Comparison of obstetric outcome in pregnant women with and without microalbuminuria

Harneet Singh, Sunita Samal, Akshaya Mahapatro, Seetesh Ghose

Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College & Research Institute, Puducherry, India

Address for correspondence: Dr. Sunita Samal, Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College & Research Institute, Puducherry - 607 402, India. E-mail: sunisamal@rediffmail.com

Abstract

Background: Maternal and neonatal outcome is an index of quality of health and life in human society. To predict serious outcomes in pregnancy various parameters are being researched so that pregnant women who are at risk are identified early and measures taken to ensure a good outcome of pregnancy. Studies have shown an association between microalbuminuria and adverse pregnancy outcome. This study was undertaken to compare obstetric outcome in pregnant women with and without microalbuminuria.

Materials and Methods: A prospective cohort study was performed on 69 pregnant women between 20 and 28 weeks of gestation. Urine tests for albuminuria and creatinine measurements were performed in all women and the albumin to creatinine ratio was calculated. The women with microalbuminuria and those without microalbuminuria were monitored until the end of their pregnancy and compared for pregnancy outcome.

Results: The age distribution in the two groups was found to be similar and comparable. Preterm labor was strongly associated with microalbuminuria group \( P = 0.001 \) strongly significant. Incidence of maternal complications were more with microalbuminuria group \( P < 0.001 \) significantly. Fetal complications were significantly more in terms of intrauterine growth restriction, prematurity, low birth weight, low Apgar score and more incidence of neonatal intensive care unit admission with microalbuminuria group \( P = 0.010 \) moderately significant. Conclusion: It was found that fetal complications were more associated with babies of pregnant women with microalbuminuria. Though maternal complications were more associated with microalbuminuria group, individual events like premature rupture of membrane, preterm premature rupture of membrane had no statistically significant association with microalbuminuria except preterm labor. However, occurrence of pre-eclampsia was more with microalbuminuria, though it didn’t carry any statistical significance.

Key words: Intrauterine growth retardation, microalbuminuria, pre-eclampsia, preterm labor, preterm premature rupture of membrane

INTRODUCTION

The development of proteinuria is accepted as a poor prognostic sign during uncomplicated pregnancy and is associated with increasing maternal and perinatal morbidity and mortality. Pre-eclampsia, gestational diabetes, preterm labor, intrauterine growth restriction (IUGR) and preterm premature rupture of membranes (PPROM) have a major impact on fetal and maternal well-being. Various researches have been done in predicting these serious events during pregnancy. Vascular dysfunction has been suggested as an etiologic precursor of pre-eclampsia, IUGR, and preterm labor and albuminuria might be a potential marker for such an endothelial dysfunction. In addition, the release of cytokines could be a trigger of preterm labor and PPROM.\(^{[1]}\) Microalbuminuria is defined as urinary excretion of albumin that is persistently above the normal range of <30 mg although below the detectable range of conventional dipstick method. Few authors have found that microalbuminuria occurs a few weeks prior to the appearance of significant proteinuria and hence is a predictor of pre-eclampsia.\(^{[2]}\) Several authors have proposed microalbuminuria as a potential predictor of pre-eclampsia.\(^{[3]}\) Other reports state that microalbuminuria might be a predictor of pre-eclampsia and eclampsia.\(^{[4-6]}\) However, according to Conde-Agudel
microalbuminuria has a sensitivity of 7.9-90% and specificity of 29.97% for the prediction of pre-eclampsia and is, therefore, of low value in the clinical practice. Preterm birth has also been linked to maternal albuminuria, with the risk of preterm labor increasing with the severity of albuminuria. Thus, conflicting results have been found regarding the importance of microalbuminuria measurement while determining an adverse pregnancy outcome. As the test is fast, inexpensive and simple there is a need to conduct further research to find good evidence for the usefulness of microalbuminuria measurement, so that we can identify at risk women and they can be managed accordingly.

