Prevalence of Microalbuminuria in Pregnancy and its Predictive Value for Development of Pregnancy Induced Hypertension at a Tertiary Care Hospital in Nepal: A Longitudinal Observation Study

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Abstract:- Introduction: Hypertensive disorders in pregnancy contribute significantly to the maternal mortality, premature birth, intrauterine growth retardation and perinatal mortality. **Objectives:** This study is done to determine if microalbuminuria can be used as a predictive marker of pregnancy induced hypertension (PIH) and adverse pregnancy and neonatal outcomes. **Materials and Methods:** This study was hospital based longitudinal observational done in pregnant women attending antenatal clinic in B.P. Koirala Institute of Health Sciences for a period of 1 year from January, 2017 to January, 2019. This study involved total of 504 women of gestational age 24-28 weeks, were evaluated for microalbuminuria, defined by spot urine albumin creatinine ratio 30-300 mg/g (Kidney Disease Improving Global Outcomes guidelines) and followed till discharge after delivery. Development of PIH and both maternal and fetal outcome were recorded. **Results:** Of the 504 patients pregnant women enrolled in our study, 89 (17.7%) had microalbuminuria. The rate of development of PIH was significantly higher in microalbuminuric women compared to non microalbuminuric (p <0.05). The Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of micro-albuminuria in predicting occurrence of PIH during Pregnancy was found to be 42.86%, 84.22%, 16.85% and 95.18% respectively. **Conclusion:** The absence of microalbuminuria was highly specific for predicting nonoccurrence of PIH during the pregnancy. However, microalbuminuria had low sensitivity for the screening of PIH and hence poor predictive value.

Keywords:- Hypertension, Microalbuminuria, Pregnancy.

I. INTRODUCTION

Hypertension is the most common medical problem encountered during pregnancy, complicating up to 10% of pregnancies.[1] Pregnancy-induced hypertension (PIH) is a syndrome of hypertension with or without proteinuria and edema, with the clinical manifestation usually occurring at 20 weeks or more gestational age of pregnancy and regressing after delivery of the conceptus, and includes gestational hypertension, pre-eclampsia, and eclampsia .[2]

Microalbuminuria is defined as detection of 30-300 mg of albumin in 24 hour urine collection or 30-300 mcg of albumin/mg creatinine in spot urine collection.[3] Studies have shown the presence of microalbuminuria earlier in pregnancy to be a poor prognostic factor, associated with an increased risk of development of pre eclampsia and severe adverse maternal and fetal outcome.[4, 5]

The aim of this study is to the prevalence of microalbuminuria among the pregnant women at and its predictive value for development of PIH and other adverse obstetric outcomes.

II. MATERIALS AND METHODS

This hospital based longitudinal observational study was carried out in Department of Obstetrics and Gynaecology, B.P. Koirala Institute of Health Sciences, a tertiary care university teaching hospital in Dharan, Nepal. The study was conducted from January 2017 to December 2018. Ethical approval was taken from the Institutional Ethical Review Board of BPKIHS. Women attending antenatal clinic between 24-28 weeks period of gestation fulfilling the selection criteria were enrolled into the study.

Selection Criteria:

Inclusion criteria:
Pregnant women with gestational age of 24-28 weeks , who were previously normotensive and non proteinuric.

Exclusion criteria:
Women with Chronic hypertension, History of preeclampsia/eclampsia in previous pregnancy, Renal disease , Overt Diabetes, Heart disease, Thyroid disorders, polyhydramnios and USG documentation of congenital malformed fetus

Sample Size:
The sample size was calculated using the following formula
$N = Z^2 PQ / L^2$,

where N= required sample size,
Prevalence (P) = 16% 6, Q= 100-P=84%
Permissible error, L= 3.2% (20% of P),
Z = confidence level at 95% (standard value of 1.96)

Consecutive sampling technique was applied. Five hundred and four women with a gestational age of 24 -28 weeks according to last menstrual period, fulfilling the inclusion criteria were enrolled after taking informed and written concent. Random spot urine sample was sent for urine albumin to creatinine ratio.Urinary creatinine and microalbumin were measured by enzymatic and immunoturbidimetric methods, respectively.

All the enrolled patients with both microalbuminuria positive or negative reports were followed up in antenatal clinic as per hospital protocol. Development of hypertension (a systolic blood pressure (SBP) $\geqslant$ 140 mmHg and/or a diastolic blood pressure (DBP) $\geqslant$ 90 mmHg) for the first time in both the groups with period of gestation was noted and patients were managed as per hospital protocol. Patients were followed up till discharge after delivery and both maternal and fetal outcome were recorded.

