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Analysis of baseline renal function tests and adverse outcomes in pregnant patients with chronic hypertension in a teaching hospital

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Conflicts of Interest: Nil

Abstract

Introduction: In the present study we observed 30 study cases to evaluate adverse outcome in pregnant patient with chronic hypertension in now rosjee Wadia Maternity Hospital, Mumbai in study duration of 18 months.

Method: This was a Prospective observational study. Result: We observed that among all cases association of low birth weight to serum creatinine and urine protein to creatinine ratio was statistically highly significant in the study.

Conclusion: The study indicates that both the parameters serum creatinine and urine protein to creatinine ratio when done in chronic hypertensive pregnant patient before 20 weeks of gestation has a reliable prediction for developing complications of neonatal morbidity and mortality. However, we have not been able to find any association with maternal complications of renal failure or Abruption placenta for similar situation.

Keywords: pregnant patients, chronic hypertension, serum creatinine, urine protein and creatinine ratio, low birth weight.

Introduction

The urinary system undergoes significant but predictable physiologic and anatomic changes during normal pregnancy. Hemodynamic and physiological changes causes a change in the Glomerular filtration rate (GFR); increases immediately after conception, to about 50% above baseline in the second trimester and then falls to about 20% above baseline in the last trimester, resulting in significant hyper filtration. Renal plasma flow also

increases significantly in early pregnancy, causing the filtration fraction to fall in mid-pregnancy. As a result the normal serum creatinine level falls, so any value above 0.8 mg/dl should be considered abnormal. Beauties et al [2003] reported that, hypertension complicates 10-15% of all pregnancies among them, 10-20% also develop proteinuria. In 2008 the Society of Obstetricians and Gynecologist of Canada [SGOC] prerelease revised guidelines that simplified the classification of hypertension in pregnancy into two categories, preexisting or gestational with the option to add with preeclampsia to either category, if additional maternal or fetal symptoms, signs, or test result support this.

Chronic hypertension in pregnancy is associated with increased rates of adverse maternal and fetal outcomes both acute and long term. Women with chronic hypertension should be evaluated either before conception or at time of first prenatal visit. Depending on this evaluation, they can be divided into categories of either "high risk" or "low risk" chronic hypertension. High-risk women should receive aggressive antihypertensive therapy and frequent evaluations of maternal and fetal well-being, and doctors should recommend lifestyle changes. In addition, these women are at increased risk for postpartum complications such as pulmonary edema, renal failure, and hypertensive encephalopathy for which they should receive aggressive control of blood pressure as well as close monitoring. In women with low-risk (essential uncomplicated) chronic hypertension, there is uncertainty regarding the benefits or risks of antihypertensive therapy. Renal insufficiency is classified as mild, moderate and severe. Patient with mild disease have a serum creatinine 1.4 mg/dl or less or 125 micro mol/l or less and no hypertension. Those with moderate renal insufficiency have a serum creatinine level of 1.5 to 2.5mg/dl, or 125 to 250 micro mol/l, and those with severe disease have creatinine those with severe disease have creatinine level of 2.5 mg/dl or more or 250 micro mol/l more. Maternal and perinatal outcomes are usually not affected with mild renal insufficiency.

Objective cut off levels are required in predicting the adverse outcomes of pregnancy when dealing with moderate and severe chronic hypertension. These models help in determining the pre pregnancy status, the suitability of continuing pregnancy and the perinatal outcome with or without the additional burden of preeclampsia. Some studies have mentioned 0.75 mg/dl or greater and a urine protein-to-creatinine ratio of 0.12 or greater as associated with adverse pregnancy outcomes. The adverse pregnancy outcome which we are interested in studying are broadly divided into two parts.

A. Maternal

- Superimposed pre- eclampsia
- Severe preeclampsia
- Preterm birth (<37 weeks)
- Iatrogenic ally induced preterm birth for worsening symptoms. (<35 weeks)

B. Neonatal

- Small for gestational age
- Primary neonatal composite. (Stillbirth, neonatal death, assisted ventilation, 5min. Apgar score <3 and neonatal seizures)

Materials and methods

Study Site

This was ahospital based prospective observational study was conducted in the Department of Obstetrics and Gynaecology in a Municipal tertiary care Centre and

teaching Hospital in Maharashtra between01/01/2017 to 30/06/2018.

Study Population

The study subjects participating in the study were the first trimester patients attending ANC OPD for the first-time outpatient department fulfilling the eligibility criteria and given such written informed consent for the participation in the study.

