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Microalbuminuria: A potential marker for adverse obstetric and fetal outcome

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Abstract
Background: Obstetric and perinatal outcome is an index of health in society. Various markers are being searched so as to increase the well being of mother and fetus in pregnancy. Several Studies [12, 13] have revealed an association between microalbuminuria and obstetric outcome. Microalbuminuria can be used as prognostic marker in evaluation of gestational hypertension, preterm labour, GDM, PPROM, IUGR.
Objective: This study was done to evaluate whether microalbuminuria which was evaluated at late second trimester could serve as marker for adverse obstetric and neonatal outcome.
Materials and Methods: A Prospective case control study was carried out on 150 people. Urine tested for urine micro albumin and creatinine and ACR ratio was calculated. Among 150 pregnant women 27 were positive for microalbuminuria and were categorised as group A. Pregnant women without microalbuminuria were considered as group B (controls). Both group A and group B were compared for obstetric outcomes.
Results: Significant association found between group A and gestational hypertension and preterm labour.
Conclusion: Microalbuminuria can be used as an early prognostic marker to detect adverse obstetric and neonatal outcome. It can be done in the late second trimester (around 18-24 weeks). It is a cheap, easily available method. Presence of microalbuminuria could therefore be a warning sign for the development of gestational hypertension and preterm delivery [14]. Hence presence of microalbuminuria needs further follow up and attention and strict blood pressure monitoring along with glycemic control in order to prevent adverse obstetric outcome of pregnancy.

Keywords: Microalbuminuria, gestational hypertension, Preterm Labour

Introduction
Microalbuminuria is defined as urine albumin level of about 30-300mg/l in spot urine sample. Microalbuminuria is compared with excretion of creatinine and is expressed as albumin creatinine ratio which is 30-300mcg/mg of creatinine. Poon *et al*. [9] reported sensitivity and specificity of ACR ratio and have concluded that it can used as a substitute for microalbuminuria measurement which in turn is more accurate. Microalbuminuria in an early uncomplicated pregnancy is found to be a poor prognostic factor [2] and is related to increased maternal and perinatal morbidity and mortality in particular gestational hypertension, preeclampsia, intrauterine growth restriction, PPROM, gestational diabetes, preterm labour which have a great impact on maternal and fetal outcome.
Vascular and Endothelial dysfunction has been suggested as etiological precursor of gestational hypertension, preeclampsia, IUGR, PPROM, preterm labour. As there is an interaction in maternal placental and fetal system placental vascular dysfunction might affect maternal physiology by inducing the release of cytokines. There will be change in glomerular filtration and vascular permeability and hence increase in urine albumin. Microalbumin as suggested by various researchers could be a sign of vascular and endothelial dysfunction.
Several authors [5, 7] have proposed microalbuminuria as a predictor of preeclampsia and also few authors proposed it occurs several weeks prior to the development of significant proteinuria [11].
Preterm deliveries may occur in pregnant women with microalbuminuria or as a consequence of preeclampsia and gestational diabetes which are seen in microalbuminuric positive patients. Studies suggest that risk of preterm labour increases with increasing severity of albumin excretion. However Mass *et al*. [8] concluded that there is no significant association between preterm delivery and urinary albumin excretion.
As compared to other markers determination of microalbuminuria is easy, fast and relatively cheap method in determining various co-morbidities.

At present only very few studies have been conducted in India and there is need to conduct further research so that pregnant women at risk can be identified earlier and assisted accordingly.

Aims

The aim of the study is to compare obstetric and fetal outcome in pregnant women with and without microalbuminuria.

Objectives

1. To study microalbuminuria in antenatal women who satisfy my inclusion criteria and who are in their late second trimester. Antenatal women with and without microalbuminuria were named as Group A and Group B respectively.
2. To follow up the pregnant women belonging to Group A & Group B till delivery and monitored for any obstetric complications.
3. To compare the obstetric and fetal outcome among the antenatal women with and without microalbuminuria.
4. To subject the results to statistical analysis.

Materials and Methods

A Prospective cohort study was performed among 150 pregnant women who are in their late second trimester attending RMMCH Department of Obstetrics and Gynaecology OPD, Annamalai University for antenatal check up during the period of November 2016 to October 2018 and who satisfy my inclusion and exclusion criteria.

Inclusion criteria: Antenatal mother without any co-morbidities in their late second trimester.

Exclusion criteria: Antenatal with gestational hypertension, GDM, BMI more than 30 and other medical disorders (chronic hypertension, kidney disorders, tuberculosis etc.) and mother on treatment with drugs and those who are not consenting for the study.

All participants were informed about the study and informed consent obtained. The study was approved by the institutional review board and the institutional ethics committee.

After selecting my cases and obtaining informed written consent, complete history was taken and examination done. All routine and specific blood investigations were done.

Random Urine sample were collected and analysed for the presence of microalbuminuria by turbidimetric immunoassay and albumin creatinine ratio was calculated. Microalbuminuria is estimated by calculating albumin creatinine ratio and microalbuminuria is expressed as 30-300mcg of albumin per mg of creatinine.

