International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Microalbuminuria Detected at Mid Term as a Marker for Adverse Pregnancy Outcome

Rachita Chawla[1], Sunita Malik[2]

[1]Senior Resident, OBG, PGIMER Rohtak
[2]Consultant OBG, Safdarjung Hospital, New Delhi

Corresponding Author: Rachita Chawla

ABSTRACT

Background: Maternal and neonatal 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. Studies have shown an association between microalbuminuria and pregnancy outcome.
This study was undertaken to find out whether microalbuminuria detected at midterm could serve as marker for adverse pregnancy outcome.
Materials and Methods: A Prospective case control study was carried out. 410 people were tested of which 30 who were positive for microalbuminuria were kept in group A.
Subjects without microalbuminuria were taken as controls (GROUP B).
They were compared for pregnancy outcome.
Results: Microalbuminuria seemed to be an important marker of pregnancy outcome.
Roughly 2/3 rd women positive for microalbuminuria were picked up before 24 weeks.
Pre eclampsia was more prevalent in the microalbuminuric group with a p value<0.05.It could be concluded that patients testing positive for microalbuminuria at midterm are likely to develop pre eclampsia roughly 10 weeks after. IUGR was also significant in the microalbuminuria positive patients. (p value<0.05). Mean duration of time elapse between detection of microalbuminuria and IUGR was 10.8 weeks. Gestational diabetes mellitus was more common in the microalbuminuric patients, although not significant. It was seen roughly 10 weeks after detection. Prom was shown to have no relation with microalbuminuria. Preterm delivery was more common in positive patients. Mean birth weight was not affected by positive patients. However it was associated with lower APGAR scores and hence the higher rate of NICU admission. Induction of labour was more commonly seen in the microalbuminuria positive patients due to co morbidities mostly pre eclampsia and prom.
Conclusion: Microalbuminuria is an important prognostic marker for adverse pregnancy outcome. It can be done around the 2nd trimester end (around 20-24 weeks). It is a cheap, easily available and cost effective method of detecting many co morbidities affecting a normal pregnancy. Presence of microalbuminuria could be a warning sign of the development of pre eclampsia, gestational diabetes which could lead to pre term delivery and the presence of IUGR. Subsequently rates of NICU admission and lower apgar scores increase with such co morbidities. In the study we found out that roughly 10 weeks period was present between detection of microalbuminuria and the onset of pre eclampsia and gestational diabetes mellitus. Therefore presence of microalbuminuria warrants attention and strict blood pressure monitoring along with glycemic control to optimize the outcome of pregnancy.
Key Words: Microalbuminuria, Pre Eclampsia, Preterm Labour, Intra Uterine Growth Retardation

INTRODUCTION

Microalbuminuria can be diagnosed from a 24-hour urine collection (between 30-300 mg/24 hours) or, more commonly, from elevated concentrations in a spot sample (30 to 300 mg/L). Both must be measured on at least two of three occasions over a two- to three-month period
The level of albumin protein can be detected by special albumin-specific dipsticks.

Pregnancy is one of the most important events in life and a poor outcome may cause serious maternal and neonatal morbidity and mortality. In particular preeclampsia, intrauterine growth retardation (IUGR), preterm premature rupture of membranes (PPROM) and gestational diabetes have a great impact on maternal and foetal safety. It is therefore necessary to detect these conditions as soon as possible to improve the prognosis of mother and foetus in the index pregnancy.

Preeclampsia is a characterised by high blood pressure and significant amounts of protein in the urine of a pregnant woman. There are different causes of this condition. Pathophysiology involves release of substances from the placenta that cause endothelial dysfunction in maternal blood vessels of susceptible women. Preeclampsia is diagnosed when a pregnant woman develops blood pressure systolic>140 and diastolic>90 (two separate readings 6 hours apart and 300 mg of protein in a 24 hour urine sample after 20 weeks of gestation.

Because of the close interactions in mother-placenta-foetus system, placental vascular dysfunction might affect maternal physiology by inducing the release of cytokines and hormones. This might result in change in glomerular filtration and vascular permeability and increase in urine albumin could therefore be an early sign of vascular dysfunction and the release of cytokines could be a trigger of pre term labour and PPROM.

Pre term deliveries (before 37 weeks of gestation) are associated with lower apgar scores indicating need for special ICU care and risk of increased neonatal mortality. Pre term deliveries may occur as a result of microalbuminuria or as a consequence of pre eclampsia and diabetes which are seen in microalbuminuria positive patients. [1]

PROM (premature rupture of membranes) is rupture of membranes prior to the onset of labour at or beyond 37 weeks of gestation. It has also been seen in association with pre term labour and microalbuminuria may serve as its marker.

Microalbuminuria is one of the markers of pregnancy outcome.

As compared to other methods determination of microalbuminuria is very easy by the test strips being used and can be done in any kind of setup. Also it is a relatively cheap modality of determining various co morbidities. Presently very few studies have been conducted in India on this subject. The work done so far is from western developed countries and there is paucity of data in our population.

MATERIALS AND METHODS

The study was conducted in the Department of Obstetrics and Gynaecology, at Vardhaman Mahavir Medical College & Safdarjung Hospital, New Delhi from September 2013 to December 2014. Before starting the study, clearance was obtained from the ethics committee of the hospital.

