Research Article

Study of urinary microalbumin/creatinine levels and ratio in gestational hypertensive patients

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Abstract

Background: Gestational hypertension (BP>140/90mmHg) or pregnancy induced hypertension usually precedes pre-eclampsia (BP>140/90mmHg associated with proteniuria). Many tests to predict pre-eclampsia are coming up on the horizon. microalbuminuria are one such tests to predict pre-eclampsia which may be present before other clinical signs and symptoms. **AIM:** To determine urinary microalbumin, urinary creatinine and urinary microalbumin/creatinine ratio in pregnancy induced hypertension and in normal pregnant women. **Material and Methods:** The study included 100 subjects with gestational age between 24-38weeks and divided into two groups viz. control group and study group. The control group included 50 subjects who were normal pregnant women and study group included 50 subjects who were gestational hypertensive patients. The urinary creatinine was estimated by Jaffe's method and urinary microalbumin was estimated by Turbidimetric Immunoassay (AGAPEE company) in all the subjects. **Results:** The estimated mean levels (mean ± SD) of urinary microalbumin, creatinine in control group were 28.1 ±25.1, 0.95 ±0.16 respectively and in patients with gestational hypertension they were 157.8 ±48.7, 1.21 ±0.37 respectively. The statistical analysis by unpaired t-test shows that the levels of urinary microalbumin were significantly increased ($p<0.001$) and the urinary creatinine were significantly increased ($p < 0.001$) in gestational hypertensive patients when compared to healthy controls. The mean urinary microalbumin/creatinine ratio in control group were 0.06±0.05 and in gestational hypertensive patients were 0.21 ±0.08. Thestatistical analysis by unpaired t-test shows that the levels of urinary microalbumin/creatinine ratio were significantly increased ($p<0.001$) in gestational hypertensive patients when compared to healthy controls. **Conclusion:** This study suggests that a regular evaluation of urinary microalbumin/creatinine ratio after 20wks of gestation may be an effective screening method for impending pre-eclampsia and may identify population at risk to be included in primary prevention programmes.

Key words: pregnancy induced hypertension; pre-eclampsia; urinary microalbumin, urinary creatinine; microalbumin/creatinine ratio.

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INTRODUCTION

Pregnancy is a physiologic state associated with substantial and, on occasion, profound alterations in metabolic and biochemical processes.[1] Hypertension and proteinuria have long been recognized to be an important complications of pregnancy. [2] Hypertension in pregnancy is the major cause of fetal growth retardation and perinatal mortality. [3]

Gestational Hypertension: is defined as elevation of BP> 140/90mmHg for the first time during pregnancy with no proteinuria and returns to normal with in 12wks postpartum.[4]

Pre-eclampsia: is diagnosed when one or more of the following maternal systemic complications accompany hypertension in second half of pregnancy: proteinuria >300mg/ day or protein/ creatinine ratio >30mg/mmol, renal impairment (plasma creatinine >100mol/lit) renal

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dysfunction (AST>50IU/L), hematologic abnormalities (platelet count<150x109/L.[5]