Statistical package for the social sciences version 20 was used for data analysis. 95% confidence interval and p value of <0.05 was taken as significant. Descriptive statistics (frequency, percentage) were used and Chi-square test was used to assess association between microalbuminuria and development of PIH and maternal and fetal outcomes.

III. RESULTS

During the study period of one year, among 504 pregnant women were enrolled in our study, microalbuminuria was present in 89 patients. The prevalence of microalbuminuria hence was 17.7% (Figure 1).
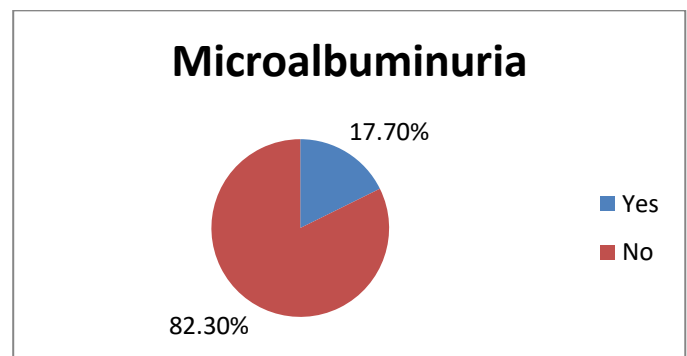

Figure 1. Prevalence of microalbuminuria among pregnant women (n=504).

In our study, microalbuminuria was found to be statistically significant with increasing age (p value <.05) and gravida (p value <0.5) (Table 1).

TABLE I. BASELINE CHARACTERISTICS OF PREGNANT WOMEN WITH MICROALBUMINURIA AND WITHOUT MICROALBUMINURIA.

Characteristics		Pregnant women without microalbuminuria Number (%)	Pregnant women with microalbuminuria Number (%)	p-value
Age	<20 yrs	51(12%)	5(6%)	0.04
	20-30 yrs	312(75%(	66(74%)	
	>30 yrs	52(13%)	18(20%)	
Gravida	Primi	215(51%)	33(37%)	0.01
	Multi	200(49%)	56(63%)	

Among 89 pregnant women who had microalbuminuria, 15 (17%) developed PIH whereas 20 of 415 (5%) developed PIH among pregnant women without microalbuminuria. The difference of prevalence of PIH among pregnant women with

Microalbuminuria and without Microalbuminuria is statistically significant with P value<0.05. The sensitivity,

specificity, PPV and NPV was found to be 42.86%, 84.22%, 16.85% and 95.18% respectively. This signifies that the absence of microalbuminuria is highly specific for predicting nonoccurrence of PIH in during the pregnancy. However, microalbuminuria has low sensitivity for the screening of PIH and hence poor predictive value (Table II).

TABLE II.   PIH AMONG PREGNANT WOMEN WITH AND WITHOUT MICROALBUMINURIA.

Microalbuminuria	PIH Present Number (%)	PIH Absent Number (%)	
Present	15 (17%)	74(83%)	P value= <0.05 Sensitivity=42.86 %(95%CI26.32%-60.65%) Specificity=84.22 %(95%CI 80.60%-87.40%) PPV=16.85 %((95% CI 11.59%-23.87%) NPV=95.18 %(95% CI 93.66%-96.35%)
Absent	`20(5%)	395(95%)	

Pregnancy outcomes among pregnant women with microalbuminuria and without microalbuminuria were not significant in terms of gestational age at delivery, mode of delivery and mode of labour (Table III).

TABLE III.   PREGNANCY OUTCOME WITH MICROALBUMINURIA AND WITHOUT MICROALBUMINURIA.

Pregnancy Outcomes	Pregnant women without Microalbuminuria N=415	Pregnant women with microalbuminuria N= 89	p-value
Gestational age at delivery			
Preterm	22(5%)	2(2%)	0.37
Term	313(75%)	72(81%)	
Post Dated	80(20%)	15(17%)	
Mode of Delivery			
Vaginal	269(64%)	61(68.5%)	0.7
Cesarean section(CS)	145(35%)	28(31.5%)	
Instrumental	1(<1%)	0	
Mode of Labour			
Spontaneous	272(65%)	56(62%)	0.79
Induced	107(26%)	26(30%)	
Elective CS	36(9%)	7(8%)	

Perinatal outcomes among pregnant women with microalbuminuria and without microalbuminuria didn't show significant relation in terms of APGAR score at birth, Birth weight or NICU admission (Table IV).

TABLE IV.   PERINATAL OUTCOMES AMONG PREGNANT WOMEN WITH MICROALBUMINURIA AND WITHOUT MICROALBUMINURIA.

