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Correlation Of Urinary Collagen IV: Urinary Albumin Ratio In The Prediction Of Preeclampsia

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Abstract

The purpose of this study was to assess the value of MA in the prediction of PE and also to compare urinary collagen IV with MA in this prediction. A total of 200 subjects (age 25±4 years, M±SC), were selected in their early pregnancy (10 to 14 weeks). Blood glucose, serum lipids, serum and urinary creatinine, urinary albumin and urinary collagen IV were measured in these subjects and they were followed up to the term for the possible development of PE, MA was defined by albumin creatinine ratio (ACR) above 32mg/g and high urinary collagen IV was defined by values above the cut-off point 2.54 ng/ml determined by the median value of the controls. The data were analyzed by grouping the subjects who developed PE in later stages of pregnancy (the PE group) and those who did not develop PE in later stages (the control group).

Out of 200 subjects 94 were primigravida and 106 were multigravida. From the total subjects 16 developed PE, which shows a prevalence of about 8.4%. The PE group showed a relatively higher value of ACR as compared to control group. 106 subjects had MA out of which 13 developed PE. The sensitivity of ACR in predicting the development of PE was 80%, specificity 49.54%, PPV 12.69% and NPV 96.42%. Regarding urinary collagen IV the PE group showed no significant difference with the value of the control group. 103 subjects had high urinary collagen IV and out of them 11 developed PE. The sensitivity of high urinary collagen IV in prediction PE was found to have no significant difference with ACR in this respect. The data suggest the following conclusions:

- Early pregnancy levels of microalbuminuria and urinary collagen IV can be used as predictors of PE with high negative value.
- Urinary collagen IV has no added advantage over MA in this respect.

Keywords : MA–Micro

Introduction

Hypertensive status in pregnancy include preeclampsia (PE)- eclampsia, chronic hypertension (either essential or secondary to renal disease, endocrine disease or other causes), chronic hypertension with superimposed PE and gestational hypertension[1].

PE as hypertension accompanied by proteinuria presenting after the 20th week of gestation. A diagnosis of eclampsia is made when a patient demonstrates seizure activity or coma in addition to signs and symptoms of PE[2].

PE occurs in about 6% of the general population; the incidence varies with geographic location (Reyanolds et al 2003). In the developing countries like Bangladesh, the incidence is expected to be higher[28].

PE is the second leading cause of maternal mortality constituting 12% to 18% of pregnancy related maternal deaths.[5] Women with PE are at increased risk for such complications as abruptio placenta, acute renal failure, cerebral hemorrhage, disseminated intravascular coagulation, pulmonary edema, criculatory collapse and eclampsia[27]. PE is strongly associated with adverse pregnancy outcome[32].

For practical purpose, most studies or potential screening test for PE have relied on clinical criteria to confirm the diagnosis. Many proposed screening tests have been found suitable for early detection of PE[10]. Clinical history is the simplest test. Others are average second trimester MAP> 90 mm of Hg, angiotension infusion test, rollover test, uterine artery doppler wave forms at 18-22 weeks[30].

Second trimester MAP has low sensitivity and low positive predictive value as an indicator of future development of PE[1]. Amgiotensin II infusion test has a high incidence of

false negative and false positive results moreover it has been found to be unsuitable and impractical for the routine evaluation of pregnant women. Supine pressor 'rollover' examination has poor sensitivity, poor specificity and limited clinical value.

Biochemical tests suggested for prediction of PE urinary calcium, urinary kallikrein to creatinine ratio, serum AFP/hcG, plasma fibronection, serum inhibin, serum urate, hematocrit, antihrombin III and plasminogen activator inhibitors[1,2]. In most cases of PE, all the above factors are found to be associated in varying frequency and combination. It is clear that no test found to be associated in varying frequency and combination. It is clear that no test reliably predicts PE.[29] Further studies are going on to detect an effective and practical early predictor of PE which will be of 'gold standard'.

All the previous studies suggested that concluded that microalbuminuria cannot be used to predict which normal woman will develop PE. These controversial results promoted the interest to detect a more suitable predictor for PE.

More recent studies have claimed that increased urinary levels of collagen IV are detected in conditions where glomerular injury is found particularly in diabetic nephropathy[22].

The aim of this study was to detect some biochemical marker that can successfully predict PE. So, here my attempt was to detect the predictive value of urinary collagen IV levels in pregnant women who are free from symptoms of PE. detection of urinary collagen IV levels is pregnant women might have more predictive value in subsequent development of PE than microalbuminuria.

