

MICRO-ALBUMINURIA AT MID PREGNANCY IN THE PREDICTION OF PREECLAMPSIA

By

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ABSTRACT

Background: Proteinuria has classically been an important finding in the diagnosis of preeclampsia and eclampsia, so in our study we use measuring microalbuminuria as a predictor of preeclampsia.

Objective: To evaluate microalbuminuria at mid pregnancy, as a predictor of preeclampsia.

Patients and Methods: This prospective observational study was carried out on 200 normotensive women, aged 18-35years, and live singleton pregnancy between 24-28 weeks at Embaba General Hospital during the period between April 2019 and February 2020. Microalbuminuria was measured in urine samples of the first micturition of the day. All were followed till delivery.

Results: Negative microalbuminuria was present in 154 patients, 6 (3.89%) developed preeclampsia. Forty six women had positive microalbuminuria and 12 (26%) of them developed preeclampsia. The sensitivity was 66.7%, specificity 81.3%, the positive predictive value was 26.1%, and the negative predictive value was 96.1%.

Conclusion: Microalbuminuria at mid pregnancy could be a significant predictor of preeclampsia.

Key Words: Microalbuminuria, prediction of preeclampsia.

INTRODUCTION

Preeclampsia (PE) is a pregnancy-specific disorder that has a worldwide prevalence of 5–8%. It is one of the main causes of maternal and perinatal morbidity and mortality globally and accounts for 50 000–60 000 deaths annually (*Gathiram et al., 2016*).

PE is a complex disease of pregnancy and it is defined by hypertension after 20

weeks gestation and proteinuria or other evidence of multisystem involvement (*Jillian et al., 2017*). However, the pathophysiology of PE remains incompletely elucidated. Circulating factors are postulated to be produced by the placenta as a result of oxidative stress. This may cause excessive systemic inflammatory response and generalized maternal endothelial dysfunction,

contributing to the maternal clinical features of PE (*Oliveira et al., 2010*).

Microalbuminuria refers to an abnormally increased excretion rate of albumin in the urine in the range of 30-299 mg/g creatinine. It is a marker of endothelial dysfunction and increased risk for cardiovascular morbidity and mortality especially, but not exclusively, in high-risk populations such as diabetics and hypertensives (*Jayaballa et al., 2015*).

We conducted this study to determine the prevalence of microalbuminuria in low risk pregnant women at mid pregnancy and its correlation with the development of preeclampsia.

PATIENTS AND METHODS

This prospective observational study was carried out on 200 pregnant women at Embaba General Hospital.

The study was approved by the ethics committee of our institute.

Inclusion criteria:

Normotensives, Age 18-35 years old, Pregnant 24-28 weeks, Live singleton pregnancy.

Exclusion criteria:

Women with history of any medical disease, Age below 18 years and above 35 years, multiple pregnancy, Patient with past history of pre eclampsia.

All patients were submitted for oral and written consents.

The study was done on 200 cases included according to the inclusion and exclusion criteria as previously described

in the period between April 2019 and February 2020. A random urine samples were collected under complete aseptic condition, preferred to be the first sample at morning then microalbumin measurement were done. All patients were followed till delivery.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Chi-square (x²) test of significance was used in order to compare proportions between qualitative parameters.
- Evaluation of Diagnostic Performance:
- Sensitivity = (true +ve) / [(true +ve) + (false -ve)].
- Specificity = (true -ve) / [(true -ve) + (false +ve)].
- PPV=(true+ve)/[(true+ve)+(false +ve)].
- NPV=(true -ve)/[(true-ve)+(false-ve)].
- Accuracy= (TP+TN)/[TP+FP+TN+FN]
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

P-value <0.05 was considered significant.

RESULTS

In this study, urinary albumin concentration in urine samples of the first micturation of the day were assayed in 200 low-risk pregnant women at gestational age of 24 – 28 weeks . Of the 200 patients, 154 had a negative microalbuminuria, 6 (3.89%) developed preeclampsia. Forty six women had

positive microalbuminuria and 12 (26%) of them developed preeclampsia and 34 (73.9%) did not. The sensitivity was 66.7%, specificity 81.3%, the positive predictive value was 26.1% and the negative predictive value was 96.1% (Table 1).