Study Design

This was prospective observational study carried out in the Department of Obstetrics and Gynaecology in a Municipal tertiary care Centre

Source of data and duration of study

Data in this study was collected from Department of Obstetrics and Gynaecology, in a Municipal tertiary care Hospital during the period January 2016 to June 2017.

Sample size: 30 patients.

Study setting

Department of Obstetrics and Gynaecology, in a Municipal tertiary care centre and teaching hospital in Maharashtra

Study Period: This study was conducted during January 2016 to June 2017.

Study Duration: One and half year.

Records includes

1. Patients OPD records
2. patients indoor hospital records
3. Laboratory reports.
4. Operation theatre master record book.

Patient selection

Inclusion criteria: All pregnant women registered in ANC clinic of this municipal tertiary care Maternity Hospital:

- Singleton fetus
- Pregnancy with chronic hypertension on antihypertensive treatment or newly

Diagnosed patients with raised blood pressure before 20 weeks of gestation.

- Patient willing for enrollment and investigations and had given such written informed consent.

Exclusion criteria

- Patients complicated with chronic hypertension due to renal causes.
- Patient not willing for investigations.
- If pregnancy complicated by fetal anomalies (Anomalous fetii are one of the important cause of small gestation outcome. Hence, its inclusion can show the data of pregnancy outcome in case of chronic hypertension)

Withdrawal Criteria: Patient refusal to participate or to continue to be a participate in the study at any point of study.

Observation and results

Table 1: Age distribution of the study subjects

Age group years	No of patients	(%)
25-28	7	23.33
29-32	14	46.67
>32	9	30
Total	30	100

Mean age was 31.13±3.19 years with minimum age 25 years and the maximum age of the patient was 38 years. Almost 47 % of the patients were having the age 29-32.

Graph 1

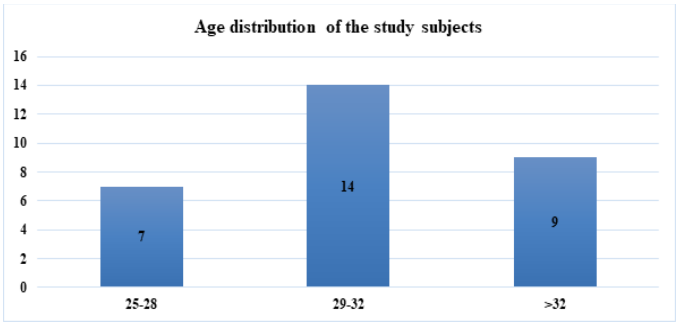


Table 2: Past history in the patients

Past History	No of patients	(%)
History of PIH	1	3.33
History of LSCS	3	10
No Significant history	26	86.67
Total	30	100

There was a single patient having past history of PIH (3.33%). 4(13.33%) had previous LSCS. Out of 30, 26 patients were not having any significant history.

Graph 2

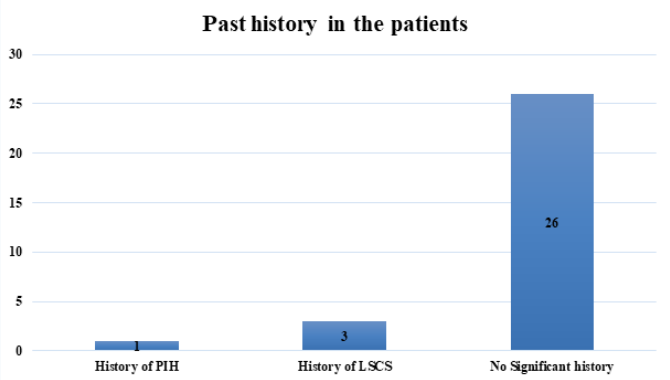


Table 3: Associated medical and surgical illness

Associated medical and surgical illness	No of patients	(%)
History of DM	1	3.33
GDM	1	3.33
Gestational Hypothyroidism	1	3.33
BOH and Protein S deficiency	1	3.33
Pre gestational hypothyroid	1	3.33
No any illness	25	83.34
Total	30	100

There was a single patient with the History of DM, GDM, Gestational Hypothyroidism, BOH and Protein S deficiency and Pregestational hyperthyroid of each. 25(83.34%) patients were not having illness.