The diagnosis of pre-eclampsia requires evaluation for proteinuria. The gold standard for this evaluation is the 24hr urine collection. However, this is a time consuming and cumbersome process that requires proper collection for accurate results. Studies have shown the urinary dipstick is a poor predictor of 24hr urine total protein level.[6] Also it is inconvenient for women, and inaccurate due to incomplete collection. In recent years, random protein/creatinine ratio has been suggested as a rapid test for prediction of pre-eclampsia.[7] The current generally accepted concept regarding the cause of pre-eclampsia is that the disease is due to endothelial cell dysfunction in morphological parameters such as endotheliosis in placental bed and uterine vessels and changes in biochemical parameters such as disturbance of prostacyclin/thromboxane A2 balance.[1] Microalbuminuria occurs when the kidney leaks small amounts of albumin into the urine. In other words, when there is an abnormally high permeability for albumin in the renal glomerulus.[8] The glomeruli are enlarged and swollen but not hypercellular, primarily as a result of hypertrophy of the intracapillary cells, which encroach on the capillary lumina, giving bloodless glomerulus. These changes may be responsible for the microalbuminuria in initially stages and later significant proteinuria seen in pre-eclampsia.[9] There is marked alteration in renal hemodynamics in pregnancy. Both GFR and renal plasma flow increase by upto 50 % above pre-pregnancy concentration. Plasma creatinine and urea concentration decrease during pregnancy and increases in 24 hr creatinine clearance (paralleling the increase in GFR) becomes apparent 4weeks after conception. Maximum increase in creatinine clearance occurs at 9-11weeks after conception. Renal function may deteriorate during pregnancy in women with preexisting renal disease or a history of preeclampsia in a previous pregnancy and hence monitoring of creatinine concentrations is advisable.[10] The majorty of women have diminished renal perfusion and glomerular filteration with corresponding elevated plasma creatinine. In severe cases it may be elevated two- to three- fold over normal values in non pregnant women.[11] Urine creatinine may also be used with a variety of other urine tests as a correction factor. Since it is produced and removed at a relatively constant rate, the amount of urine creatinine can be compared to the amount of another substance being measured. Examples of this are when creatinine is measured with protein to calculate urine protein/creatinine ratio (UP/CR) and when it is measured with microalbumin to calculate microalbumin/creatinine ratio (also known as albumin/creatinine ratio, ACR). These tests are used to evaluate kidney function as well as to detect other urinary tract disorders.[12] The purpose of the present study is to determine the presence of microalbuminuria or high microalbumin/creatinine ratio in gestational hypertensive patients when compared to normal pregnant patients.

MATERIAL AND METHODS

A total number of 100 subjects participated in the present study which included 50 gestational hypertensive patients between 24-38weeks of pregnancy. 50controls were healthy pregnant women between 24-38weeks of gestation, without any major illness. The subjects included both primi and multigravida pregnant women from Bapuji Hospital and Chigateri General Hospital, Davangere (both attached teaching hospitals for J.J.M. Medical College, Davangere). Each gave informed consent and this study was approved by Ethical and Research Committee of J.J.M. Medical College, Davangere to use human subjects in the research study.

Exclusion criteria

Patients with history of chronic hypertension, diabetes, renal diseases, and other chronic medical illness History was taken regarding age, parity, socioeconomic status, past, family, and personal history. General examination was done for blood pressure, odema and weight gain. Examination was conducted in all the cases according to the proforma. Routine investigations were done in all the cases 50.

The early morning first urine sample from all patients was collected in calcium free vials.10ml of urine was collected and 0.2ml HCL was added to prevent calcium salt precipitation. Creatinine was estimated in the collected samples. Separate sample was collected for microalbumin estimation. Sample was tested within 24hrs of collection. If urine was turbid then it was centrifuged at 2000rpm for 10min, and clear supernatant was used for testing.

Statistic analysis: Results are expressed as mean ±SD. Unpaired 't' test was used for intergroup Comparison and paired 't' test for intra group comparison. $p < 0.05$ was considered as statistically Significant.

RESULTS

Table 1: Descriptive Information of Subjects

Number Of Subjects		50	50
AGE (years)	MEAN± SD	22.4±2.9	22.3±2.8
	RANGE	18-28	18-32
POG(weeks)	20-24	20(39%)	30(59%)
	25-28	24(47%)	15(29%)
	30-34	7(14%)	6(12%)
Parity	NULLI	32(63%)	29(57%)
	MULTI	19(37%)	22(43%)

Table 2: Comparison of urinary microalbumin levels between cases and controls

Groups		Urinary Microalbumin (mg/L)
Controls	MEAN ±SD	28.1 ± 25.1
	RANGE	8.0 – 120.0
Cases	MEAN±SD	157.8 ± 48.7
	RANGE	62.2 – 260.4
Cases Vs Controls	MEAN DIFFERENCES	129.6
	t value*	16.9
	P value	<0.001, HS

*- unpaired t- test, HS- highly significant

Table 3: Comparison of urinary creatinine levels between cases and controls

Groups		Urinary Creatinine (gm/day)
Controls	MEAN ±SD	0.95 ± 0.16
	RANGE	0.8 – 1.6
Cases	MEAN±SD	1.21 ± 0.37
	RANGE	0.80 – 1.88
Cases Vs Controls	MEAN DIFFERENCES	0.26
	t value*	4.63
	P value	<0.001, HS

