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Assessment of Correlation of Serum Lipid Profile and Urinary Protein Creatinine Ratio with Occurrence of Gestational Hypertension in Pregnant Mothers in a Tertiary Care Hospital, Kolkata

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ABSTRACT

After 18 months study from 1st April, 2021 to 30th September, 2022 on the pregnant mothers in a tertiary care hospital, i.e., in R.G. Kar Medical College & Hospital, Kolkata, we have observed that there is significant rise of Urinary Protein Creatinine ratio in spot urine sample of Gestational hypertensive women in comparison to normotensive pregnant women. We may opine that, measurement of Spot Urinary Protein Creatinine Ratio as well as Serum Triglyceride, Total Cholesterol, different components of Cholesterol and calculation of their ratios may be used as precautionary steps, to take the necessary actions to prevent the complications of Gestational hypertension, i.e., graver grades of Pregnancy Induced Hypertension (PIH), namely, Preeclampsia and Eclampsia.

Keywords: Serum lipid profile; Urinary protein creatinine ratio; Gestational hypertension; Cholesterol; Pregnancy induced hypertension.

1. Introduction

Pregnancy is a very important physiological phenomenon in life of every woman though it concerns the whole family and society too. Normal human pregnancy (i.e. gestation) lasts approximately 40 weeks, as measured from the first day of the last normal menstrual period (LMP).

Hypertension is one of the common medical complications of pregnancy which contributes significantly to maternal and perinatal morbidity and mortality. Early identification of this clinical entity and its effective management play a significant role in the outcome of pregnancy, both for the mother and the baby. This entity on many occasions remains undetected till major complications supervene, particularly in undeveloped countries, with inadequately cared pregnancy.

During pregnancy a woman undergoes dramatic physiologic and hormonal changes. The large quantities of oestrogens, progesterone, prolactin, and corticosteroids produced during pregnancy affect various metabolic and endocrine systems [1]. In addition, the woman experiences (1) an increase in resistance to angiotensin, (2) a predominance of lipid metabolism over glucose use, and (3) increased synthesis by the liver of thyroid- and steroid-binding proteins, fibrinogen, and other proteins characteristic of pregnancy [2], [3], [4].

Gestational Hypertension, if not treated properly progresses to different strata of pregnancy induced hypertension, at first proceeds to preeclampsia, and followed by eclampsia. Gestational hypertension is a pregnancy condition characterized by hypertension which can occur any time after 20 weeks (although there are cases occurring at less than 20 weeks in abnormal pregnancies such as molar pregnancies). It affects 3% to 5% of pregnancies and continues to be a major cause of maternal and perinatal mortality [5]. The disorder manifests with placental

ischaemia and endothelial dysfunction that leads to intravascular deposition of fibrin with subsequent end organ damage. Most maternal deaths are due to central nervous system complications but ischemic liver damage may also occur [6]. If gestational hypertension cases are not treated properly and disease aggravates then only cure for this condition is delivery of the placenta.

Abnormal lipid metabolism has a basic role in the pathogenesis of PIH (Pregnancy induced Hypertension) where endothelial cell damage is one of the earliest hallmarks. Lipoproteins levels increase more in PIH than in normal pregnancy and cause damage to endothelium that may result in high blood pressure and proteinuria. In pregnancy there is an increase in oestrogen levels which is the main factor behind hypertriglyceridemia [7].

Gestational hypertension if further proceeds as untreated may put both maternal and foetal health at risk. Hypertensive disorders of pregnancy (HDPs) contribute globally to approximately 30,000 maternal deaths annually [8]. According to National Health Portal, India 2016, the prevalence of HDPs in India was 7.8%.

Chronic hypertension is present in up to 5% of pregnant women and is defined as hypertension present before pregnancy or before 20 weeks of gestation. In a multicentre study conducted by National High Blood Pressure Education Program, approximately 30% of HDPs were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension [9].