Graph 3

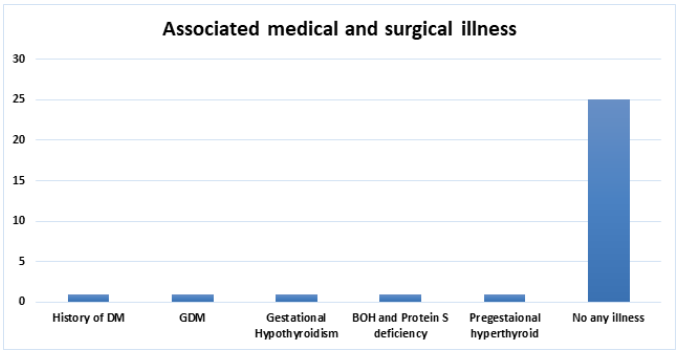


Table 4: Blood pressure distribution in the study

Blood Pressure	No of patients	(%)
Raised	23	76.67
Normal	07	23.33
Total	30	100

(Raised BP ≥140 systolic or ≥90 diastolic or both}

In the study out of total 30 patients, 23(76.67%) patients had raised BP and 7(23.33%) had normal BP.

Graph 3

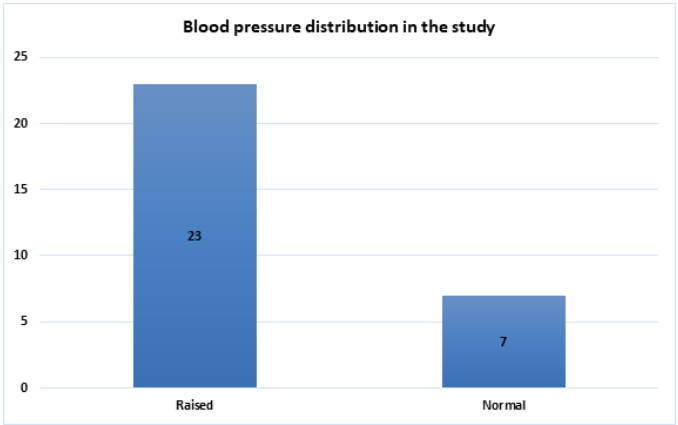


Table 5: Level of serum creatinine in the study subjects

Level of serum creatinine	No of patients	(%)
≤1mg%	17	56.67
>1mg%	13	43.33
Total	30	100

Level of Serum creatinine >1 mg% was present in 13(43.33%) patients of the chronic hypertension.

Graph 4

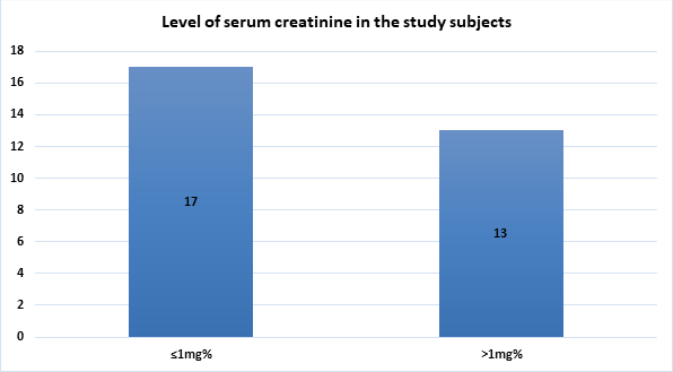


Table 6: Proteinuria (Urine protein to creatinine ratio) in the study subjects

Urine protein to creatinine ratio	No of patients	(%)
≥0.3	9	30
<0.3	21	70
Total	30	100

In 9(30%) of the patients the Urine protein to creatinine ratio was ≥0.3 suggestive of proteinuria.

Graph 5

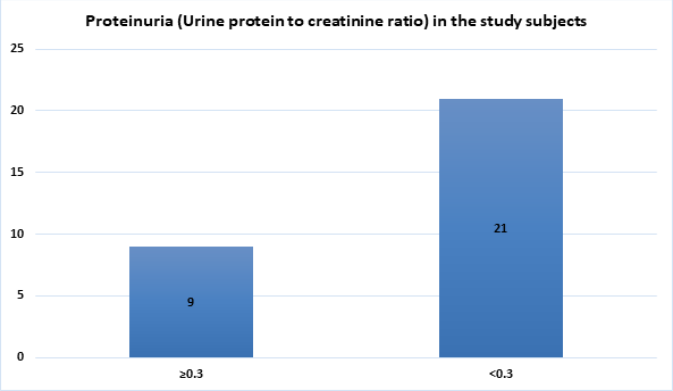


Table 7: Gestational age at time of delivery

Gestational age at time of delivery	No of patients	(%)
Preterm	11	36.67
Term	19	63.33
Total	30	100

Mean gestational age in the study was 36.80 ±2.08weeks Highest was 39 weeks and lowest was 31.6 weeks. There were total 11(36.67%) patients who delivered at preterm and rest 17(63.33%) who were delivered at term.