It was a prospective case control study.

The sample size was decided assuming prevalence of microalbuminuria to be 7.8% (with an error margin of 20%). Alpha value of study was 0.05 with power of study to be 80 % and loss to follow up to be 10%. 410 people were tested of which 30 who were positive for microalbuminuria were kept in group A.

Subjects without microalbuminuria were taken as controls (group B).

Nulliparous gravid women with singleton pregnancy attending the outpatient department of Safdarjung hospital were selected. All eligible women were approached consecutively. Those who were willing to participate and gave written informed consent were asked to provide baseline information on demographic, socioeconomic factors (age, address, husband's name, education and occupation of both, contact number and per capita income).

Group A(Cases): 30 nulliparous women coming to ANC OPD at 20-28 weeks testing positive for microalbuminuria

Group B(Controls): 30 nulliparous women in the same bracket (matched for age and

gestational age) testing negative for microalbuminuria.

INCLUSION CRITERIA were Nulliparous women with gestational age 20-28 weeks with Blood pressure <140/90 mm Hg with Serum creatinine <0.8 mg/dl and Serum uric acid<4.5 mg/dl.

EXCLUSION CRITERIA was patients with Polyhydramnios**,** Foetal anomaly, patients with presence of any systemic disease like hypertension, diabetes, kidney disease, asthma, tuberculosis, active urinary tract infections**,** gross albuminuria were excluded.

First early morning voided urine was recommended as specimen material. After a detailed history and ensuring that all inclusion criteria are fulfilled, all women were asked to give morning urine samples subsequently. All patients were counseled regarding the correct method of collecting the urine sample.

The urine samples were tested for microalbuminuria by "MICRAL" test strips

TEST COMPONENTS:

Test strip contained per cm2 – monoclonal antibodies against human albumin (immunoglobulin G) labelled with colloidal gold: 6 microgram, fixed albumin: 9.5 microgram.

Participants were followed in each antenatal visit till the time of delivery as per hospital protocol. They were screened for development of preeclampsia and gestational diabetes or any other co morbidities like pre term deliveries, premature rupture of membranes and IUGR. Neonatal outcome was seen in terms of Birth weight, NICU admission and Apgar score.

STATISTICAL ANALYSIS:

Qualitative data was analysed by Chi square test and Fischer exact test. The quantitative data was analysed by t test and skewed data by Mann Whitney U test. P value of less than 0.05 was taken as significant.

RESULTS AND OBSERVATIONS

This study was conducted in the Department of Obstetrics and Gynaecology, Vardhman Mahavir Medical College and Safdarjung Hospital, Delhi between September 2014 and December 2015.

410 women were tested and subsequently 60 consecutive women attending the outpatient department of Obstetrics and Gynaecology department of Vardhman Mahavir Medical College and Safdarjung Hospital, Delhi who fulfilled all inclusion criteria and did not fall under any of the exclusion criteria were recruited for the study.

Prevalence of microalbuminuria was found to be 7.31%. Over a period of 1 year 410 patients were examined of which 30 came out to be positive for microalbuminuria.

Table 1- Period of gestation (in weeks) at the time of detection of microalbuminuria

POG in weeks(at detection of microalbuminuria)		
< 21	10	33.33%
21-22	15	50%
23-24	5	16.7%

Maximum number of people developed microalbuminuria between 21-22 weeks 15 (50%), around 10(33.3%) cases between <21 weeks and 5 (16.7 %) between 23-24 weeks. [table 1]

Distribution according to period of gestation (in weeks) at the detection of microalbuminuria [figure 1]

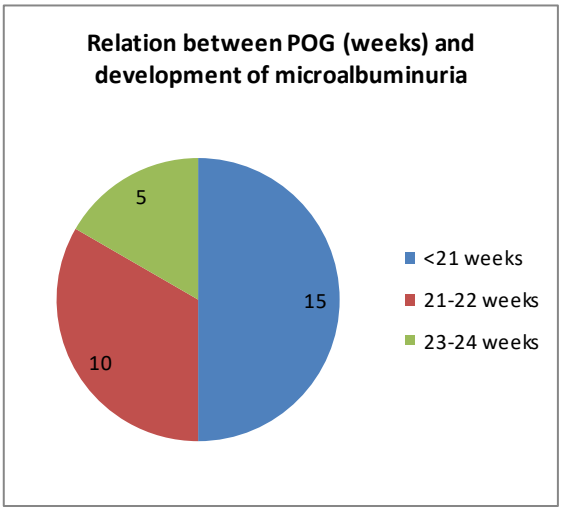

Figure 1

Pre eclampsia was found in 14 (46.7%) patients in the group A. However, only 3 patients (10%) patients in group B developed pre eclampsia. Pre eclampsia was significantly more common in group A (46.7%) than group B (10%) (p value 0.02) [TABLE 1]. It wasfound out that 8 (26.7 %) patients who were positive for microalbuminuria developed gestational diabetes mellitus in the index pregnancy. However, only 2 (6.7%) patients who were microalbuminuria negative developed gestational diabetes mellitus. The p value was 0.07 which was not significant [TABLE 2]. Premature rupture of membranes (PROM) was found in 26% of the cases whereas around the same % was found in the control group.Pre term labour was found in 11(36.7 %) patients in group A and 5 patients in group B (16.7%). However, this difference was not statistically significant (p value 0.08) [TABLE 3]. IUGR was found in 14 (46.7%) patients in group A and 3 (10 %) patients in group B. This difference was statistically significant with a p value of 0.02. [TABLE 4]. 22/30 cases (73.3%) went into spontaneous labour while labour had to be induced in 8 cases. However in the control group27 (90%) patients went into spontaneous labour. (FIGURE 2)