Another one important and well-known clinical feature of dreaded preeclampsia and eclampsia cases is proteinuria. So increased Protein- creatinine ratio in urine may be an early hallmark of detection of preeclampsia associated with proteinuria greater than 300 mg/24 h or PCR (Protein: Creatinine Ratio) more than 30mg/mmol or more than 0.3 after 20 weeks of gestation [10]. One of the early pathophysiological hallmarks in pre-eclampsia is endothelial cell damage. Proteinuria is a marker of endothelial dysfunction in glomerular as well as renal tubules of nephrons and is associated with essential hypertension, obesity, diabetes and renal disease. Persistent proteinuria indicates a high probability of damage of the glomerular filtration capacity of the kidney and is of major diagnostic importance in pregnancy as a possible predictor of developing Preeclampsia [11]. Although the 24-h collection of urine is the gold standard for quantifying urinary albumin excretion, it is cumbersome to collect the sample and results in a delay of at least 24 h in diagnosis. Many previous studies have measured microalbuminuria to predict pre-eclampsia in early pregnancy, postulating that the stage of gross proteinuria is preceded by the stage of microalbuminuria. This study is an attempt to evaluate the role of single spot urinary protein/creatinine ratio as prediction of pre-eclampsia in asymptomatic pregnant women in early pregnancy [12] which is a less costly parameter than microalbumin (ACR- albumin creatinine ratio).

So, over all this present study is based on two types of assays (1) serum lipid profile and (2) spot urine protein-creatinine ratio. Two groups are taken- (1) healthy pregnant women and (2) Gestational hypertensive cases (same age group as Group Number 1) and Group 1 is taken as control. This study will estimate lipid profile and spot urine protein creatinine ratio in both group to find any association between lipid profile and urine protein creatinine ratio with pregnancy induced hypertension cases with comparison to healthy pregnant women so that the results of these parameters may guide the obstetricians to take the necessary measures at an early stage of Gestational hypertension before attaining the dreaded stages of pregnancy induced hypertension i.e preeclampsia and eclampsia.

2. Aims and Objectives

The current study aimed to see the analysis of serum biomarkers -lipid profile (Triglyceride, total cholesterol, High density lipoprotein cholesterol-HDL-C, low density lipoprotein cholesterol- LDL-C and very low density lipoprotein cholesterol- VLDL-C) and spot sample of urinary protein – creatinine ratio in between two groups- Gestational hypertension cases and in normotensive pregnant cases in a tertiary care hospital, Kolkata and comparative assessment of these parameters in between two groups.

2.1. Specific Objectives

1. Estimation of serum lipid profile (Triglyceride, total cholesterol, High density lipoprotein cholesterol- HDL-C, low density lipoprotein cholesterol- LDL-C and very low-density lipoprotein cholesterol- VLDL-C) separately in Gestational hypertension cases and in normotensive pregnant cases.

2. Estimation of urinary protein creatinine ratio (UPCR) separately in Gestational hypertension cases and in normotensive pregnant cases.

3. Comparative assessment in these two groups to find out any association between Gestational hypertension cases with estimated serum lipid profile and estimated spot sample of UPCR.

3. Materials and Methodology

An observational case-control study was conducted in the Department of Biochemistry after getting approval from the West Bengal University of Health Sciences and the Institutional ethics Committee, in collaboration of the Department of Gynecology and Obstetrics of R.G. KAR Medical College and Hospital, Kolkata. After obtaining the ethical clearance the study was started from 1st April 2021 and continued till 30th September 2022, total – 18 months.

Clinically diagnosed Gestational Hypertension cases who have not start the treatment along with apparently healthy pregnant women matched age as controls.

76 gestational hypertension cases recruited from outpatient and inpatient Department of Gynaecology & Obstetrics R.G.KAR Medical College and Hospitals, Kolkata, following set of fixed inclusion and exclusion criteria. Side by side, 76 normotensive pregnant who are otherwise normal had been taken as control in our study.