Table (1): Pregnancy out come in normo-albuminuric cases and micro-albuminuriccases

Groups	Total (n=200)		Normo-albuminuric (n=154)		Micro-albuminuric (n=46)		x ²	p-value
	No.	%	No.	%	No.	%		
Pre-Eclampsia								
Present	18	9%	6	3.9%	12	26.1%	8.682	<0.001
Absent	182	91%	148	96.1%	34	73.9%		

There was a statistically significant relation between albuminuric cases and pre-eclampsia and the sensitivity was 66.7%, specificity 81.3%, the positive

predictive value was 26.1% and the negative predictive value was 96.1% (Table 2).

Table (2): Diagnostic performance for prediction of pre-eclampsia using the micro-albuminuria

Groups	Pre – Eclampsia				Total (n=200)		Sensitivity	Specificity	PPV	NPV	Accuracy
	Present (n=18)		Absent (n=182)								
	No.	%	No.	%	No.	%					
Micro-albuminuria											
Present	12	66.7	34	18.7	46	23	66.7%	81.3%	26.1%	96.1%	80.0%
Absent	6	33.3	148	81.3	154	77					

DISCUSSION

Pre-eclampsia remains a major cause of perinatal and maternal morbidities and mortality, and is one of the most common medical complications of pregnancy (Senna and Abonar, 2017).

Preeclampsia and eclampsia occur in up to 10% of all pregnancies. Preeclampsia describes a common syndrome that occurs in the second half of pregnancy and often manifesting with hypertension and proteinuria. It is the

second leading cause of maternal mortality worldwide, constituting 12-18% of pregnancy related maternal deaths (Pontius and Vieth, 2019).

Proteinuria has classically been an important finding in the diagnosis of preeclampsia and eclampsia. However, customary dipstick methods for detecting proteinuria fail to detect minimal elevation in urinary excretion of albumin that may be present before other clinical signs and symptoms of preeclampsia with radioimmunoassay and other sensitive

methodology for detection of microalbuminuria, it is now possible to detect minimal elevation in albumin excretion that have gone unnoticed in the past. Microalbuminuria refers to sub-clinical elevation of urinary albumin excretion (*Parving and Rossing, 2020*).

In current study the majority of studied cases 38.0% were gravida 2, while 28.0% had one or three gravidity, and only 6.0% were 4 gravida. As regarding to parity, 38.0% of cases were para 1, while 28.0% of them either had no or two parity and 6.0% of cases.

This finding was supported by *Divya (2017)* who reported that young primi 30 years of age are said to have increased chance of preeclampsia. Primigravida are 15 times more affected than multigravida.

These figures were similar to those seen by *Jensen et al. (2010)* whose median ages were 27 years for microalbuminuria group and 28 years for non-microalbuminuria group. They found that micro-albuminuria was more frequently seen among nulliparous versus multiparous women, but with a non-significant difference, on the other hand, our study population were much younger than those seen by *Sandvik et al. (2013)* whose patients' mean age was 37.9 years among cases with preeclampsia and 39 years among cases without preeclampsia.

This study showed a statistically significant relation between presence of microalbuminuria and incidence of pre-eclampsia (26.1% of cases developed preeclampsia had microalbuminuria versus 3.9% had normoalbuminuria). This can be explained by persistent micro albuminuria is indicative of huge possibility of impairment of the filtration

capability of the glomeruli of the kidney, and it is of great importance as a likely forecaster of preeclampsia in pregnancy (*Rafi et al., 2019*).

In harmony with current study, prospective case control study by *Chawla and Malik (2018)* showed that Pre-eclampsia was more prevalent in the microalbuminuric group 46.7% and 10% of patients in group B developed pre-eclampsia with significant difference between both groups.

In agreement with the present study, *Senna and Abonar (2017)* reported that microalbuminuria might be used as an early marker of endothelial dysfunction in pre-eclampsia, before the onset of the overt syndrome, as it is likely that overt proteinuria is preceded by a microalbuminuric phase. The difference was highly significant among the groups.

Moreover, *Divya (2017)* showed a relationship of microalbuminuria and development of pre- eclampsia. 36% of patients with microalbuminuria 30-300 mg/l developed pre- eclampsia and 63.8% didnot develop pre-eclampsia even with microalbuminuria positive. *Sobh et al. (2016)* showed that the proportion of women with microalbuminuria who developed preeclampsia was greater compared with those with normoalbuminuria.