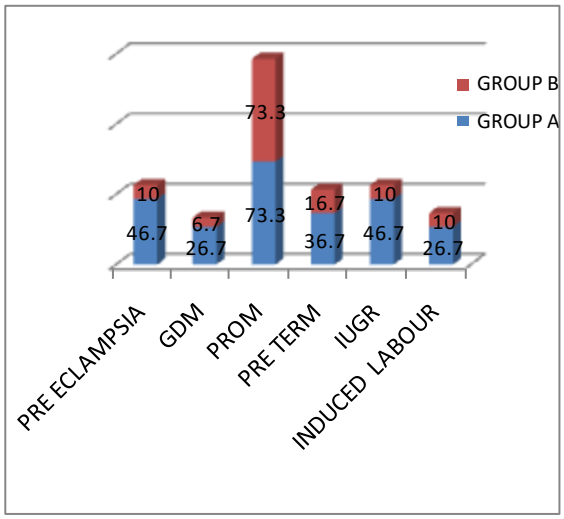

Figure 2- distribution of various study parameters in microalbuminuria positive and negative groups

Mean fetal weight was 2.5 kg in the case group and 2.42 in the control group. The mean apgar score at 1 minute was 6.4 in case group and 7.1 in control group which was found to be statistically significant (p value 0.016), whereas at 5 minutes it was 7.90 in case group and 8.17 in control group which was statistically non significant (p value 0.128)[TABLE 5]. NICU admission was found in 9 cases (30%) and 3 controls (10%) which is statistically significant (p value = 0.053) [TABLE 6] (FIGURE 3).

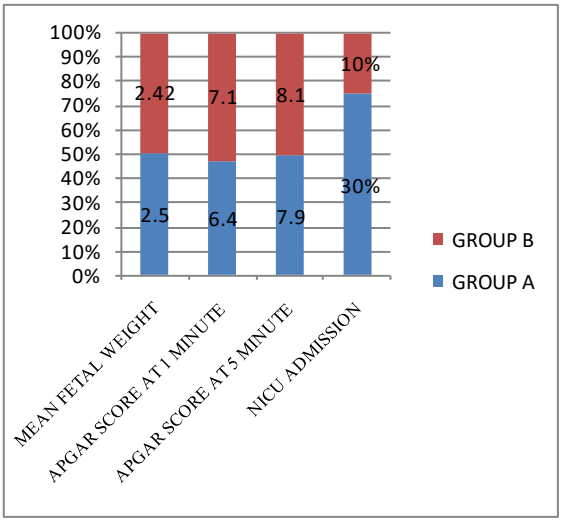

Figure 3- DISTRIBUTION OF VARIOUS FETAL PARAMETERS IN BOTH GROUPS

Mean duration of time elapse between detection of microalbuminuria and pre eclampsia was 10.5 weeks. Mean duration of time elapse between detection of microalbuminuria and gestational diabetes mellitus was 10.1 weeks. Mean duration of time elapse between detection of microalbuminuria and premature rupture of membranes was 9 weeks. Mean duration of time elapse between detection of microalbuminuria and IUGR was 10.8 weeks. (FIGURE 4)

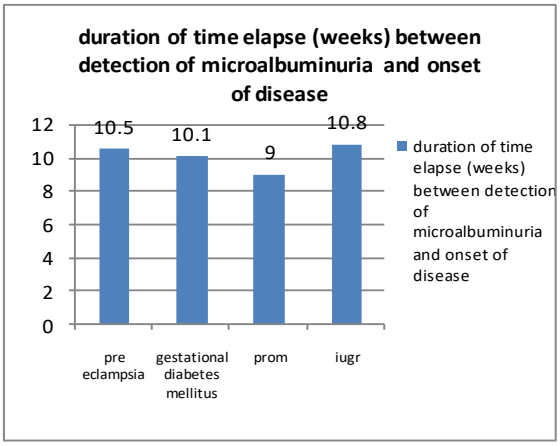

Figure 4 –TIME ELAPSE BETWEEN DETECTION OF MICROALBUMINURIA AND ONSET OF DISEASE

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. The sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria for the prediction of gestational diabetes mellitus was 80%, 56%, 26.6%, 93.3% respectively. The sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria for the development of PROM was found to be 50%, 50%, 26.6% and 73.3% respectively. The sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria for detection of pre term labour was 68.75%, 56.8%, 36.6%, 83.3% respectively. The sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria for detection of IUGR was 82.3%, 62.7%, 46.6%, 93.3% respectively (figure 5,6)