Parameters measured in this study are-serum Total Cholesterol, Triglyceride, High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Very Low-Density Lipoprotein Cholesterol (VLDL-C) and Calculation of spot Urinary Protein Creatinine Ratio (UPCR)

4. Results

The following parameters are taken as main indicators of our study. The parameters are compared in Gestational Hypertension and Normotensive pregnant women group as follows-

1. Total serum Cholesterol

2. Serum Triglyceride

3. Serum High Density Lipoprotein cholesterol (HDL-C)

4. Serum Low Density Lipoprotein cholesterol (LDL-C)

5. Serum Very Low-Density Lipoprotein cholesterol (VLDL-C)

6. Serum calculated Non-High-Density Lipoprotein cholesterol (Non-HDL-C)

7. Serum calculated Cholesterol-HDL-C Ratio

8. Serum calculated LDL-C: HDL-C

9. Serum calculated VLDL-C: HDL-C and

10. Spot sample urine Protein- Creatinine Ratio

Steps of Statistical Significance

1. At first Tests of Normality done where it has been seen that whether the samples of these above parameters are showing normal distribution or skewed distribution. For these two tests can be done-

(i) KOLMOGOROV – SMIRNOV test (where sample size > 50)

(ii) SHAPIRO- WILK test (where sample size < 50)

2. Here 76 samples are taken from both two groups. So, KOLMOGOROV – SMIRNOV test is accepted.

3. Here if Null Hypothesis is accepted that means the distribution is Normal if Null Hypothesis is rejected that means here the distribution is not normal or skewed to one side.

4. If p value is found < 0.05 that means statistically significant or Null hypothesis rejected so distribution skewed.

5. Then if Distribution is found normal than t test could be done and if the distribution is found as skewed, then Man- Whitney U test is to done.

6. If these results are significant that is p value is < 0.05 then Null Hypothesis is rejected that means Urinary protein-creatinine ratio in Hypertensive pregnant group is significantly higher than that of normotensive group. In case of serum lipid profile also if p value is < 0.05 then total cholesterol and other components of total cholesterol like Triglyceride, LDL, VLDL are significantly higher in Gestational hypertensive group in comparison to normotensive pregnant group.

7. All data are to be compiled in SPSS version 20 (Statistical Package for Social Sciences) method.

(1) Tests of Normality

Here result in test of Normality accepted in Kolmogorov-Smirnov test as sample size is 76 (more than 50).

At first all parameters for lipid profile done.

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Table 1. Tests of normality

	V1	Kolmogorov–Smirnov[a]			Shapiro–Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Chol HDL ratio	1	.086	76	.200*	.961	76	.021
	2	.116	76	.014	.927	76	.000
Total Cholesterol	1	.114	76	.016	.961	76	.019
	2	.135	76	.002	.905	76	.000
TG	1	.127	76	.004	.951	76	.005
	2	.218	76	.000	.742	76	.000
HDL	1	.142	76	.001	.945	76	.003
	2	.188	76	.000	.892	76	.000
LDL	1	.064	76	.200*	.984	76	.439
	2	.129	76	.003	.930	76	.000
VLDL	1	.137	76	.001	.948	76	.004
	2	.219	76	.000	.743	76	.000
Non HDL	1	.111	76	.021	.962	76	.021
	2	.139	76	.001	893	76	.000

Distributions are found skewed for all the above parameters.

Test of normality done by Kolmogorov-Smirnov test in serum LDL-C: HDL-C and VLDL-C: HDL-C and found in these two parameters sample distributions are normal.