Antenatal who were screened were categorized as Group A (with microalbuminuria) and Group B (without microalbuinuria). The obstetric and fetal outcome of Pregnant women belonging to Group A and Group B were followed up until delivery and obstetric outcomes in terms of Gestational hypertension, Preterm labour, PPROM, IUGR, Gestational diabetes were compared and analysed.

Data and Results

The pregnancy outcomes were analysed using Chi-square test of association. The entire statistical analysis were carried our using statistical packages of social sciences spss-21.

The mean age of the study women was 25.20±4.03 yrs.

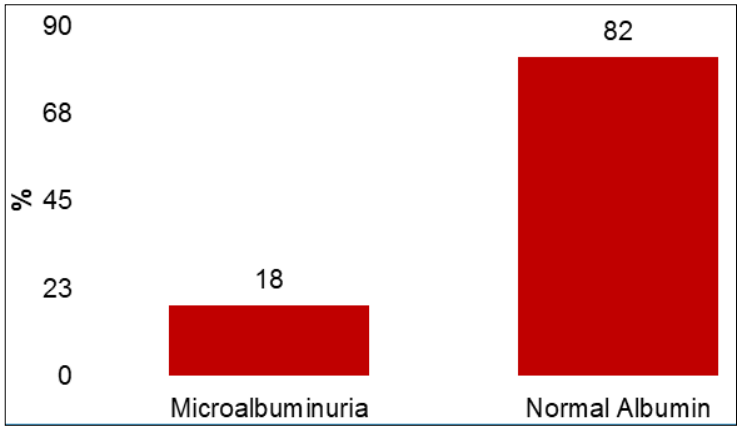

Chart 1: Incidence of Microalbuminuria

Microalbuminuria were observed in 18% of the study women. Microalbumin was negative in 82% of the women.

Table 1: Microalbuminuria values and associated outcomes.

Microalbuminuria values	Total	PIH	Preterm	IUGR	PPROM
30-40 mcg/mg	14	1	2	-	1
40-50 mcg/mg	5	1	1	1	-
50-70 mcg/mg	2	1	1	-	-
70-100 mcg/mg	4	2	-	-	-
100-150mcg/mg	1	-	1	-	-
>400(421)mcg/mg	1	-	-	-	-

It was found that no significant correlation between microalbuminuria levels and obstetric outcomes.

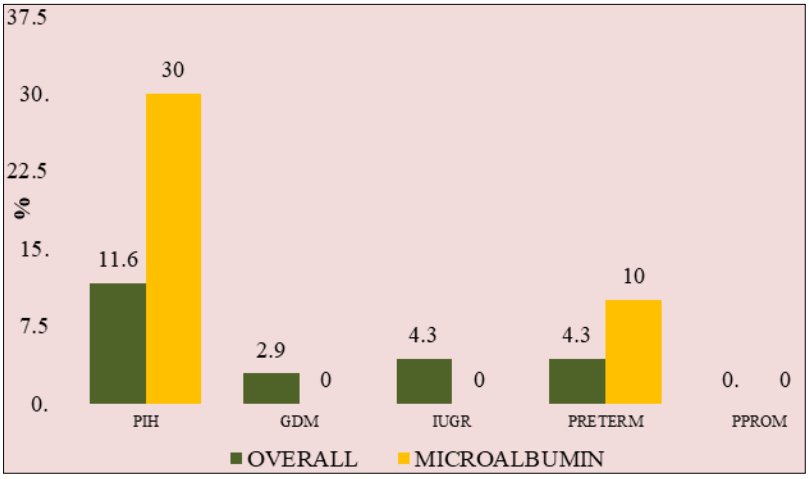

Chart 2: Overall incidence of obstetric complications among group A and B

Table 2: Overall Obstetric Outcome.

	Group A	Group B	Total
GHT	5	7	12
GDM	-	5	5
Preterm Labour	5	8	13
PPROM	1	2	3
IUGR	1	7	8

The Chi square test of association is statistically significant (X^2=4.95, p=.03). Therefore, there is significantly higher incidence of gestational hypertension among microalbuminuric group.

Table 3: Incidence of gestational hypertension

	Group A	Group B
Multigravida	2	2
Primi	3	5

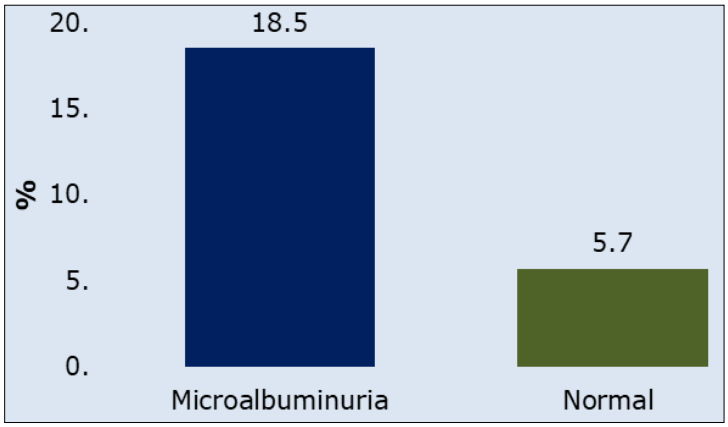

Chart 2: Incidence of gestational hypertension

The Chi square test of association is statistically significant (x2-4.95, p=0.03)