Graph 6

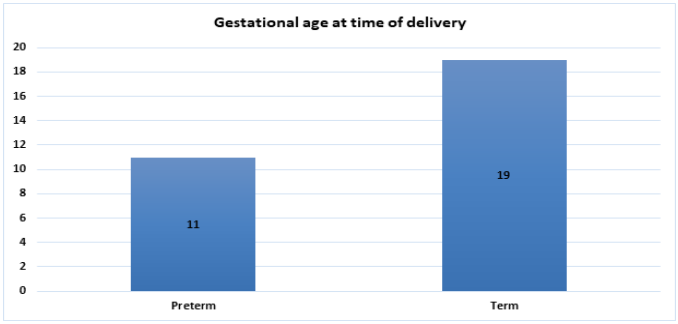


Table 8: Apgar score

Apgar Score (at 0 min)	No of patients	(%)
7or below	8	26.67
>7	22	73.33
Total	30	100

APGAR score in neonates at 0 minutes was 7 or less in 8(26.67%) of the cases and >7 in rest 22(73.33%)

Graph 7

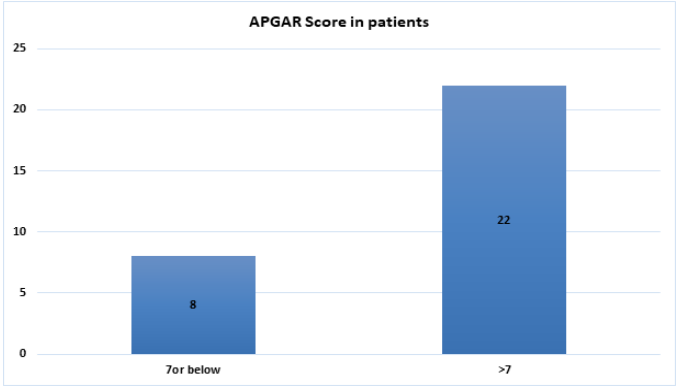


Table 9: Incidence of LBW in the study subjects

Weight at birth in kg	No of patients	(%)
<2.5 kg	13	43.33
≥2.5	17	56.67
Total	30	100

Mean weight was 2.43± 0.54kg Highest was 3.44kg and lowest was 0.956kg.

Incidence of LBW i.e., birth weight <2.5kg was 43.33% in the study.

Graph 8

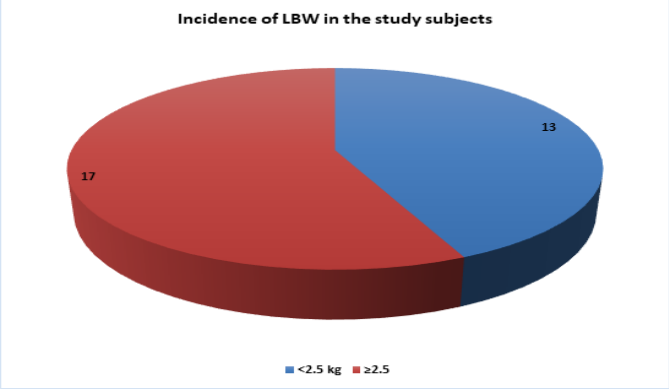


Table 10: Neonatal mortality in the study subjects

Neonatal mortality	No of patients	(%)
Yes	2	6.67%
No	28	93.33%
Total	30	100

Neonatal mortality was reported to be 6.67% in the study. There were 2 deaths in neonates