Table 2. LDL-C: HDL-C Value

	Kolmogorov-Smirnov test value	P value	Inference
Gestational hypertension group	0.06203	0.91405	As p value is > 0.05 so distribution is normal
Normotensive pregnant group	0.11788	0.22336	As p value is > 0.05 so distribution is normal

Table 3. VLDL-C: HDL-C Value

	Kolmogorov- Smirnov test value	**P value**	**Inference**
Gestational hypertension group	0.12511	0,16942	As p value is > 0.05 so distribution is normal
Normotensive pregnant group	0.15109	0.05582	As p value is > 0.05 so distribution is normal

Table 4. Spot Urine Protein: Creatinine ratio

	Kolmogorov-Smirnov test value	**P value**	**Inference**
Gestational hypertension group	0.16125	0.02031	As p value is < 0.05 so distribution is skewed.
Normotensive pregnant group	0.26441	0.00001	As p value is < 0.05 so distribution is skewed.

(2) Compilation in SPSS software package

Here tests of normality done with above parameters by SPSS software package.

V1 is taken as Gestational hypertension group that is group1 and Normotensive group is taken as 2. If p value is found <0.05 in any of these two groups for any parameter then it can be called that the distributions are skewed.

(3) Normal or Skewed

Here in all the parameter p value is found < 0.05 and so in all parameter's distribution is to taken as, skewed in both Hypertensive and Non-hypertensive pregnant cases.

(4) T test or Mann- Whitney Test

Now as in all parameters except serum LDL-C: HDL-C ratio and VLDL-C: HDL-C ratio are found Skewed distribution. So, Man-Whitney test is to be done for each parameter except those two. And for LDL-C: HDL-C ratio and VLDL-C: HDL-C ratio unpaired T test is done. Following results are found by SPSS software package.

MANN-WHITNEY TEST:

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Table 5. For Lipid profile except LDL-C: HDL-C ratio and VLDL-C: HDL-C ratio

Ranks

	V1	N	Mean Rank	Sum of Ranks
TOTAL CHOLESTEROL	1	76	101.34	7702.00
	2	76	51.66	3926.00
	Total	152		
TG	1	76	109.50	8322.00
	2	76	43.50	3306.00
	Total	152		
HDL	1	76	54.41	4135.50
	2	76	98.59	7492.50
	Total	152		
LDL	1	76	98.47	7484.00
	2	76	54.53	4144.00
	Total	152		
VLDL	1	76	109.57	8327.50
	2	76	43.43	3300.50
	Total	152		
Chol HDL ratio	1	76	110.15	8371.50
	2	76	42.85	3256.50
	Total	152		
Non HDL	1	76	104.87	7970.00
	2	76	48.13	3658.00

(5) Null hypothesis accepted or rejected

Now it has to be decided whether Null hypothesis is accepted or rejected. If in any parameter p value is found < 0.05 then for that parameter Null hypothesis will be rejected i.e amount of analytes in sample of one group (for current study Hypertensive group) is significantly higher than that of other group (for current study Normotensive group).

All the results are found by SPSS version 20 software package.

All results (mean) and level of significance are in a single row in below-

	Total cholesterol (TC) mg/dl	**Triglycerides mg/dl**	**HDL-C mg/dl**	**LDL-C mg/dl**	**VLDL-C mg/dl**	**Non-HDL-C mg/dl**	**TC: HDL-C**	**LDL-: HDL-C**	**VLDL-C : HDL-C**	**UPCR**
Gestational hypertension group	227	258	39	137	52	188	5.8	3.5	1.31	0.26
Normotensive pregnant group	169	139	45	94	27	123	3.7	2.1	0.62	0.16
Level of Significance	Significant	Significant	Significant	Significant	Significant	Significant	Significant	Significant	Significant	Significant

This is one of the key factors in our study to see any significant difference between these two proposed groups. It was earlier discussed that if Urinary protein- creatinine ratio is found more than 0.3 in gestational hypertension it is

suggestive of **PROTEINURIA**. In our current study it was also found that in spot sample urine of Gestational hypertension group PCR (protein- creatinine ratio is (0.26) is more than that of normotensive pregnant group (0.16).