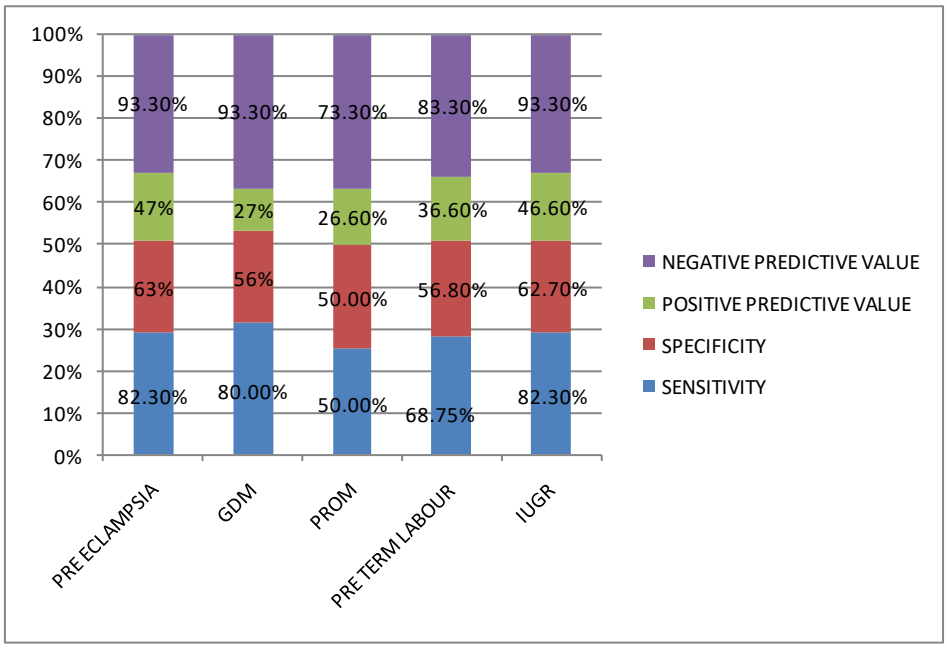

FIGURE 5- NEGATIVE PREDICTIVE VALUE, POSITIVE PREDICTIVE VALUE, SENSITIVITY AND SPECIFICITY OF MICROALBUMINURIA FOR VARIOUS MATERNAL PARAMETERS

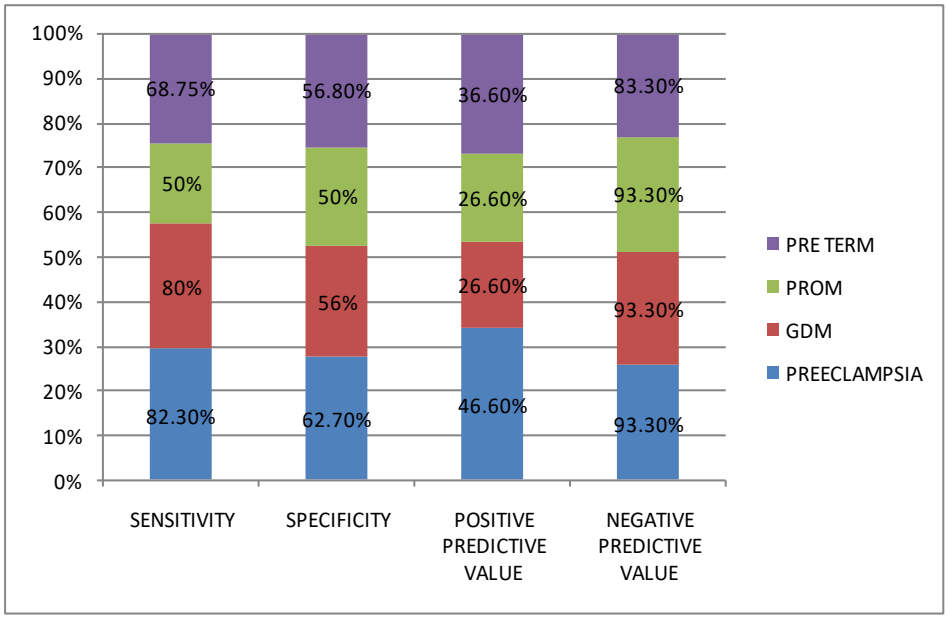

Figure 6- SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUE OF MICROALBUMINURIA FOR VARIOUS MATERNAL PARAMETERS

