rate between the first and third trimesters ($P < 0.05$) and also the second and third trimesters ($P < 0.02$) were statistically significant. The third trimester value just failed to attain statisti-

between 81 to 120 ml/minute, 2 cases had values above 120 ml/minute and 2 cases had creatinine clearance rate between 61 to 80 ml/minute. In the second trimester 86.6% had creatinine clearance rate between 81 to 120 ml/minute, 1 case had a value between 61 to 80 ml/minute and 3 cases had value above 120 ml/minute. In the third trimester 78% had creatinine

TABLE III
Creatinine Clearance Values in Controls in Normal Pregnancy

Groups	No. of cases	Range ml/min.	Mean ml/min.	S.D.	't' value	'P' value
Controls	15	83.3-123.8	101.93	13.0	—	—
1st trimester	15	61.3-146.6	105.0	20.9	1.4	>0.10
2nd trimester	30	77.6-127.4	101.81	13.4	.024	>0.90
3rd trimester	50	38.5-139.5	91.91	17.8	1.64	>0.05
Normal pregnancy (as a whole)	95	38.5-146.6	97.20	17.9	1.0	>0.05

1st trimester vs 2nd trimester 't'—0.61 'P' >0.50

2nd trimester vs 3rd trimester 't'—2.3 'P' <0.05

2nd trimester vs 3rd trimester 't'—2.5 'P' <0.02

TABLE IV
Distribution of Creatinine Rates in Controls in Normal Pregnancy

Groups	No. of cases	Creatinine clearance rates in ml/minute						Above 140
		Below 40	41-60	61-80	81-100	101-120	121-140	
Controls	15	—	—	—	8	6	1	—
1st trimester	15	—	—	2	2	9	1	1
2nd trimester	30	—	—	1	13	13	3	—
3rd trimester	50	1	1	6	30	9	3	—
		(2.0%)	(2.0%)	(12.0%)	(60.0%)	(18.0%)	(6.0%)	

clearance rate between 81 to 120 ml/minute, 6 cases had value between 61 to 80 ml/minute and 2 cases had values below 61 ml/minute. (Table IV). In the group of normal pregnancy as a whole 80% had clearance rate between 81 to 120 ml/minute, 11.6% had values below 81 ml/minute and only 2 cases had values below 61 ml/minute.

Creatinine clearance rates decreased significantly ($P < 0.001$) in all the groups of toxaeemias except in cases of essential hypertension. The fall in creatinine clearance was dependent upon the severity of toxaeemia. Thus in mild pre-eclampsia, the average creatinine clearance rate was 61.28 ± 8.88 ml/minute, in hypertension with superimposed toxaeemia it was 55.4 ± 11.2 ml/minute, in severe pre-eclampsia the value was 48.8 ± 10.75 ml/minute and the maximum fall was observed in cases of eclampsia in whom the value was 41.3 ± 12 ml/minute. (Table V).

than 60 ml/minute. In severe pre-eclampsia 75% and in eclampsia all the cases had clearance rate less than 60 ml/minute. In eclampsia 70% had values below 40 ml/minute. In hypertension all the cases had values above 60 ml/minute and 58.3% had levels above 80 ml/minute. But in the group of hypertension with superimposed toxaeemia again all the 12 cases had clearance rate of less than 80 ml/minute, and in 8 cases the rates were less than 60 ml/minute. (Table VI).

Kuhlback and Widholm (1966) got the mean value of serum creatinine at 0.73 mg%, in normal pregnancy. This is in accordance with our mean value of $0.82 \pm .14$ mg% in normal pregnancy. George and Kalyani Kutty (1970) got higher values (1.6 mg%). Serum creatinine level depends on many factors such as diet, muscle mass and physical activity. Difference in the method of estimation of this parameter might partly explain the discrepancy in results.

TABLE V
Creatinine Clearance Values in Toxaeemias of Pregnancy

Groups	No. of cases	Range ml/min.	Mean ml/min.	S. D.	t value	P value
Normal pregnancy third trimester	50	38.5-139.5	91.91	17.8	—	—
Mild pre-eclampsia	40	43.7-81.8	61.28	8.88	10.01	<0.001
Severe pre-eclampsia	16	35.0-69.2	48.8	10.75	9.3	<0.001
Eclampsia	10	32.5-72.2	41.3	12.0	8.6	<0.001
Hypertension	12	63.2-129.1	90.0	15.9	0.49	>0.60
Hypertension with superimposed toxaeemia	12	32.5-72.2	55.4	11.2	6.8	<0.001

In the third trimester of normal pregnancy, 42 cases (84%) had creatinine clearance rate more than 80 ml/min., whereas in mild preeclamptic toxaeemia 97.5% (39 cases) had value below 80 ml/min. and 35% had clearance rate of less

The high serum creatinine level obtained in the later half of pregnancy can be explained on the basis of negative nitrogen balance. Our patients who belong to poor socioeconomic group are mainly taking vegetarian diet. Due to this nega-

TABLE VI
Distribution of Creatinine Clearance Values in Toxaemias of Pregnancy

Groups	No. of cases	Creatinine clearance values in ml/minute					
		Below 40	41-60	61-80	81-100	101-120	121-140
Normal pregnancy third trimester	50	1 (2.0%)	1 (2.0%)	6 (12.0%)	30 (60.0%)	9 (18.0%)	3 (6.0%)
Mild pre-eclampsia	40	—	14 (35.0%)	25 (62.5%)	1 (2.5%)	—	—
Severe pre-eclampsia	16	3 (18.7%)	9 (56.2%)	4 (25.0%)	—	—	—
Eclampsia	10	7 (70.0%)	2 (20.0%)	1 (10.0%)	—	—	—
Hypertension	12	—	—	5 (41.6%)	6 (50.0%)	—	1 (8.3%)
Hypertension with superimposed toxemia	12	1 (8.3%)	7 (58.3%)	4 (33.3%)	—	—	—

tive protein balance body protein is broken down leading to formation of more creatine which is then converted into creatinine.

Creatinine clearance rate is increased in early pregnancy followed by a reduction in the later part of pregnancy. This can be explained by changes in glomerular filtration rate and renal blood flow which increases in early pregnancy but comes down in later weeks. Other workers also have noticed high levels of serum creatinine in toxemia but their values are higher. In cases of eclampsia serum creatinine level in present series was $1.27 \pm .16$; George and Kalayan Kutti (1970) 2.52 mg%; Nayar (1940) 4.4 mg% in comparison to present findings. But, then the serum creatinine levels in controls and in normal pregnancy were also comparatively low in the present series. There is low creatinine clearance rate in all the groups of toxemia and it is due to reduced glomerular filtration. In cases of uncomplicated essential hypertension the glomerular filtration is nor-

mal or increased inspite of reduction in renal blood flow because maximum spasm perhaps occurs in the efferent glomerular arterioles which increases the intraglomerular pressure and thereby enhances filtration (Hayashi 1956).

Summary

In toxemia of pregnancy, the serum creatinine levels were increased significantly in all the groups including cases of essential hypertension. Creatinine clearance rate is higher in early pregnancy followed by reduction in the later part. The creatinine clearance rate decreased significantly in all the cases of toxemia except hypertension.

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