5. Discussions

BP ≥140/90 mm Hg for the first time in pregnancy measured two times with at least 6-hour interval after 20 weeks, without Proteinuria [13].

From NHP (National Health Portal) it is found that in India prevalence of Gestational hypertension is 7.8 %. In one study Magee LA et al found that Gestational hypertension incidence was lower in Pakistan (9.3%) than India (10.3%), Mozambique (10.9%), or Nigeria (10.2%) (p = 0.001). Most hypertension was diastolic only (46.4% in India, 72.7% in Pakistan, 61.3% in Mozambique, and 63.3% in Nigeria) [14].

The cause of gestational hypertension is unknown. Some conditions may increase the risk of developing the condition, including the following:

- Pre-existing undiagnosed hypertension
- Kidney disease
- Diabetes
- Hypertension with a previous pregnancy
- Mother's age younger than 20 or older than 40
- Multiple foetuses (twins, triplets)
- African-American race

Main concern of Gestational hypertension is with high blood pressure, there is an increase in the resistance of blood vessels. This may hinder blood flow in many different organ systems in the expectant mother including the liver, kidneys, brain, uterus, and placenta.

There are other problems if gestational hypertension is overlooked or neglected or remains untreated or inadequately treated. Placental abruption (premature detachment of the placenta from the uterus) may occur in some pregnancies. Gestational hypertension can also lead to foetal problems including intrauterine growth restriction (poor foetal growth) and stillbirth.

Furthermore, if untreated, severe gestational hypertension may cause dangerous seizures (eclampsia) and even death in the mother and foetus. Because of these risks, it may be necessary for the baby to be delivered early, before 37 weeks gestation.

From previous worker's study it has been revealed that there are some factors which have some influence on gestational hypertension. One of these influential factors is maternal age. Though it is not our focus of the study but Dietl A et al., on 2015 worked on it and found some association of Gestational hypertension with advanced maternal age [15].

Gudeta TA et al., on 2019 worked on women attending delivery service at Mizan-Tepi University Teaching Hospital, Tepi General Hospital and Gebretsadik Shawo Hospital, and found gestational age were predictors of Gestational hypertension [16].

In our current study we also found that mean age in gestational hypertension is 25.6 yrs. which is significantly higher than normotensive group that is 23.6 yrs. In Mann-Whitney U test p value is found 0.0005 which is far below than 0.05.

We conducted our current study by taking 76 cases of Hypertensive pregnant women and side by side similar number of normotensive pregnant women are chosen as control. In both groups Urinary protein- creatine ratio was done from spot urine sample as well as from serum sample measurement of Total cholesterol, Triglyceride, HDL-C, LDL-C, VLDL-C, Non-HDL-C, total cholesterol: HDL cholesterol ratio, LDL cholesterol: HDL cholesterol ratio and VLDL cholesterol: HDL cholesterol ratio was done and comparison done between these two groups and found significant different.

These ideas are taken from some previous research works done in India or outside of India. Varghese S et al., on 2020 have found that abnormal pregnancy lipid profile is shown to have a positive correlation with endothelial dysfunction which in turn leads to development of hypertensive disorder of pregnancy [17].

This lipid profile means total cholesterol and its different components are our study interests. In a case control study done at Central India where Singh B et al., on 2018 Singh B have found that the subjects who are suffering from dyslipidaemia are more prone to Hypertension [18]. They showed that mean cholesterol, triglyceride, LDL-C, VLDL-C, value is analysed with control group showing significantly increase ($p<0.0001$) and HDL-C value significantly decreased in pre-eclampsia patient in comparison to the normal control group ($p<0.0001$).

Evruke C et al., in 2004 studied on relationship between gestational hypertension and occurrence of hyperlipidaemia and concluded that in gestational hypertension cases, hyperlipidaemia is more profound than in the normotensive group. Lipid levels increase parallel to the severity of the disease being improved in normotensive group compared with the gestational hypertensive group [19].