MATERIALS AND METHODS

A prospective cohort study, conducted in Mahatma Gandhi Medical College and Research Institute from December 2011 to March 2013. Pregnant women between 20 and 28 weeks of gestation who fulfilled the inclusion criteria of blood pressure <140/90 mm of Hg, normal one step glucose tolerance test and no pre-existing renal conditions were recruited after informed consent for their participation. Pregnant women with history of hypertension, diabetes mellitus and preterm labor in a previous pregnancy, multiple pregnancy, history of systemic disorder for which they had received drug treatment, urinary tract infection were excluded from the study. A total of 69 cases were studied. All participants were fully informed about the study and provided written informed consent at the time of enrollment. A detailed history was taken, general physical and systemic examination including obstetric examination were done. Random morning urine samples obtained from participants and the urine albumin and creatinine concentrations were determined by Jaffe method. Albumin creatinine ratio (ACR) is a ratio between two measured substances (urine albumin mg/dl/urine creatinine g/dl). Unlike a dipstick test for albumin, it is unaffected by variation in urine concentration. ACR was calculated to evaluate the presence of microalbuminuria. ACR calculated to evaluate the presence of microalbuminuria.

- ACR <3 mg/g - absence of microalbuminuria.
- ACR 3-20 mg/g - mild microalbuminuria.
- ACR >20 mg/g - severe microalbuminuria.

Women were monitored until delivery for the development of pre-eclampsia, preterm labor, PPROM and gestational diabetes and fetus for IUGR, preterm birth and fetal distress. Patients were followed up directly who delivered in our institution. Descriptive statistical analysis had been carried out in the present study. Results on continuous measurements were presented on mean ± SD (min-max) and results on categorical measurements were presented in a number (%). Significance was assessed at 5% level of significance. Statistical software: The statistical software namely Statistical analysis system 9.2, StatisticalPackage for Social Science 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver. 2.11.1 were used for the analysis of the data.

RESULTS

A total of 69 pregnant women between 20 and 28 weeks period of gestation (POG) were recruited after satisfying the inclusion and exclusion criteria. Group-1 included pregnant women with microalbuminuria and Group-2 included pregnant women without microalbuminuria. Age distribution in the two groups was similar and comparable [Table 1]. Mean POG is significantly less in pregnant women with microalbuminuria ($P = 0.001^{**}$) [Table 2]. A/C ratio was significantly more associated with pregnant women with microalbuminuria with $P \leq 0.001^{**}$ [Table 3]. Microalbuminuria group had 38.5% of induced labor, whereas the other group had only 14.3% ($P = 0.045^{*}$). PPROM was the leading indication of induction in both the groups [Table 4]. Cesarean

### Table 1: Age distribution

| Age in years | Pregnant women without microalbuminuria (%) | Pregnant women with microalbuminuria (%) |
|--------------|--------------------------------------------|------------------------------------------|
| <20          | 2 (3.5)                                    | 1 (7.6)                                  |
| 21-25        | 33 (58.9)                                  | 9 (69.2)                                 |
| 26-30        | 18 (32.1)                                  | 3 (23.07)                                |
| 31-35        | 3 (5.3)                                    | nil                                       |
| Total        | 56                                          | 13                                        |

### Table 2: Fetal maturity

| Maturity | Pregnant women without microalbuminuria (%) | Pregnant women with microalbuminuria (%) | Total (%) |
|----------|--------------------------------------------|-----------------------------------------|-----------|
| Preterm  | 7 (12.5)                                   | 7 (53.8)                                | 14 (20.3) |
| Term     | 49 (87.5)                                  | 6 (46.2)                                | 55 (79.7) |
| Total    | 56 (100)                                   | 13 (100)                                | 69 (100)  |