Graph 9

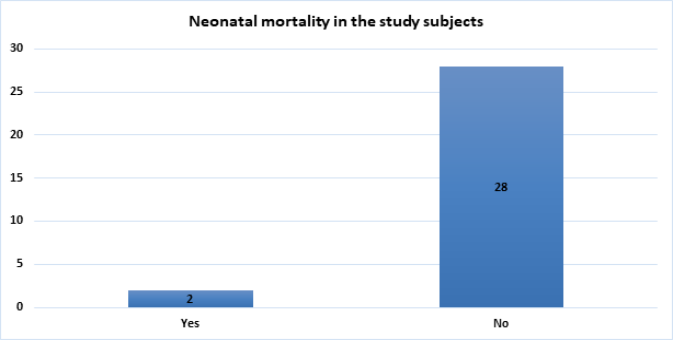


Table 11: Association of LBW with Serum creatinine in the study subjects

LBW	Serum creatinine		Total	P value
	≤1mg%	>1mg%		
Yes	2	11	13	0.000066
No	15	2	17	Significant
Total	17	13	30	

The proportion of LBW in patients with raised creatinine was 11 out of 13 patients and 2 out of total 17 patients having normal creatinine level of 1mg%. This association of LBW to the serum creatinine level was statistically highly significant in the study.

Graph 10

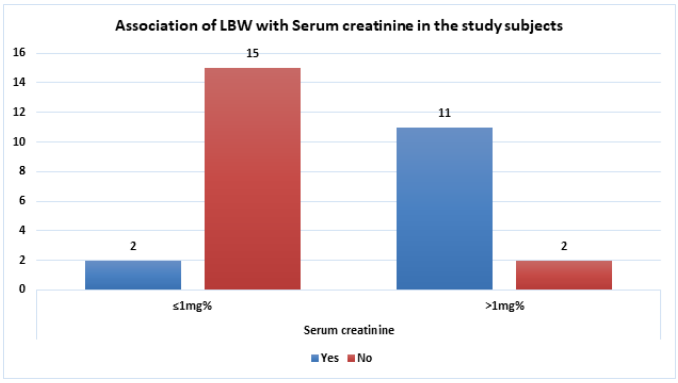


Table 12: Association of LBW with Urine Protein: creatinine in the study subjects

LBW	urine Protein: creatinine		Total	P value
	≥0.3	<0.3		
Yes	8	5	13	0.00097
No	1	16	17	Significant
Total	9	21	30	

The proportion of LBW in patients with raised urine Protein: creatinine ratio was 8 out of total 9 patients and 5 out of total 21 patients having normal urine Protein: creatinine ratio. This association of LBW to the urine Protein: creatinine ratio was statistically highly significant in the study.

Graph 11

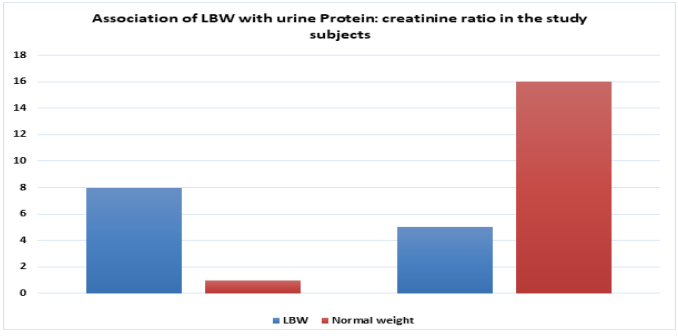


Table 13: Neonatal mortality with Urine Protein: creatinine ratio in the study subjects

Neonatal Mortality	Urine Protein: creatinine		Total	P value
	≥0.3	<0.3		
Yes	2	0	02	0.025
No	7	21	28	Significant
Total	9	21	30	

There were 2 neonatal deaths out of total 9 patients with raised Urine Protein: creatinine ratio (≥0.3). No neonatal death was reported among 21 patients having normal Urine Protein: creatinine ratio. The association of Neonatal Mortality to the Serum Protein: creatinine ratio found to be statistically significant in the study.