TABLE 1- DISTRIBUTION OF PRE ECLAMPTIC PATIENTS AMONG 2 GROUPS

	GROUP A	GROUP B	P VALUE
NEGATIVE FOR MICROALBUMINURIA	16	27	O.O2 SIGNIFICANT
POSITIVE FOR MICROALBUMINURIA	14	3	

TABLE 2- DISTRIBUTION OF GESTATIONAL DIABETES MELLITUS AMONG 2 GROUPS

	GROUP A	GROUP B	P VALUE
NEGATIVE FOR MICROALBUMINURIA	22	28	0.07
POSITIVE FOR MICROALBUMIURIA	8	2	NON SIGNIFICANT

TABLE 3- DISTRIBUTION OF PRE TERM LABOUR AMONG 2 GROUPS

	GROUP A	GROUP B	P VALUE
NEGATIVE FOR MICROALBUMINURIA	25	14	0.08
POSITIVE FOR MICROALBUMINURIA	5	16	NON SIGNIFICANT

TABLE 4- DISTRIBUTION OF IUGR IN 2 GROUPS

	GROUP A	GROUP B	P VALUE
NEGATIVE FOR MICROALBUMINURIA	16	27	0.02
POSITIVE FOR MICROALBUMINURIA	14	3	SIGNIFICANT

TABLE 5 – APGAR SCORES IN 2 GROUPS

	APGAR SCORE AT 1 MINUTE	APGAR SCORE AT 5 MINUTES
	GROUP A	GROUP B
NEGATIVE FOR MICROALBUMINURIA	7.1	8.17
POSITIVE FOR MICROALBUMINURIA	6.4	7.90
P VALUE	0.016 (SIGNIFICANT)	0.128 (NON SIGNIFICANT)

TABLE 6 – NICU ADMISSION IN 2 GROUPS

	GROUP A	GROUP B	P VALUE
NEGATIVE FOR MICROALBUMINURIA	21	27	0.053
POSITIVE FOR MICROALBUMINURIA	9	3	SIGNIFICANT

DISCUSSION

Microalbuminuria has been the focus of many studies but studies pertaining to pregnant woman have been very few. The studies done have been conducted in the western population, whose data may not pertain to the Indian scenario. Also the results have not been very conclusive.
Hence this study was carried out.

Maternal complications in pregnancy like pre eclampsia and gestational diabetes are on a rise and hence it is of utmost importance to detect them and treat them early for an optimum outcome of pregnancy thus decreasing the maternal and fetal morbidity.

Previous studies have showed the association of microalbuminuria with several co morbidities like pre eclampsia, gestational diabetes, intra uterine growth restriction and preterm labour.

In the present study the prevalence of microalbuminuria was found to be 7.31%. Over a period of 1 year 410 patients were examined of which 30 came out to be positive for microalbuminuria. Similar results were obtained by Bahasadri S et al in 2011 in which 490 women were followed up to delivery. Of these, 38 (7.8%) women were positive for microalbuminuria (exposed group). [2]

Pre eclampsia

The prevalence of pre eclampsia among microalbuminuric patients was found to be 46.7 % which is comparable to a study done by Bahasadri S et al in 2011 in which 50% (19 out of 38 patients) in the exposed group developed pre eclampsia subsequently. [2]

In our study pre eclampsia had a statistically significant relation with the presence of microalbuminuria. 46% (14/30) of cases and only 10% controls developed preeclampsia. (p value 0.02). Of these the cases had relatively early onset and severe pre eclampsia as compared to the controls which had late onset and mild pre eclampsia.

Mean duration of time elapse between detection of microalbuminuria and pre eclampsia was 10.5 weeks.

A study by Rodriguez MH et al demonstrated the data for Eighty-eight normotensive gravid women between 24 and 34 weeks of gestation who underwent urine evaluation for the presence of microalbuminuria. Preeclampsia subsequently developed in 83% of patients with a high level of microalbuminuria (greater than or equal to 11 micrograms/ml). Conversely, 94% of women who did not demonstrate high microalbuminuria remained normotensive at the time of delivery [3] which is comparable to our study in which 90% patients who did not have microalbuminuria remained normotensive.

Sibai BM et al depicted a clear relation between the two variables by demonstrating that pre eclampsia was more common among women who had proteinuria at baseline (28% v/s 18%, Odds ratio, 1.75). [4]

In 2001 a study conducted by Shaarawy et al determined whether the presence of microtransferrinuria and microalbuminuria detected in pregnant women who are free of symptoms can predict the subsequent development of preeclampsia. [5] One hundred fifty five pregnant women were successfully followed from 10 weeks gestation up till delivery. Pre-eclampsia developed in 31 women (17(54.8%) mild and 12 (38.7%) severe pre-eclampsia), whereas 124 women remained normotensive (controls). This is in comparison to our study in which pre eclampsia developed in 17 women of which 12 (70.4%) were mild and 5(29.4%) severe pre eclampsia.

In 2003 Salako BL conducted another study and demonstrated that there was an increased incidence of preeclampsia with an increase in urine albumin and this was statistically significant ($P<0.05$). [1] There was increased incidence of preeclampsia with an increase in albumin excretion and this was statistically significant (P value < 0.05).

In a study conducted by Weerasekara et al in 2003, Serum uric acid, creatinine and microproteinuria levels were determined in 256 women attending the antenatal clinic at 28 weeks of pregnancy. Subsequently they were followed-up at 2-weekly intervals until 36 weeks and Fifty-nine women developed blood pressures of 140/90 mmHg or more during the study period. [6] Microproteinuria levels of more than 375 mg/l were recorded in 43women (72.8%) before elevation of their blood pressure. sixty five women of 197 who remained normotensive had microproteinuria levels of more than 375 mg/l. in our study microalbuminuria was present in 14 out of 17(82.3 %) of women with blood pressure ≥140/90 mm hg. This difference might be seen due to a larger sample size in our study.

The sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria for the prediction of pre eclampsia in our study was 82.3%, 62.7%, 46.6%, 93.3% respectively which is comparable to a study done by Salako B. et al in which with single urinary microalbumin excretion estimation at booking, the sensitivity, specificity, positive and negative predictive values of albuminuria were 88.9%, 67.9%, 22.2% and 98.3% respectively. [1]

In 2001, in a study done by Shaarawy et al, microalbuminuria as a predictor of pre eclampsia had a sensitivity, specificity, positive predictive value, negative predictive value of 50%, 58%, 50% and 91%, respectively. [5] The similarity in the negative predictive value of microalbuminuria suggests its effectiveness as a diagnostic tool of pre eclampsia.

IUGR

One of the major causes of IUGR is placental factor which includes vascular dysfunction that might lead to insufficient supply of nutrients and blood supply to the fetus thus leading to IUGR. Placental vascular dysfunction by inducing the release of hormones and cytokines leads to changes in GFR and hence increase in urine albumin,

of which microalbuminuria is a early marker.

In the present study the presence of IUGR was also found to be statistically significant with a p value of 0.02. IUGR among the microalbuminuria positive group was seen in 14/30 cases (46%) and 3/30 controls (10%). Mean duration of time elapse between detection of microalbuminuria and IUGR was 10.8 weeks.

This is comparable to a study done by SH Bahasadri in which IUGR was seen in 15 (39.47%) microalbuminuria positive and 30 (6.63%) microalbuminuria negative subjects. [2]

Also similar results were demonstrated in a study by Harneet Singh et al in which he found IUGR in 30.8% cases as compared to 3.6% without microalbuminuria this difference was found to be statistically significant. [7]

The sensitivity, specificity, negative predictive value and positive predictive value of microalbuminuria was 82.3%, 62.7%, 93.3%, 46.6%, respectively which is comparable to a study by Gaucherand et al. in which sensitivity was 79.4%, specificity 83.4%, the negative predictive value (NPV) 95.1% and the positive predictive value (PPV) 50%. [8]

The high sensitivity and negative predictive value of microalbuminuria suggest its importance as a diagnostic tool.

GESTATIONAL DIABETES

There have been various studies which show the presence of albumin in urine after the development of diabetes but very few researches have shown the presence of microalbuminuria before the development of gestational diabetes.

In the present study the presence of gestational diabetes was present in more number of microalbuminuria positive patients (26% v/s 6%) but this difference was not found to be statistically significant. This might have been due to the fact that nephropathy due to diabetes occurs only on long standing disease and microalbuminuria is only a very early marker of the onset of nephropathy which is corrected in gestational diabetes soon after the termination of pregnancy.

Similar result was found in a study done by Go RC et al where they concluded that those women with MA had higher rates of diabetes (63.8 vs. 28.6%, odds ratio [OR] = 4.4, $P < 0.05$). [9]

A similar conclusion was also drawn by Bomback AS et al where they found that. women with GDM had a higher rate of microalbuminuria but not macroalbuminuria than their nondiabetic peers (10.0 vs. 7.7%). [10]

In our study the sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria was 80%, 56%, 26.6%, 93.3% respectively. It was also found out that the mean gestational age was 31 weeks for the development of gestational diabetes. Mean duration of time elapse between detection of microalbuminuria and gestational diabetes mellitus was 10.1 weeks

PRETERM LABOUR

In the present study preterm labour was found to be present in more number of microalbuminuria positive patients than the other group 11(36%) v/s 5(16%), however this was not found to be statistically significant.

In 2000 a study done by Sibai BM et al showed a similar result where frequency of pre term delivery at <35 weeks of gestation rose in women with proteinuria at baseline (29% v/s 13%, Odds ratio 2.6). [4] frequency of preterm delivery at <35 weeks' gestation rose greatly with increasing severity of diabetes (P =.0002) and had small-for-gestational-age infants (14% vs 3%; odds ratio, 5. 4; 95% confidence interval, 2.7-17.7), and they were less likely to have large-for-gestational-age infants (14% vs 40%; odds ratio, 0.2; 95% confidence interval, 0.1-0.5).

This difference might have been found due to a larger sample size in the study conducted by Sibai in which 462 women were recruited.

In our study 1 out of 30 cases testing positive for microalbuminuria (33.3%) had both pre eclampsia and diabetes and subsequently had a pre term delivery which is comparable to a study conducted by Carr et al of pregnancies complicated by diabetic nephropathy with "Above Target" mean arterial pressure (> or = 100 mm Hg; N = 21) and "Below Target" mean arterial pressure (< 100 mm Hg; N = 22). [11] They concluded that The Above Target group had more proteinuria (4.69 +/- 1.08 v 1.65 +/- 0.43 g/24 h; P = .007) and higher serum creatinine levels (1.23 +/- 0.17 v 0.85 +/- 0.06 mg/dL; P = .02). The Above Target group was more likely to deliver at < 32 weeks' gestation (38.1% v 4.6%; P = .007). The increased risk of preterm delivery remained significant after adjusting for duration of diabetes and glucose control.

In a study by P. Ekbom et al wherein increased perinatal morbidity associated with preterm delivery was seen as a major problem in pregnancy complicated by type 1 diabetes. [12] Of all deliveries in women with microalbuminuria, 62, (P < 0.001), respectively, were preterm. in our study 50% of patients with GDM who were microalbuminuria positive had pre term deliveries.