Aims And Objective

The objectives of the present study were:

To measure the urinary levels of albumin and collagen IV during first trimester of pregnancy and to determine whether the presence of the above molecules in the urine of asymptomatic pregnant women can predict the subsequent development of PE.

Materials And Methods

Place of the study:

The prospective study was conducted at the Department of Obstetrics and Gynecology, DMCH, BSMMU, BIRDEM, during the period of Jan 2007 to December 2008.

Subjects

A total number of 200 pregnant women at 10-14 weeks of pregnancy were selected on the basis of availability.

Inclusion criteria:

- All women at their 10 to 14 weeks of pregnancy.
- Women at their reproductive age, having no other complications or associated disease.

Results

In the present study, 200 women were included. All were at their 10-14 weeks of pregnancy without any complication or any known risk factors for developing preeclampsia. Among them PE developed in 16 patients. The rest 184 patients remained normotensive (Controls). The prevalence of PE among the study group was 8%.

Table- 1: Anthropometric and clinical parameters of the study subjects.

Group	Age Years	BMI kg/m²	SBP mmHg	DBP mmHg	MAP mmHg
Control n=184	25±4	22.68±3.49	105±11	67±9	80±8
PE n= 16	26±5	24.54±4.35	134±11	92±10	106±9
t/p value					
Control vs. PE	0.68/0.49	1.58/0.11	7.7/0.001	8.80/0.001	9.30/0.001

BMI, Body Mass Index; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MAP, Mean Arterial Pressure; n, number of subjects. Results are expressed as mean ±SD, t/p value was calculated using by Student's unpaired t-test;

Table- 2: Percentage of PE among Collagen IV and ACR positive case.

	Total	Control %	PE	PE%
Coll-IV+	103	88.53	11	11.47
ACR +	106	87.30	13	12.69

Coll-IV, Urinary collagen IV; PE, Preclampsia; ACR, Albumin Creatinine Ratio.

Table-3 : The sensitivity, specificity and predictive values of ACR for PE.

	PE		
ACR	+	-	Total
+	13	93	106
-	3	91	94
Total	16	184	200

Table- 4: The sensitivity, specificity and predictive values of collagen IV for PE.

	PE		
Coll-IV	+	-	Total
+	11	91	103
-	5	93	97
Total	16	184	200

Table- 5: Comparison of collagen IV against ACR as a predictor of PE.

	PE		
Coll- IV	+	-	Total
+	61	42	103
-	45	52	97
Total	106	94	200

Discussion

Prediction of PE in the early stages of pregnancy can be very helpful in preventing the disorder or in decreasing its severity. It has, thus, become a major focus of research in PE.

An albumin excretion between 25 and 250 mg/day is defined as MA and its presence indicates glomerular dysfunction resulting from generalized microvascular damage[1].

The sensitivity of prediction PE by measuring MA in early pregnancy varied between 50% to 68%, the specificity varied between 58 to 97%, PPV varied between 26 to 61% and the NPV varied between 87-94%[8,10].

Out of 200 pregnant subjects screened 16 developed PE in later stages; thus the prevalence is about 8.4% which is little lower than the usual values in the developing world, but seems to be reasonable is an urban setting. The present data shows that the group of pregnant subjects who developed PE in later stages had significantly higher values of ACR as compared to cases who did not develop PE.

In the absence of reference range of ACR in early pregnancy the ACR cut-off point for normal subjects (32 mg/g) was taken as the cut-off point in our subjects.[22] Using this criteria 106 patients had MA, among whom 13 developed PE in later pregnancy and 93 did not develop PE.

The sensitivity of MA as a predictor of PE was found to be 80% which lies above the values reported by various authors. The specificity in the present study 49.54%, however, was slightly lower. The NPV in the present study was 96.42% which corresponds to the values of 94.40% as reported by Bar et al 1996 and the PPV was 12.69% which is much lower than that reported by Das et al (1996)[3,13].

In the present study the urinary collagen IV level in the pregnant subjects who developed PE in later stages [2.74 (1.60-7.5) ng/ml, p= 0.244]. Since there is no published data on the reference ranges of urinary collagen IV in early pregnancy we used the median value in normal subjects (2.54 ng/ml) as a cut-off point. Using these criteria 103 (88.53%) patients had high collagen (IV) and out of those 11 (11.47%) developed PE in later pregnancy. The sensitivity of urinary collagen IV in predicting PE was 70%, specificity 50.50%, PPV 11.50% and NPV 94.8%.

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