Graph 12

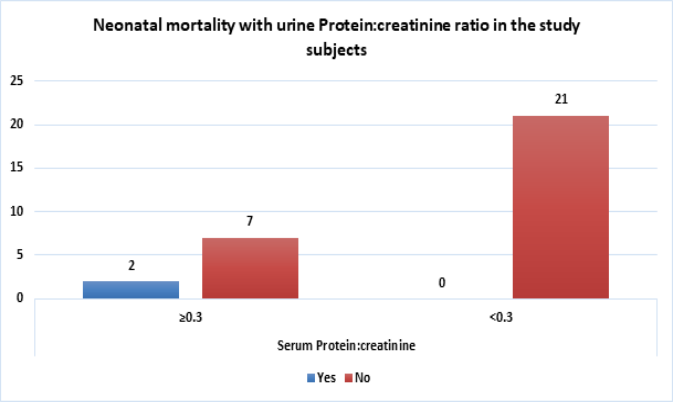
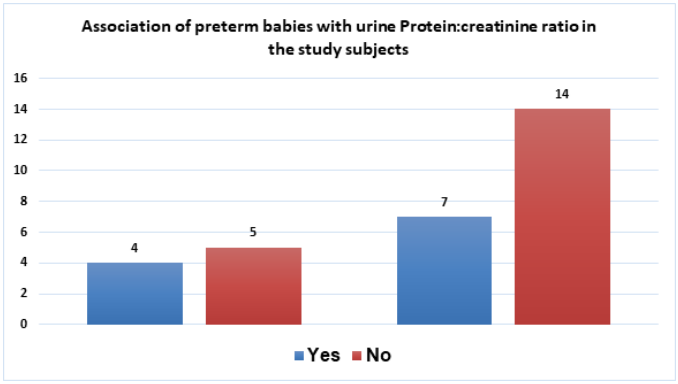


Table 14: Association of preterm babies with Urine Protein: creatinine in the study subjects

Preterm or not	Urine Protein: creatinine		Total	P value
	≥0.3	<0.3		
Yes	4	7	11	0.5627
No	5	14	19	Not Significant
Total	9	21	30	

The proportion of preterm births in patients with raised Urine Protein: creatinine ratio was 4 out of total 9 patients and 7 out of total 21 patients having normal urine Protein: creatinine ratio. This association of preterm births to the Serum Protein: creatinine ratio was statistically not significant in the study.

Graph 13



Discussion

This prospective observational study was conducted in a municipal tertiary care hospital and teaching institute. Total 30 pregnant patients who were chronic hypertensive were included in the study as per the study criteria. All necessary ethical permissions were taken.

Mean age was 31.13±3.1 years with minimum age 25 years and the maximum age of the patient was 38 years. Nearly half (47%) of the patients were between the age 29-32 yrs.

There was only one patient having past history of Pregnancy induced hypertension (3.33%). 4(13.33%) had previous LSCS. Out of 30, 26 patients were not having any significant contributory history. In other studies, given in the table 3 the proportion of preeclampsia was ranging from 10% to 25% which was far greater than 3.33% in our study. The sample size in all studies was quite large and so was the study period. It is pertinent to note that this study is a sample of the representation of the population affected.

There was a single patient with the History of DM, GDM, Gestational Hypothyroidism, BOH and Protein S deficiency and Pregestational hypothyroid of each (3.33% each). Most of the patients were not having any

preceding history. This has to do more with the social reasons and poor follow up which our pregnant women do. In the following studies, the associated morbidities were as follows:

	Preeclampsia	Abruption Placentae (%)	Delivery at 37 wk. (%)	SGA (%)
Sibai et al(n=211)	10	1.4	12.0	8.0
Rey and Couturier (n=337)	21	0.7	34.4	15.5
McCowan et al(n=142)	14	NR	16.0	11.0
Sibai et al(n=763)	25	1.5	33.3	11.1
Lydakis et a(n=213)	16	--		
Mabie et al.(n=169)	34.3	1.8		

The rate of the abruption placentae in these studies ranged from 0.7% to 1.4%. In our study not a single patient of abruption placentae was noted. The incidence of abruption placentae depends upon a number of factors, this conclusion of our study does not rule out the fact that Abruption placentae does form a serious morbid condition both for the mother and fetus and a high degree of suspicion is needed in order to tackle this emergency.

40% of the patients had BMI ≥25 and rest normal BMI i.e. <25. BMI didn't play a significant difference in the outcome. In the study out of total 30 patients, 23(76.67%) patients had raised BP and 7(23.33%) had well controlled blood pressure on medications.

There were 7 patients having the edema. In those 7 patients Grade 1 edema was present in 3 and Grade 2 was 4(13.33%) patients. Level of Serum creatinine >1 mg% was present in 13(43.33%) patients of the chronic hypertension. In 9(30%) of the patients the Urine protein to creatinine ratio was ≥0.3 suggestive of proteinuria. Total 13(43.33%) patients were delivered by LSCS of which 9(30%) were emergency LSCS. Israeli study of >100 000 deliveries reported an odds ratio of 2.7 (95% CI, 2.4–3.0) for caesarian section even after adjustment for superimposed preeclampsia. Mean gestational age in the study was 36.80 ±2.08weeks Highest was 39 weeks and lowest was 31.6 weeks.