In 2010 Dorte M. Jensen et al studied the same relation to find out the association between microalbuminuria and pre term deliveries in pregnant women. [13] The frequencies of pre term deliveries before 34 weeks in the microalbuminuric group was (13%) significantly higher than in normoalbuminuric group (6%).

In 2015, a study conducted by Harneet singh et al Preterm birth was more common with pregnant women with microalbuminuria 53.8% as compared to 12.5% in pregnant women without microalbuminuria (*P* = 0.001**). [7]

In our study, the sensitivity, specificity, positive predictive value and negative predictive value of microalbuminuria for the prediction of pre term labour was 68.75%, 56.8%, 36.6%, 83.3% respectively.

PREMATURE RUPTURE OF MEMBRANES

PROM is associated with preterm labour and infections which induce the release of inflammatory cytokines which is also the mechanism of placental vascular dysfunction thus leading to changes in gfr and hence excretion of albumin in urine.

In the present study premature rupture of membranes was not found to have any relation with the presence of microalbuminuria. Mean duration of time elapse between detection of microalbuminuria and premature rupture of membranes was 9 weeks.

A similar conclusion as that of ours was drawn by Harneet Singh et al where they concluded that events like premature rupture of membrane, preterm premature rupture of membrane had no statistically significant association with microalbuminuria. [7] 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.

However previous studies such as that done by Bahasadri S et al have shown significant relation of premature rupture of membranes with microalbuminuria. (31.6% versus 10.2%). [2]

POST PARTUM HAEMORRHAGE

In the present study the rate of post partum haemorrhage was higher in the expose dgroup than the control group. This may be secondary to complications like pre eclampsia which is known to be associated with PPH. [14]

INDUCTION OF LABOUR

In our study, Labour was spontaneous in 22/30 cases (73.3%) and induced (26.7%) cases. however in the control group 90% patients went into spontaneous labour.

The reason for induction of labour was PROM in 5 cases (62.5%) and severe pre eclampsia in 3 cases (37.5%).

The reason for induction in the control group was PROM only (100%).

The mode of delivery was vaginal in 93.3% cases, 3.3% instrumental and 3% caeserian section in the cases whereas 100% controls had vaginal delivery

Similar results were found in a study by Harneet Singh et al in 2015 where. 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. [7] Cesarean section was more associated with microalbuminuria as the induction rate was also more in the same group ($P \leq 0.001$**)

BIRTH WEIGHT

In our study microalbuminuria was found to have no effect on the mean birth weight. In group A mean birth weight was 2.5 kg ± 0.5335kg and in group B it was 2.4 kg ± 0.3411 kg. The mean birth weight was slightly more due to the presence of macrosomia in the GDM patients in group A.

However, prior studies do not echo a similar picture. In a study done by Renu Singh et al in 2012 the mean birth weight (kg ± standard deviation) was significantly lower in the microalbuminuria group (2.45 ± 0.6) as compared to the normoalbuminuria group (2.8 ± 0.37), $P < 0.001$. [15]

In a study done by Harneet Singh et al in 2015, 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) [7]

APGAR SCORE

In our study the mean apgar score at 1 minute was 6.4 ± 1.3 in group A and in group B it was 7.1± 0.1. This was found to be statistically significant. However the 5 minute apgar score was also higher in the control group but did not carry any statistical significance.

Our results were comparable to a study done by Harneet Singh et al in which fetal complications were significantly more in terms of low Apgar score and more incidence of neonatal intensive care unit admission with microalbuminuria group (P = 0.010*) moderately significant wherein 94% subjects without microalbuminuria had an Apgar score of 8-10 whereas the number in the same category in microalbuminuria positive group was 60%. [7]

NICU ADMISSION

In the present study, NICU admission was found to be significantly higher in the case group than the control group. 30% NICU admission rate was found in the microalbuminuric group whereas only 10% was found in the normoalbuminuric group.

Similar results were shown by the study by Harneet Singh et al in which the NICU admission was significantly higher (53%) in the exposed group than the control group (5%). [7]

Most of the neonates had respiratory distress due to low birth weight and prematurity (60%), out of which 20% landed in hypoxic ischaemic encephalopathy and rest had septicemia mean duration of stay in NICU was 8 days.

CONCLUSIONS AND RECOMMENDATIONS

Microalbuminuria seemed to be an important marker of pregnancy outcome.

Roughly 2/3 rd women positive for microalbuminuria were picked up before 24 weeks.

- Pre eclampsia was more prevalent in the microalbuminuric group with a p value<0.05.
- It could be concluded that patients testing positive for microalbuminuria at midterm are likely to develop pre eclampsia roughly 10 weeks after.
- IUGR was also significant in the microalbuminuria positive patients. (p value<0.05). Mean duration of time elapse between detection of microalbuminuria and IUGR was 10.8 weeks
- Gestational diabetes mellitus was more common in the microalbuminuric

patients, although not significant. It was seen roughly 10 weeks after detection.