### Table 3: Albumin/creatinine ratio

| Albumin/creatinine ratio | Pregnant women without microalbuminuria (%) | Pregnant women with microalbuminuria (%) | Total (%) |
|--------------------------|--------------------------------------------|-----------------------------------------|-----------|
| <3                       | 56                                         | Nil                                     | 63 (91.3) |
| 3-20                     | Nil                                        | 10                                      | 6 (8.7)   |
| >20                      | Nil                                        | 3                                       | 69 (100)  |
section was more associated with microalbuminuria as the induction rate was also more in the same group (P ≤ 0.001**) [Table 5]. Preterm birth was more common with Group-1, 53.8% compared to 12.5% in pregnant women without microalbuminuria (P = 0.001**) [Table 6]. Majority of the pregnant women with microalbuminuria had delivered low birth weight babies (1500-2500 g) (61.5%) while Group-2 had babies birth weight between 2500 and 3500 g (64.3%) (P = 0.007**) [Table 7]. IUGR found in 30.8% of pregnant women with microalbuminuria and only in 3.6% of Group-2 [Table 8]. Low Apgar score was also significantly associated with pregnant women with microalbuminuria (P = 0.005**) [Table 9]. So the incidence of neonatal intensive care unit (NICU) admission were more with Group-1 (P ≤ 0.001**) [Table 10]. In microalbuminuria group 69.2% had complications like premature rupture of membrane (PROM), PPROM, pre-eclampsia while only 12.5% of women had these complications in the other group [Table 11]. With reference to specific maternal complication, PPROM had occurred in almost same frequency in both groups (55.6%/57.1%). PROM was not seen in any pregnant women with microalbuminuria and only in two women (28.6%) in without microalbuminuria group. Pre-eclampsia was reported in 44.4% of Group-1 and in only 14.3% of Group-2 [Table 11].

**DISCUSSION**

Several studies have been attempted to predict adverse outcomes in pregnancy by different clinical, biophysical and biochemical tests. A total of 69 women were recruited and microalbuminuria was checked between 20 and 28 weeks of pregnancy and divided into two groups. First group comprised of pregnant women with microalbuminuria and the second group included pregnant women without microalbuminuria.