There were total 11(36.67%) patients who delivered at preterm and rest 19(63.33%) who were delivered at term. These finding were opposite to that of Rey and Couturier (n= 337) and Sibai et al (n= 763) which had term deliveries of 34.4% and 33.3% respectively. The proportions of term deliveries were 12% and 16% in the studies by Sibai et al(n=211) and McCowan et al(n=142) respectively

APGAR score in neonates at 0 minutes was 7 or less in 8(26.67%) of the cases and >7 in rest 22(73.33%)

Mean weight was 2.43± 0.54kg Highest was 3.44kg and lowest was 0. 956kg.Incidence of LBW that is. birth weight <2.5kg was 43.33% in the study.

Neonatal mortality was reported to be 6.67% in the study. There were 2 deaths in neonates. In a study by Sibai et al. there were 2 stillbirths and 4 neonatal deaths for an overall perinatal mortality of 28.1/1000 which was greater than in our study 6.67%.Zetterström and colleagues conducted an analysis of >800000 Swedish birth records, including those in 4749 women with chronic hypertension, and reported an odds ratio of 2.71 (95% CI, 1.96–3.73) for intrauterine demise (stillbirth) and an odds ratio of 2.89 (95% CI, 1.95–4.83) for

neonatal death among the group with chronic hypertension.

In all of the emergency LSCS patients the serum creatinine was raised. Serum creatinine was raised in only 3 out of 17 patients of FTND and in 1 out of 4 patients of Elective LSCS. This association of mode of delivery to the serum creatinine level was statistically significant.

Urine Protein: creatinine was ≥0.3 (Proteinuria) in 7 out of 9 patients of the emergency LSCS patients It was also raised in 1 out of 17 patients of FTND and in 1 out of 4 patients of Elective LSCS. This association of mode of delivery to the urine Protein: creatinine ratio was statistically significant.

The proportion of LBW in patients with raised creatinine was 11 out of 13 patients and 2 out of total 17 patients having normal creatinine level of 1mg%. This association of LBW to the serum creatinine level was statistically highly significant in the study. The proportion of LBW in patients with raised urine Protein: creatinine ratio was 8 out of total 9 patients and 5 out of total 21 patients having normal urine Protein: creatinine ratio. This association of LBW to the urine Protein: creatinine ratio was statistically highly significant in the study.

There were 2(22.2%) neonatal deaths out of total 9 patients with raised urine Protein: creatinine ratio (≥0.3). No neonatal death was reported among 21 patients having normal Serum Protein: creatinine ratio. The association of Neonatal Mortality to the urine Protein: creatinine ratio found to be statistically significant in the study.

Also in a study by Ferrazzani S et al. Perinatal mortality rate was extremely higher in the group with protein uric preeclampsia which was 12.9%

The proportion of preterm births in patients with raised urine Protein: creatinine ratio was 4 out of total 9 patients and 7 out of total 21 patients having normal urine Protein: creatinine ratio. This association of preterm births to the urine Protein: creatinine ratio was statistically not significant in the study.

Rates for chronic hypertension during pregnancy between 0.6% and 2.7% have been reported. There may be under-reporting in population datasets for this diagnosis, with the rate more likely to be nearer 2%.

The rate for gestational hypertension is almost certainly under-reported, with rates between 4.2% and 7.9% recorded. Both chronic hypertension and gestational hypertension can progress to pre-eclampsia. Rates for pre-eclampsia are better known, though a range of 1.5% to 7.7% has been reported. The rate depends on the distribution of parity in the population: the rate for primigravida women is 4.1% and in women in their second pregnancy 1.7%. It is likely that up to 10% of pregnancies are complicated by hypertensive disorders and there is evidence that the rate may be increasing. The standards of care and substandard care (where different management might have been expected to prevent death) have been identified in the majority of cases. These failures of care have not just occurred in the critical care environment. Hypertensive disorders during pregnancy may result in substantial maternal morbidity, and maternal death is the tip of the iceberg. A study reported that one-third of severe maternal morbidity was a consequence of hypertensive conditions,[116]and another study found that over half of admissions for acute kidney failure, one-quarter of admissions for coagulopathy and nearly one-third of admissions for ventilation or cerebrovascular disorders occurred in women with hypertensive disorders.[24]A study reported that 1 in 20

