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Predicting adverse outcomes in hypertensive obstetric cases by using spot urine calcium: Creatinine ratio

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Abstract
Background: Hypertensive disorders complicate upto 5-10% of pregnancies, 3.9% is preeclampsia the leading cause of both direct maternal and perinatal mortality. Mostly preeclampsia is diagnosed only after pathological changes are already established. The study being carried out to investigate the significance of urinary calcium-creatinine ratio in predicting the outcomes with hypertensive disorder of pregnancy.
Methods: All women between the gestational ages 20 -28 weeks were taken into the study, spot urine sample was taken to measure the urinary calcium-creatinine-ratio. Ratio less than or equal to 0.04 was considered test positive and those with ratio of >0.04 was considered test negative.
Results: 218 normotensive, 17Gestational hypertension, and 21Preeclampsia were recruited fir the study. Urinary creatinine excretion among gestational hypertension and preeclampsia is more than normotensive women. Calcium excretion is low in preeclampsia compared to normotensive women. CCR was positive 87.69% of preeclampsia and 40% in gestational hypertension. We found that CCR was a better predictor of preeclampsia than gestational hypertension, with sensitivity of 73.81%, specificity of 95.18%.More maternal complications such as abnormal Doppler studies and HELLP syndrome among preeclampsia, and lower birth weight were noted among women with preeclampsia. More number of abnormal APGAR at 1' and 5' were noted in preeclampsia group.
Conclusion: Spot Urine calcium-creatinine ratio of ≤0.04 in asymptomatic pregnant women between 20-28 weeks of pregnancy is a good predictor for hypertensive disorders of pregnancy, especially preeclampsia. We can also conclude that there is increased maternal and fetal morbidity among women complicated with hypertension than normotensive women.

Keywords: HDP, calcium-creatinine ratio, complications, hypertension, morbidity

Introduction
Hypertensive disorders of pregnancy (HDP) have been a challenge to obstetricians and researchers since many centuries and remain a major public health problem worldwide. Hypertensive disorders complicate up to 5-10% of all pregnancies. Of which 3.9% is preeclampsia. It is the leading cause of both direct maternal and perinatal mortality. 16% of maternal mortality rate is due to hypertensive disorders in pregnancy [1].
The lower the creatinine clearance, the severe is the renal disease. This has been shown to parallel the decline in urinary calcium in preeclampsia, even before the clinical appearance of signs and symptoms. Though the exact reason for this phenomenon is not clear, it has been speculated that the renal changes in preeclampsia are the basis for using urinary calcium-to-creatinine ratio as a screening test [2]. Hypertensive disorders complicate up to 5-10% of all pregnancies. Of which 3.9% is preeclampsia. It is the leading cause of both direct maternal and perinatal mortality. In most cases, preeclampsia is diagnosed only after the pathological changes are already established. Hence, not many treatment options are left for the treating obstetrician. Hence, the present study is being carried out to investigate the significance of urinary calcium-creatinine ratio in predicting hypertensive disorders of pregnancy and to study the maternal and fetal outcomes of mothers with hypertensive disorder of pregnancy.

Material and Methods
All the singleton pregnancy, who came for antenatal check-up at Justice K S Hegde Charitable Hospital with a period of gestation between 20 to 28 weeks of pregnancy at the booking visit were recruited into the study from December 2015- January 2020. Were included in the study grouped into two groups: those who develop hypertensive disorders of pregnancy and those who remained normotensive.

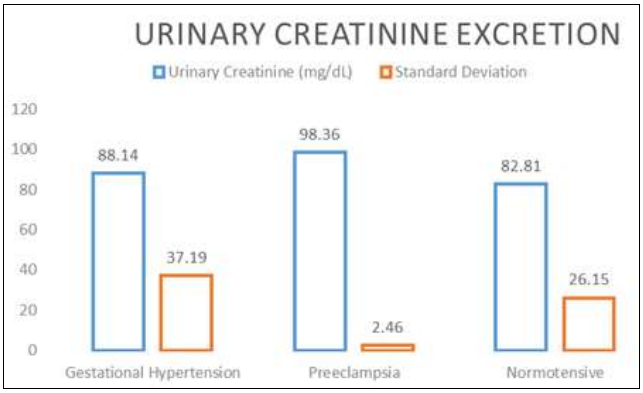
They were also followed until delivery and asked about signs and symptoms of preeclampsia during each visit.
Urinary calcium-creatinine ratio and BP were measured in both the groups and correlated. Maternal and the fetal outcomes were noted.

Results

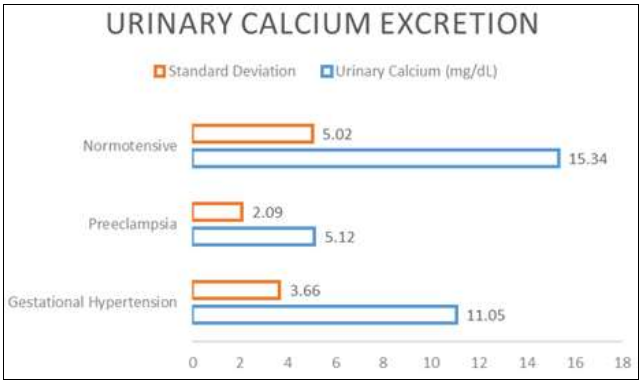
A total of 218 normotensive, 17 Gestational hypertension, and 21 Preeclampsia were recruited fir the study. Most of the participants belonged to the age group 26-30 years35.35% belonged to the age group between 26-30 years. (Table 1), both groups had higher number of primigravidae (Table 2), lower-middle socio-economic status. Urinary creatinine excretion among gestational hypertension and preeclampsia is more than normotensive women. The urinary calcium creatinine excretion among gestational hypertension and preeclampsia was statistically significantly more than normotensive women (ANOVA p = 0.031). (Graph 1 & 2) Also shows that calcium excretion is low in preeclampsia compared to normotensive women. CCR was positive among 87.69% of preeclampsia and 40% in gestational hypertension group. We found that CCR was a better predictor of preeclampsia than gestational hypertension, with sensitivity of specificity of 91.89% PPV of 97.14% and NPV of 25% more maternal complications such as abnormal Doppler studies and HELLP syndrome among preeclampsia, and lower birth weight were noted among women with preeclampsia. More number of abnormal APGAR at 1' and 5' and neonatal complications were noted in preeclampsia group. (Graph 3).