The pregnant women in the two groups were age matched (P = 0.536). Bahasadri et al. also found comparable age groups in their study.[9] Mean POG was significantly less in pregnant women with microalbuminuria (P = 0.001**). Hence, our study regarding preterm labor is consistent with the study by Franceschini et al. who showed that preterm labor was related to microalbuminuria in a dose-response manner.[1] However, Massé et al. did not find any relationship between the gestational age at the time of delivery and the amount of urine albumin. They concluded that urine albumin would not be a good marker for preterm labor.[10] With regard to maternal complication in this study, incidence was more with microalbuminuria group (P < 0.001**). However, individual complications like PROM and PPROM were not associated with microalbuminuria. Though the occurrence of pre-eclampsia was more with microalbuminuria group (44.4%) as compared to those without microalbuminuria (14.3%), it was not statistically significant (P = 0.308). A similar study was done by Bahasadri et al., a prospective cohort study...
study which included 490 nulliparous women who were at the end of the second trimester of pregnancy. PPROM was reported in 58 (11.8%) women, pre-eclampsia in 58 (11.8%), IUGR in 45 (9.2%), gestational diabetes in 24 (4.9%), and 83 (16.9%) women delivered preterm. Preterm labor, pre-eclampsia, IUGR, and PPROM were more common in the exposed group, but gestational diabetes occurred with the same frequency in both groups. Univariate and multivariate logistic regression analysis showed that microalbuminuria increased risks for preterm labor and pre-eclampsia. In this study, it was found that microalbuminuria was not a predictor of pre-eclampsia \((P = 0.308)\). With regard to pre-eclampsia, Salako et al. have reported that microalbuminuria might be a good predictor of this condition with a high sensitivity but a low positive predictive value. By contrast, Lara González et al. showed that microalbuminuria is not a good predictor of pre-eclampsia. Bar et al. have reported that microalbuminuria early in the third trimester of pregnancy is a good predictor of hypertensive complications in pregnancy and birth weight, but that it cannot predict IUGR and neonatal outcome. Poon et al. proposed that the appearance of clinical proteinuria in pre-eclampsia is preceded by a microalbuminuria phase. However, these authors observed microalbuminuria (determined during 11-13 weeks of pregnancy) in 55% of normal pregnancies and in only 75% of pregnancies that complicated by pre-eclampsia. The authors concluded that ACR measurement during 11-13 weeks of pregnancy does not have any more predictive value than assessment of other maternal risk factors such as race and age. The results by Poon et al. do not contradict the results of the present study because urine sampling in their study occurred earlier during pregnancy than in the present study (20-28 weeks of pregnancy), and the microalbuminuria phase might begin after 11-13 weeks of pregnancy. In the present study, incidence of induced labor \((P = 0.045)\) and cesarean section \((P < 0.001)\) was more associated with microalbuminuria group, which could be due to significant association of maternal complication \((P < 0.001)\) in the same group. With respect to fetal complication, IUGR was significantly more in babies of microalbuminuria group \((P = 0.010)\). It was also found that prematurity, low birth weight, low Apgar score and more incidence of NICU admission in babies of pregnant women with microalbuminuria. In several studies, it has been concluded that pregnancy outcome is related to renal function and the risks of pre-eclampsia, IUGR and preterm labor are increased with reduced kidney function. Gestational diabetes mellitus was not found in any of the group. But several studies have been performed in patients with diabetes who have microalbuminuria. Ekborn et al. evaluated the pregnancy outcome among women with type 1 diabetes and found that the prevalence of preterm labor was significantly increased in the group of women who had microalbuminuria. However, the researchers proposed that this could be due to pre-eclampsia. The authors also concluded that the classification of women with type 1 diabetes according to urinary albumin is superior to the White classification in predicting preterm labor. Gangaram et al. compared the diagnostic value of the micro ACR with that of the 24-h urine protein test when screening for proteinuria among pregnant women with hypertension. They reported that the value of the two tests in this context was the same and concluded that measurement of the micro ACR may be a good substitute for a random urine protein test. In the present study comparison of ACR with 24-h urinary protein was not done. However, the relationship of maternal complications like pre-eclampsia and preterm labor with microalbuminuria is still controversial. Further research with a large sample size is needed to have established relationship between microalbuminuria and maternal complication.

**Table 9: Apgar score**

| Apgar score | Pregnant women without microalbuminuria (%) | Pregnant women with microalbuminuria (%) | Total (%) |
|-------------|--------------------------------------------|----------------------------------------|-----------|
| 1-5         | 0 (0)                                      | 1 (7.7)                                | 1 (1.4)   |
| 6-7         | 3 (5.4)                                    | 4 (30.8)                               | 7 (10.1)  |
| 8-10        | 53 (94.6)                                  | 8 (61.5)                               | 61 (88.4) |
| Total       | 56 (100)                                   | 13 (100)                               | 69 (100)  |

**Table 10: NICU stay**

| NICU stay | Pregnant women without microalbuminuria (%) | Pregnant women with microalbuminuria (%) | Total (%) |
|-----------|--------------------------------------------|----------------------------------------|-----------|
| No        | 53 (94.6)                                  | 6 (46.2)                               | 59 (85.5) |
| Yes       | 3 (5.4)                                    | 7 (53.8)                               | 10 (14.5) |
| Total     | 56 (100)                                   | 13 (100)                               | 69 (100)  |

**Table 11: Specific maternal complication**

| Maternal complications | Pregnant women without microalbuminuria \((n = 7)\) (%) | Pregnant women with microalbuminuria \((n = 9)\) (%) | Total \((n = 16)\) (%) | \(P\) value (%) |
|------------------------|--------------------------------------------------------|---------------------------------------------------|------------------------|-----------------|
| PPROM                  | 4 (57.1)                                               | 5 (55.6)                                          | 9 (56.3)               | 1.000           |
| PROM                   | 2 (28.6)                                               | 0                                                  | 2 (12.5)               | 0.175           |
| PE                     | 1 (14.3)                                               | 4 (44.4)                                          | 5 (31.3)               | 0.308           |

PPROM: Preterm premature rupture of membranes, PROM: Premature rupture of membranes, PE: Pre-eclampsia
CONCLUSION

It was found that fetal complications were more associated with babies of pregnant women with microalbuminuria. Maternal complications were also more with microalbuminuria group, but individual events like PROM, PPROM had no statistically significant relation with microalbuminuria group except with preterm labor. Though occurrence of pre-eclampsia was more with microalbuminuria, it didn’t carry any statistical significance.