As there is a strong relationship between High lipid profile and general hypertension so it is obvious to think about association between serum high lipid status with gestational hypertension. In an USA based study it was found by Sakurai M et al., on 2011 that with sequential models to control for multiple possible confounders (dietary, other), linear regression analyses showed that dietary cholesterol was directly related to systolic blood pressure for all participants and for normotensive pregnant individuals. With adjustment for 12 variables, estimated systolic blood pressure differences with 2 standard deviation higher cholesterol intake (131.0 mg/1,000kcal) were 0.9 mmHg ($p<0.05$) for all participants, and 1.1 mmHg ($p<0.01$) for non-hypertensive individuals [20].

Daniel A et al., on 2016 studied on this similar subject on 2016 and found that women who subsequently developed preeclampsia had 10.4%, 13.6%, and 15.5% higher concentrations of LDL cholesterol, triglycerides, and LDL cholesterol: HDL cholesterol ratios, respectively, than did control subjects ($P < .05$). The HDL cholesterol concentrations were 7.0% lower in women with preeclampsia than in control subjects ($P < .05$) [21].

In our current study we also found that mean total cholesterol in gestational hypertension is 227 mg/dl which is significantly higher than normotensive group that is 169 mg/dl. In Mann-Whitney U test p value is found 0.0007 which is far below than 0.05.

Some scholars Ray et al., on 2006 in British territory found an association between serum Triglyceride and Hypertension in gestational status [22].

In a study Siddiqui I et al., on 2006 showed that women with gestational hypertension exhibited higher serum triglyceride levels compared with normal pregnant women ($P < 0.01$). They recommend that any pregnant female with higher serum triglyceride concentrations may be further investigated and followed up carefully as there is a chance of developing hypertension [23].

Guan P et al., studied the effect of serum triglyceride on gestational hypertension on 2012 and concluded that maternal TG levels are associated with gestational hypertension, and a wide range of TG levels is sufficient for foetal growth within a given gestational week [24].

Research was done by Ray J G et al., in 2006 on maternal triglycerides as a factor for pre-eclampsia and found that the mean TG concentration was significantly higher among pre-eclamptic cases than among unaffected controls. The risk of pre-eclampsia typically doubled with each increasing TG category [25].

In our current study we also found that mean serum triglyceride in gestational hypertension is 258 mg/dl which is significantly higher than normotensive pregnant group that is 139 mg/dl. In Mann-Whitney U test p value is found 0.0006 which is far below than 0.05.

Recent China based studies Hwang YC et al., on 2019 have suggested that high density lipoprotein cholesterol (HDL-C) cholesterol is inversely associated with the development of hypertension. After 10 years study they have shown that HDL cholesterol more specifically HDL-C 2 is inversely associated with occurrence of hypertension [26].

In our current study we also found that mean serum High density lipoprotein Cholesterol in gestational hypertension is 39.7 mg/dl which is significantly lower than normotensive pregnancy group that is 45.1 mg/dl. In Mann-Whitney U test p value is found 0.0007 which is far below than 0.05.

Rajesh A et al., of India on 2020 found in their study the mean serum total cholesterol (TC) level was significantly higher in Gestational hypertension group than that of normotensive pregnant group with p value < 0.001. Triglyceride and LDL cholesterol were also significantly higher in Gestational hypertension women as compared to normotensive pregnant women [27].

Shihab A et al., in a recent study on first quarter of 2022 found that LDL cholesterol and other bad cholesterol like VLDL cholesterol are high in pregnancy induced hypertension cases. He Statistically showed significant differences in LDL cholesterol and other bad components of Lipid profile(TG,TC and VLDL) in PIH patients as compared to normal controls [28].

In our current study we found that mean serum LDL cholesterol in gestational hypertension is 137 mg/dl which is significantly higher than normotensive group that is 94 mg/dl. In Mann-Whitney U test p value is found 0.0006 which is far below than 0.05.