Table 1: Gravida status

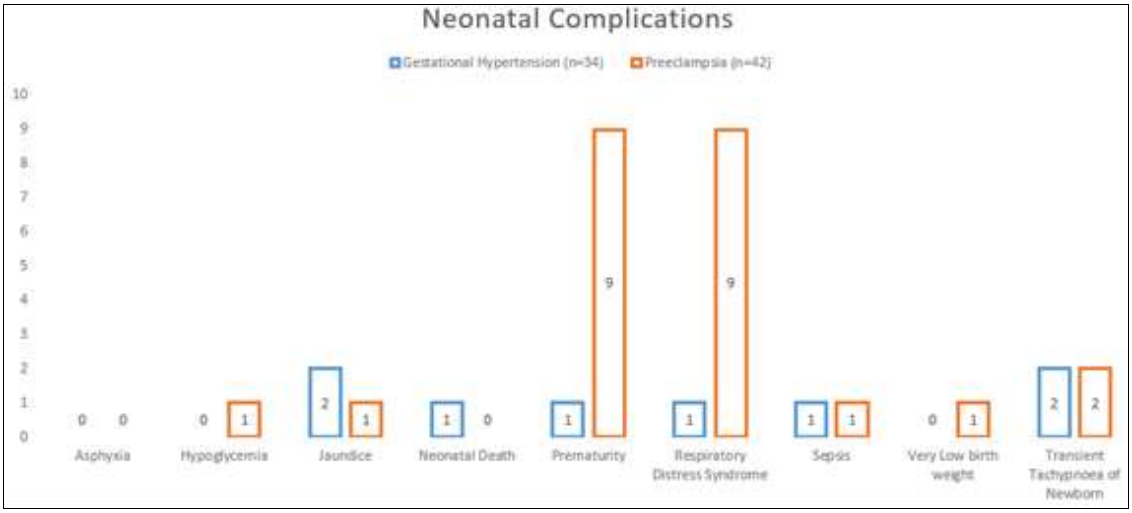
Gravida Group	Normotensive (n=436)	Gestational Hypertension (n=34)	Preeclampsia (n=42)	p Value
Primigravida	81.88%	4.82%	86.70%	0.29
Multigravida	18.12%	2.98%	21.10%	



Graph 1: Urinary creatinine excretion



Graph 2: Urinary calcium excretion



Graph 3: Neonatal complications and hypertensive status

Discussion

According to the World Health Organization (WHO), 20% of the 15 million preterm births reported each year are related to PE [3]. This situation is particularly important in developing countries where the incidence of hypertensive disorders of pregnancy is higher and maternal mortality rates and preterm births are 20 times higher than those reported in developed countries [4, 5].
Unfortunately, the pathophysiology of this multisystem disorder, characterized by abnormal vascular response to placentation, is still unclear. Delivery is the only curative treatment for pre-eclampsia. In most cases, preeclampsia is diagnosed only after the pathological changes are already established.
The prediction of preeclampsia is a worthwhile goal because identification of patients at risk could result in earlier diagnosis of the disease, monitoring the mother and fetus at risk, and implementing preventive strategies. Calcium-to-creatinine ratio has been suggested by many to be a good screening test for preeclampsia [6]. Creatinine clearance is an indicator of the renal damage in pregnancy hypertension J Kar *et al.* [7] noted that the

CCR had a Sensitivity of 75%, Specificity of 94.4%, PPV of 64.2%, NPV of 96.5%, Vahdat *et al.* [8] noted that the Sensitivity of 77%, Specificity of 78% 54%, Dutt *et al.* [9], Sensitivity of 40% Specificity of 86.7%.

Munge AM *et al.* [10] noted that the CCR had a Sensitivity of 63.6, Specificity of 94.9% < PPV of 77.8 and NPV 90.2.

The present study noted that the CCR HAD A Sensitivity of 91.89%, Specificity of 50%, PPV of 97.14% and NPV 25%.

Table 2: Urinary calcium creatinine excretion as predictive factor for gestational hypertension

Statistic	Value	95% CI
Sensitivity	91.89%	78.09% to 98.30%
Specificity	50.00%	1.26% to 98.74%
Positive Likelihood Ratio	1.84	0.46 to 7.37
Negative Likelihood Ratio	0.16	0.03 to 0.94
Disease prevalence (*)	94.87%	82.68% to 99.37%
Positive Predictive Value (*)	97.14%	89.45% to 99.27%
Negative Predictive Value (*)	25.00%	5.42% to 65.96%
Accuracy (*)	89.74%	75.78% to 97.13%

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