(5%) women with severe pre-eclampsia. Hypertensive disorders also carry a risk for the baby. In the recent UK perinatal mortality report, about 1 in 20 (5%) stillbirths in infants without congenital abnormality occurred in women with pre-eclampsia. While this may be an improvement from the late 1990s (7%), it still represents a significant burden. A similar trend in the stillbirth rate has been seen in other countries. About 10% of women with severe pre-eclampsia give birth before 34 weeks. The contribution of pre-eclampsia to the overall preterm birth rate is substantial: 1 in 250 (0.4%) women in their first pregnancy will give birth before 34 weeks as a consequence of preeclampsia14 and 8–10% of all preterm births result from hypertensive disorders. Half of women with severe pre-eclampsia give birth preterm.

Summary and conclusions

This data was analyzed by SPSS version 20.0.

Mean age was 31.13±3.19 years with minimum age 25 years and the maximum age of the patient was 38 years. Almost half of the patients were having the age 29-32.

There was a single patient having past history of PIH (3.33%). 4(13.33%) had previous LSCS.

In our study, 26(86.67%) patients were not having any significant history.

Each one patient had the history of DM, GDM, Gestational Hypothyroidism, BOH and Protein S deficiency and Presentational hypothyroid of each.

Higher levels of Serum creatinine >1 mg% was present in 13(43.33%) patients of the chronic hypertension.

In 9(30%) of the patients the Urine protein to creatinine ratio was ≥0.3 suggestive of proteinuria.

Total 13(43.33%) patients were delivered by LSCS of which 9(30%) were emergency LSCS. Mean gestational age in the study was 36.80 ±2.08weeks Highest was 39 weeks and lowest was 31.6 weeks.

There were total 11(36.67%) patients who delivered at preterm.

APGAR score in neonates at 0 minutes was 7 or less in 8(26.67%) of the cases and >7 in rest 22(73.33%)

Mean weight was 2.43± 0.54kg Highest was 3.44kg and lowest was 0.956kg.

Incidence of LBW that is birth weight <2.5kg was 43.33% in the study.

Neonatal mortality was reported to be 6.67% in the study. There were 2 deaths in neonates

In all of the emergency LSCS patients the serum creatinine was raised. This association of mode of delivery to the serum creatinine level was statistically significant.

Serum Protein: creatinine was ≥0.3 (Proteinuria) in 7 out of 9 patients of the emergency LSCS patients. The association of mode of delivery to the Serum Protein: creatinine ratio was statistically significant.

Incidence of LBW in patients with raised creatinine was 11 out of 13 patients and 2 out of total 17 patients having normal creatinine level of 1mg%. Thus, the association of LBW to the serum creatinine level was statistically highly significant in the study.

The proportion of LBW in patients with raised Serum Protein: creatinine ratio was 8 out of total 9 patients and 5 out of total 21 patients having normal Serum Protein: creatinine ratio. This association of LBW to the Serum Protein: creatinine ratio was statistically highly significant in the study.

There were 2 neonatal deaths out of total 9 patients with raised urine Protein: creatinine ratio (≥0.3). The association of Neonatal Mortality to the urine Protein: creatinine ratio found to be statistically significant in the study.

The proportion of preterm birth in patients with raised urine protein to urine creatinine ratio was 4 out of total 9 patients and 7 out of total 21 patients having normal urine protein to urine creatinine ratio. This association of preterm births to the urine protein to urine creatinine ratio was statistically not significant in study.

In conclusion the study indicates that both the parameters of Serum Creatinine and Urine Protein to Creatinine ration when done in chronic hypertensive pregnant patients before 20 weeks of gestation has a reliable prediction for developing complications of neonatal morbidity and mortality. However, we have not been able to find any association with maternal complications of Renal failure or Abrutio placenta for the similar situation.

As with nearly all small studies, the sample size is a significant hindrance in coming to a final significant outcome. Further other parameters like renal involvement as a cause for chronic hypertension, which would have formed a major bulk of patients with secondary hypertension was not included in the study. The study also lacked a significant proportion of patients with detailed accurate pregestational history and evaluation which could have helped in identifying more cases of chronic hypertension. The social norm of registering later in pregnancy confuses the picture between pregnancy induced hypertension and chronic hypertension with superimposed preeclampsia.

To validate the study, a larger recruitment with multicenter involvement would be the most appropriate. It will also help to give more accurate predictive cut-off levels of the two parameters on whose basis effective counseling and antenatal monitoring of such patients can be undertaken.

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