- Prom was shown to have no relation with microalbuminuria
- Preterm delivery was more common in positive patients.
- Mean birth weight was not affected by positive patients. However it was associated with lower Apgar scores and hence the higher rate of NICU admission
- Induction of labour was more commonly seen in the microalbuminuria positive patients due to co morbidities mostly pre eclampsia and prom.
- Therefore we recommend that microalbuminuria is an important prognostic marker for adverse pregnancy outcome.

It can be done around the 2nd trimester end (around 20-24 weeks).

It is a cheap, easily available and cost effective method of detecting many co morbidities affecting a normal pregnancy. Presence of microalbuminuria could be a warning sign of the development of pre eclampsia, gestational diabetes which could lead to pre term delivery and the presence of IUGR. Subsequently rates of NICU admission and lower Apgar scores increase with such co morbidities.

In the study we found out that roughly 10 weeks period was present between detection of microalbuminuria and the onset of pre eclampsia and gestational diabetes mellitus. Therefore presence of microalbuminuria warrants attention and strict blood pressure monitoring along with glycemic control to optimize the outcome of pregnancy.

REFERENCES

1. Salako BL, Olayemi O, Odukogbe AT, Adedapo KS, Aimakhu CO, Alu FE, Ola B. Microalbuminuria in pregnancy as a predictor of pre eclampsia and eclampsia. West Afr J Med 2003; 22:295-300.
2. Bahasadri S, Kashanian M, Khosravi Z. Comparision of pregnancy outcome among nulliaparas with and without microalbuminuria at the end of second trimester. International journal of gynaecology and obstetrics 2011;115:34-36.
3. Rodriguez MH, Masaki DI, Mestman J, Kumar D, Rude R. Calcium/creatinine ratio and microalbuminuria in the prediction of preeclampsia. Am J Obstet Gynecol 1988;159(6):1452-5.
4. Sibai BM, Caritis S, Hauth J, Lindheimer M, VanDorsten JP, MacPherson C. Klebanoff M, Landon M, Miodovnik M, Paul R, Meis P, Dombrowski M, Thurnau G, Roberts J, McNellis D. Risks of preeclampsia and adverse neonatal outcomes among women with pregestational diabetes mellitus. Am J Obstet Gynaecol 2000;182:364-9.
5. Shaarawy M, Salem ME. The clinical value of microtransferrinuria and microalbuminuria in the prediction of pre-eclampsia. Clin Chem Lab Med 2001 Jan;39(1):29-34
6. Weerasekera DS, Peiris H. The significance of serum uric acid, creatinine and urinary microprotein levels in predicting pre-eclampsia. J Obstet Gynaecol 2003;23(1):17-9.
7. Singh H, Samal S, Mahapatro A, Ghose S. Comparison of obstetric outcome in pregnant women with and without microalbuminuria. Journal of natural science, biology and medicine. 2015;1(6):120-124.
8. Gaucherand P, Salle B, Sergeant P, Guibaud S, Rudigoz RC. Micro-albuminuria analysis and pregnancy. An approach to detect placentary insufficiency?. Eur J Obstet Gynecol Reprod Biol. 1996 ;70(1):49-52.
9. Go RC, Desmond R, Roseman JM, Bell DS, Vanichanan C, Acton RT. Prevalence and risk factors of microalbuminuria in a cohort of African-American women with gestational diabetes. Diabetes Care2001;24(10):1764-9.
10. Bomback AS, Rekhtman Y, Whaley-Connell AT, Kshirsagar AV, Sowers JR, Chen SC, Li S, Chinnaiyan KM, Bakris GL, McCullough PA. Gestational diabetes mellitus alone in the absence of subsequent diabetes is associated with microalbuminuria:

results from the Kidney Early Evaluation Program (KEEP). 2010 Dec; 33(12):2586-91. DOI: 10.2337/dc10-1095

11. Carr DB, Koontz GL, Gardella C, Holing EV, Brateng DA, Brown ZA, Easterling TR Diabetic nephropathy in pregnancy: suboptimal hypertensive control associated with preterm delivery. Am J Hypertens. 2006;19(5): 513-9
12. Ekbom P, Damm P, Rasmusssen BU, Rasmussen FU, Molvig J, Mathiesen RE. Pregnancy outcome in type 1 diabetic women with microalbuminuria. Diabetes care 2001;24:1739-44.
13. Jensen DM, Damm P, Ovesen P, Pedersen LM, Beck-Nielsen H, Westergaard JG et al. Microalbuminuria, preeclampsia, and pre term delivery in pregnant women with type 1 diabetes. Diabetes care 2010;33:90-94.
14. Altenstadt VS, Hukkelhoven CPWM, Roosmalen JV, Bloemenkamp KWM. Pre-eclampsia increases the risk for postpartum haemorrhage: a nationwide cohort study among more than 3,40,000 deliveries. AJOG 2012;206(1):S68.
15. Singh R, Tandon I, Deo S, Natu SM. Does microalbuminuria at mid-pregnancy predict development of subsequent pre-eclampsia? J Obstet Gynaecol Res. 2013;39(2):478-83.

How to cite this article: Chawla R, Malik S. Microalbuminuria detected at mid term as a marker for adverse pregnancy outcome. Int J Health Sci Res. 2018; 8(2):41-52.

****