*- unpaired t- test, HS- highly significant

Table 4: Comparison of urinary microalbumin/creatinine ratio between cases and controls

GROUPS		URINARY MICROALBUMIN/ CREATININE RATIO
Controls	MEAN ±SD	0.06 ± 0.05
	RANGE	0.01 – 0.24
Cases	MEAN±SD	0.21 ± 0.08
	RANGE	0.06 – 0.43
Cases Vs Controls	MEAN DIFFERENCES	0.15
	t value*	10.3
	P value	<0.001, HS
	CUT OFF VALUE	>0.14

*- unpaired t- test, HS- highly significant

DISCUSSION

In the present study urinary microalbumin and creatinine levels in gestational hypertensive patients were statistically highly increased compared to normotensive pregnant women. The renal lesion that is characteristic of preeclampsia is termed glomerular endotheliosis. The glomeruli are enlarged and swollen but not hypercellular, primarily as a result of hypertrophy of the intracapillary cells, which encroach on the capillary lumina, giving bloodless glomerulus. These changes may be responsible for the microalbuminuria in initially stages that is in gestational hypertensive patients and later significant proteinuria seen in pre-eclampsia.[9] The predominant pathology, which is endothelial dysfunction sets in as early as 8-18week, however, the signs and symtoms appear in the late midtrimester. In order to arrest the disease process in the initial stages or to prevent complications especially in women predisposed to pre-eclampsia, various predictors have been proposed time and again.[16] Proteinuria and alterations in calcium excretion are common features of various forms of hypertension and renal disorders.[17] Microalbuminuria is defined as urinary excretion of albumin that is persistently above normal, but cannot be detected by urine dipstick methods.[18] Microalbuminuria is diagnosed either from a 24-hour urine collection (20 to 200 µg/min) or more commonly, from elevated concentrations (30 to 300 mg/L) on at least two occasions. An albumin level above these values is called "macroalbuminuria" or albuminuria.[8] To compensate for variations in urine concentration in spot-check samples, it is more typical in the United Kingdom to compare the amount of albumin in the sample against its concentration of creatinine. This is termed the albumin/creatinine ratio (ACR) and microalbuminuria is defined as ACR _2.8 mg/mmol (female) or _2.0 mg/mmol (male).[8] Creatinine (from the Greek *kreas*, flesh) is a break-down product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass). Chemically, creatinine is a spontaneously formed cyclic derivative of creatine. Creatinine has a molecular weight of 113Da and is present in all body fluids and secretions and is freely filtered by the glomerulus.[19] A combination of serum and urine creatinine levels may be used to calculate a creatinine clearance. This test measures how effectively kidneys are filtering small molecules like creatinine out of blood.[19] The amount of microalbumin in the sample is compared against its concentration of creatinine which is termed the microalbumin/creatinine ratio is the preferred test for screening for microalbuminuria. This is because creatinine which is byproduct of muscle metabolism is normally excreted in urine on a constant basis. Its level in urine is relatively stable. Since the concentration (or dilution) of urine varies throughout the day, this property of creatinine allows its measurement to be used as a corrective factor in random/spot samples.[76] In the present study the urinary microalbumin/ creatinine ratio was higher in women with gestational hypertension when compared to normotensive pregnant women. The cut off value was 0.14. A ratio of more than 0.14 was seen in women with gestational hypertension. This was statistically significant with a p-value less than 0.001.

CONCLUSION

The study shows a close relationship between urinary calcium as well as creatinine excretion and the gestational hypertensive patients. The current study supports that the levels of urinary calcium are significantly decreased in gestational hypertensive patients compared to normotensive pregnant women, where as urinary creatinine are increased in gestational hypertensive patients compared to normotensive pregnant women. It is also emphasized from the study that a regular evaluation of urinary calcium/creatinine ratio after 20weeks of gestation may be an effective screening method for impending pre-eclampsia and may identify population at greater risk to be included in primary prevention programmes.

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