Similarly, in *Kattah et al. (2013)* found that women with severe preeclampsia had an ever-higher risk of developing microalbuminuria, with an 8-fold increase over women with uncomplicated pregnancies. *Singh et al. (2013)* found out that the microalbuminuria in second trimester was highly linked with development of pre-eclampsia, late in

pregnancy. Moreover, *Jensen et al. (2010)* found a highly significant rise of blood pressure among patients with microalbuminuria compared to those with non-microalbuminuria. They found that preeclampsia was seen in 41% of patients with microalbuminuria, compared to only 12% of patients with non-microalbuminuria, with a significant difference.

This study showed that, microalbuminuria can predict development of preeclampsia with diagnostic accuracy of 80%, sensitivity of 66.7% specificity of 81.3% positive predictive value of 26.1% and negative predictive value of 96.1%. Our results was in line with *Chawla and Malik (2018)* who found the sensitivity, specificity, positive predictive value, negative predictive value of microalbuminuria for the prediction of developing pre-eclampsia was 82.3%, 62.7%, 46.6%, 93.3% respectively. Moreover, according to *Senna and Abonar (2017)* the predictive values of microalbuminuria in the pathogenesis of preeclampsia were: sensitivity 80%, specificity 72.2%, positive likelihood ratio 288%, negative likelihood ratio 22.7%, positive predictive value 24.2%, negative predictive value 97%, Odd's ratio 10.4 and lastly accuracy 76.1%. *Sobh et al. (2016)* found that testing for microalbuminuria was accurate in predicting preeclampsia in almost 85% of cases.

In accordance with current study, microalbuminuria has the sensitivity of 7 to 90 % and specificity of 29 to 97 % in predicting pre-eclampsia as in study by *Conde-Agudelo et al. (2015)*.

However, one of the reasons of this variability is the lack of strict criteria regarding the selection of the PE subjects and in most of the cases the PE was mixed up in different proportions.

CONCLUSION

The prevalence of microalbuminuria in low risk pregnant woman is high (23%) and microalbuminuria in mid pregnancy could be a significant predictor of development of preeclampsia.

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تقييم الزلال البولي الضئيل (الميكروألبومين) فى فترة منتصف الحمل ودوره فى توقع حدوث تسمم الحمل

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خلفية البحث: يعد اكتشاف بروتين البول عاملاً مهمًا فى تشخيص تسمم الحمل، لذلك نعتمد فى دراستنا على تقييم الزلال البولي الضئيل (الميكروألبومين) كإشارة إلى توقع حدوث تسمم الحمل.

الهدف من البحث: تقييم الزلال البولي الضئيل (الميكروألبومين) فى فترة منتصف الحمل ودوره فى توقع حدوث تسمم الحمل.

المرضى وطرق البحث: تم إجراء هذه الدراسة فى مستشفى إمبابة العام ف الفترة من أبريل 2019 إلى فبراير 2020، وتم إدراج 200 حالة وفقاً لمعايير الاشتمال والاستبعاد تم متابعتهم حتى ميعاد الولادة، حيث تم سحب عينات بول عشوائية من الأمهات تحت ظروف التعقيم ثم تم قياس نسبة الميكروألبومين وكان الناتج يتراوح ما بين 30-299مجم/جم فى الحالات التى لديها زلال بولي ضئيل.

نتائج البحث: خضعت 200 حالة للدراسة 46 حالة منهم فقط كان لديها زلال بولي ضئيل اما 154 حالة لم يكن لديهم زلال بولي ضئيل. تم متابعة الحالات (بعد تحديد عمر الحمل عن طريق الأشعة التلفزيونية او حسابات الأم) حتى الولادة ووجد أن 12 حالة من 46 أصيبت بتسمم الحمل ووجد أيضاً أن 6 حالات فقط من 154 اللاتى لم يكن لديهم زلال بولي ضئيل اصيبت بتسمم الحمل.

الإستنتاج: تبين من البحث أن الزلال البولي الضئيل يوجد فى نسبة عالية من السيدات الحوامل اللاتى ليس لديهن خطورة (23%)، و أن الزلال البولي الضئيل فى منتصف الحمل يعتبر دلالة ذات أهمية فى التنبؤ بحدوث تسمم الحمل.

الكلمات الدالة: تقييم الزلال البولي الضئيل (الميكروألبومين)، تسمم الحمل.