REFERENCES

1. Franceschini N, Savitz DA, Kaufman JS, Thorp JM. Maternal urine albumin excretion and pregnancy outcome. Am J Kidney Dis 2005;45:1010-8.
2. Bar J, Hod M, Erman A, Friedman S, Gelerenter I, Kaplan B, et al. Microalbuminuria as an early predictor of hypertensive complications in pregnant women at high risk. Am J Kidney Dis 1996;28:220-5.
3. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams Obstetrics. 23rd ed. New York, USA: McGraw Hill; 2010.
4. Salako BL, Olayemi O, Odukogbe AT, Adedapo KS, Aimakhu CO, Alu FE, et al. Microalbuminuria in pregnancy as a predictor of pre-eclampsia and eclampsia. West Afr J Med 2003;22:295-300.
5. Lara González AL, Martínez Jaimes A, Romero Arauz JF. Microalbuminuria: Early prognostic factor of preeclampsia? Ginecol Obstet Mex 2003;71:82-6.
6. Shaarawy M, Salem ME. The clinical value of microtransferrinuria and microalbuminuria in the prediction of pre-eclampsia. Clin Chem Lab Med 2001;39:29-34.
7. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002;39 2 Suppl 1:S1-266.
8. Risberg A, Larsson A, Olsson K, Lyrenäs S, Sjöquist M. Relationship between urinary albumin and albumin/creatinine ratio during normal pregnancy and pre-eclampsia. Scand J Clin Lab Invest 2004;64:17-23.
9. Bahasadri S, Kashanian M, Khosravi Z. Comparison of pregnancy outcome among nulliparas with and without microalbuminuria at the end of the second trimester. Int J Gynaecol Obstet 2011;115:3-6.
10. Massé J, Forest JC, Moutquin JM. Microalbumin as a marker of premature delivery. Obstet Gynecol 1996;87:661-3.
11. Poon LC, Kametas N, Bonino S, Vercellotti E, Nicolaides KH. Urine albumin concentration and albumin-to-creatinine ratio at 11(+0) to 13(+6) weeks in the prediction of pre-eclampsia. BJOG 2008;115:866-73.
12. Munkhaugen J, Lydersen S, Romundstad PR, Widerøe TE, Vikse BE, Hallan S. Kidney function and future risk for adverse pregnancy outcomes: A population-based study from HUNT II, Norway. Nephrol Dial Transplant 2009;24:3744-50.
13. Ekboom P, Damm P, Feldt-Rasmussen B, Feldt-Rasmussen U, Mølvig J, Mathiesen ER. Pregnancy outcome in type 1 diabetic women with microalbuminuria. Diabetes Care 2001;24:1739-44.
14. Gangaram R, Naicker M, Moodley J. Comparison of pregnancy outcomes in women with hypertensive disorders of pregnancy using 24-hour urinary protein and urinary microalbumin to creatinine ratio. Int J Gynaecol Obstet 2009;107:19-22.
15. Conde-Agudele A, Lede R, Belizan J. Evaluation of methods used in the prediction of hypertensive disorders of pregnancy. Obstet Gynecol Survey 1994;49:210-22.

How to cite this article: Singh H, Samal S, Mahapatro A, Ghose S. Comparison of obstetric outcome in pregnant women with and without microalbuminuria. J Nat Sc Biol Med 2015;6:120-4.

Source of Support: Nil. Conflict of Interest: None declared.