Fetal Outcome	Pregnant women without microalbuminuria	Pregnant women with microalbuminuria	P value
APGAR score at birth			
>6	414(99.7%)	89(100%)	0.82
<6	1(0.3%)	0	
Birth weight			
<2.5 kg	28(6%)	5(5%)	0.2
2.5-4 kg	374(90%)	78(88%)	
>4kg	13(4%)	6(7%)	
NICU admission			
Yes	3(0.7%)	0(0%)	0.5
No	412(99.3%)	89(100%)	

IV.   DISCUSSION

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 have revealed an association between microalbuminuria and obstetric outcome. Microalbuminuria

can be used as a predictive marker of PIH and adverse pregnancy and neonatal outcomes in women.[4-6] Bar et al described a phase of microalbuminuria that preceded clinical proteinuria and that this test has some predictive value for severe disease.[7]

In our study, the prevalence of microalbuminuria among pregnant women attending BPKIHS was found to be 17.7 % , similar to previous studies done by Salako et.al , Kour. G et al and A.Senna et. al, where the prevalence of microalbuminuria were 23.7%, 16 % and 14.3 % respectively.[8,6,9]

Our study revealed that microalbuminuria is less common below 20 years of age whereas it increases as the age of the pregnant women increases which was in contrast in the study done by S. Harneet et al.2015 where the age distribution in the two groups was found to be similar and comparable.[10] Our study also showed that the presence of microalbuminuria is higher in multigravida than in primigravida. Hence multigravida with increasing age was more likely to have microalbuminuria . However previous study by A. Senna et. al. and Masse J et.al reported no significant association between microalbuminuria with increasing gravida. [9, 11]

In our study, the overall prevalence of PIH was found to be 6.9%. Development of PIH was significantly higher in pregnant women who had microalbuminuria compared to those who hadn't . Previous studies also reported significant association of microalbuminuria with development of PIH. [6, 8,9] .Hoewever no significant relationship between microalbuminuria and hypertension was reported in some studies. [10]

The Sensitivity, specificity, Positive Predictive value(PPV) and Negative Predictive value(NPV) of microalbuminuria in predicting development of PIH was found to be 42.86%, 84.22 %, 16.85%and 95.18 % respectively. This showed high specificity and negative predictive value of microalbuminuria for development of PIH and low sensitivity. So we concluded that microalbuminuria is a poor screening tool for PIH due to its low sensitivity. This finding is also in accordance with the study done by Shaarawy M et.al. 2001 , which showed the sensitivity of microalbumin in predicting Preeclampsia was between 50% to 68%, the specificity varied between 58 to 97%, PPV varied between 26 to 61% and the NPV varied between 87-94%. [12] However the sensitivity of microalbuminuria as a predictor of Preeclampsia was found to be 80% in a study done by K. Fatema et.al and 87.5% in a study by V Mishra et al which lies above the values reported by various other authors.[13 , 14] In contrast to our study, L.González et al also reported the sensitivity of microalbuminuria in the development of pregnancy induced hypertension to be 79%, specificity 63%, the positive predictive value 46% and the negative predictive value to be 88%, and concluded that microalbuminuria is not a good predictor of pre-eclampsia.[15]

In this study, Pregnancy outcomes among pregnant women with microalbuminuria and without microalbuminuria was not significant in terms of gestational age at delivery, mode of delivery and mode of labour , similar to the study done by A. Senna et. al .2017.[9]

Our study tried to compare the various maternal and perinatal outcomes among the patient with microalbuminuria and without microalbuminuria. The study did not reveal significant difference in the maternal outcomes. Only 2 pregnant women without microalbuminuria developed severe disease which was statistically not significant. This was similar to the study done by Harneet singh et al.2015 where they have found no statistically significant association between microalbuminuria and obstetric complications except for preterm labour. [10] Other maternal complications like Acute Kidney Injury, APH, Preterm labour, PPROM were also not seen among the studied sample. In contrast, study done by Dr. K Lavanyakumari et.al , Kour G et.al and S.Bahasadri et.al reported that maternal complications like Preterm labor, PPROM, APH, PPH were more common in the microalbuminuria positive group.[4,6, 16]

Similarly our study didn't show significant difference in perinatal outcomes like IUGR, poor APGAR score, IUFD, Low birth weight and NICU admissions. , which was in contrast to different studies done by H. Singh et al, Kour G et.al, M. Jayaballa et.al where microalbuminuria had significant association with the poor perinatal outcomes as described above.[6,10,17]

Single centered study and small study population are the limitations of the present study. Large scale and multi-centered study are needed to further evaluate the role of microalbuminuria in estimating their risks and implications in pregnancy.

V. CONCLUSIONS

The absence of microalbuminuria at 24-28 weeks period of gestation firmly excludes the development of PIH in later part of pregnancy as the value of microalbuminuria in predicting PIH is poor and there is no association between microalbuminuria and various maternal and perinatal outcomes.

Conflict of Interest: None.

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