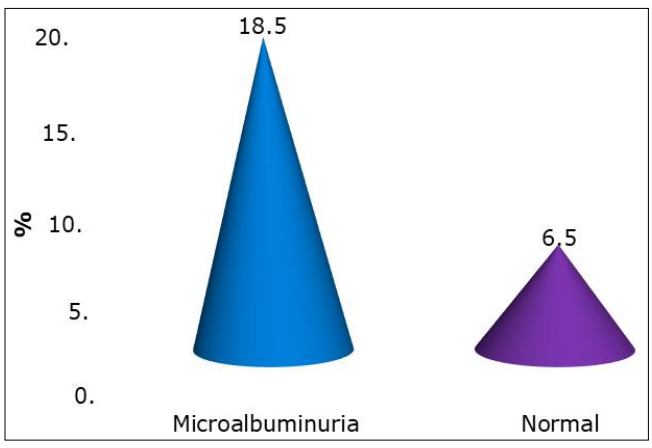

Chart 3: Preterm

Overall 8.67% of the women had preterm delivery.

Table 4: Incidence of preterm

	Group A		Group B
	No	%	
Multigravida	4	23.5%	3
Primi	1	10%	5

Incidence of preterm labour is about 7 times higher in primi belonging to group a (women with microalbuminuria) and it is about 3 times higher in multigravida belonging to group A. It is statistically significant (p=0.04).

Table 5: Comparison of birth weight

Birth Weight	Group A		Group B	
	No	%	No	%
< 2.5 kg	3	11.11%	13	10.5%
>2.5kg	24	88.8%	109	88.6%

No significant association between microalbuminuria and birth weight.

Discussion

In my study, a total of 150 pregnant women was selected, out of which 27 were positive for microalbuminuria. Microalbuminuria is evaluated in normal antenatal women (150 nos) without any comorbidities. All these case were followed up till delivery and occurrence of various obstetric complications like gestational hypertension, GDM, IUGR Preterm labour, PPROM were recorded and analysed.

In my study, Gestational hypertension was observed in 11 patients out of total 150 cases. Microalbuminuria was positive in 5 patients. 18.5% of pregnant women with microalbuminuria developed gestational hypertension [10] during follow up whereas gestational hypertension was observed in only 5.7% of pregnant women with normal range of albumin excretion. Salako *et al*. [1] have concluded microalbuminuria could be a effective predictor of preeclampsia with high sensitivity. It was found that there is significant association between microalbuminuria and subsequent development of gestational hypertension.

By contrast lara gonzalez *et al* reported that microalbuminuria is not a good predictor of preeclampsia.

Incidence of GDM among my study population is observed in only 3.3% all GDM cases in total 5 patients were in group b. the chi square test of association is statistically insignificant (x2=1.14, p=0.29). No significant association between microalbuminuria and GDM was found in my study. In contrast to a study [15] by Rachita *et al*. they have reported gestational hypertension among pregnant women with microalbuminuria and higher incidence of GDM in microalbuminuria positive patients.

Ekbom *et al*. [4] have reported increased incidence of preterm labour in pregnant women with microalbuminuria among type 1 diabetes mother [5].

In my study, both groups were followed up for incidence of threatened preterm /preterm delivery. Out of total study population 13 of the patients developed preterm labour. Overall 8.67% of the women had preterm labour. The incidence of preterm were high (total of 5 patients) among group A. On analysis there is statistical significant (p=0.04 x2=4.04) between microalbuminuria and preterm delivery. Similar results given by franceschini *et al*. [6] who concluded preterm labour was found among women with microalbuminuria group in a dose concentration manner.

In my study the incidence of IUGR was only 1 patient among microalbuminuria positive patient. IUGR was found in 5.33% of total population. The chi square test association in statistically not significant. (X^2=1.86, p=0.17).

PPROM was observed in 3.7% of group A and in 1.6% of group B. The chi square test of associaton is statistically insignificant. In a study by Harneet singh *et al*. [3], they have reported significant association with fetal complications and found no statistically significant association between microalbuminuria and obstetric complications except for preterm labour but overall incidence of preeclampsia was higher.

The relationship of microalbminuria and maternal complications like preterm labour and gestational hypertension is still controversial. Further research is needed with large sample size ignorer to establish a clear association between microalbuminuria and adverse obstetric outcomes.

Conclusion

Microalbuminuria was observed in 18% of the pregnant women studied and it was found in 14.5% of the primigravida.

The development of gestational hypertension in microalbuminuric group was found to be statistically significant.

Preterm labour was found associated significantly in women with microalbuminuria.

Hence it is concluded that microalbuminuria can be considered as a prognostic marker and can be used as a screening tool for early detection of gestational hypertension, preeclamsia and preterm labour.

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