Research done by Sparklane C N et al., on 2013 and the objective of this meta-analysis was to test the association between preeclampsia and maternal total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), non-HDL-C, and triglyceride levels measured during pregnancy. Seventy-four studies met all eligibility criteria and were included in the meta-analysis. Weighted mean differences in lipid levels were calculated statistically. Preeclampsia was associated with elevated total cholesterol, non-HDL-C, and triglyceride levels, regardless of gestational age at the time of blood sampling, and with lower levels of HDL-C in the third trimester [29].

Tesfa E et al., had done research on 2020 and in this review, the maternal serum levels of TG, TC, LDL-c and VLDL-c were significantly associated with the risk of preeclampsia. However, HDL-cholesterol was not significantly associated but it was lower in pre-eclamptic women. Further, large scale prospective studies should verify these outcomes and it is recommended that lipid profiles should be included as a routine diagnostic test for pre-eclamptic women [30].

As non-HDL cholesterol is called ‘bad cholesterol’ so it can be assumed that it may be associated with hypertension. In our current study we found that mean serum non-HDL cholesterol in gestational hypertension is 187 mg/dl which is significantly higher than normotensive group that is 123 mg/dl. In Mann-Whitney U test p value is found 0.0006 which is far below than 0.05.

In our study it has been revealed that increased amount serum total cholesterol is associated with gestational hypertension whereas HDL cholesterol is inversely associated. So, if I combine both parameters, it should reveal that serum cholesterol – HDL cholesterol ratio is positively associated with Gestational hypertension. We have found mean Cholesterol -HDL ratio in gestational hypertension is 5.77 whereas in normotensive pregnant women it is 3.75. So, by Mann-Whitney U method p value is found 0.005 which is far below than 0.05. So, Cholesterol-HDL cholesterol ratio is significantly higher in pregnancy Induced hypertensive group in comparison to normotensive group.

On other side Hypertension is both a cause and effect of CKD (chronic kidney disease) and affects most CKD patients. Control of hypertension is important in those with CKD as it leads to slowing of disease progression as well as reduced CVD risk.

High levels of protein in urine over a period may be the first sign that kidney disease or another condition has damaged the filters in kidneys. A protein in urine test can help us to find kidney damage early so we can make changes to protect our kidneys. So, we can say that urine protein is associated with hypertension.

Ahmed Aziz KM et al., on 2019 invented regression models for the excretion of urinary protein from the kidney with elevated SBP (systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure) and PP (Pulse Pressure) were highly significant ($p < 0.0001$ for all) [31].

Duka I et al., on 2008 published an article and from this review provides a summary of current evidence regarding the associations of blood pressure with microalbuminuria [32].

Same type of conclusions came when multiple researchers from different site worked on same topics like relation between urine protein and Gestational hypertension.

Qualitative and quantitative measurement of urine protein excretion is one of the most common tests performed during pregnancy which is necessary for the diagnosis of preeclampsia which may occurred in untreated Gestational hypertension. From a recent experiment done by Fishel B M and his co-workers the classic cut-off cited to define proteinuria during pregnancy is a value of >300 mg/24 hours [33].

One of the most reliable types of evidence of chronic kidney disease is Urinary Protein- Creatinine ratio in spot sample of urine. Now a days it mostly replaced 24 hours protein excretion in urine. Ramos JG et al., on 1999 have done a cross-sectional study of 47 hypertensive patients who had been pregnant for 20 weeks or more seen at the Maternity of the University Hospital of Porto Alegre. The protein/creatinine ratio measured in a single urine sample that is 0.3 is taken at random from hypertensive pregnant women showed good sensitivity and specificity for the diagnosis of 24-h proteinuria > or = 300 mg and was strongly correlated with 24-h proteinuria [34].

Sanchez-Ramos L et al., on 2013 worked on Spot urine sample to find Protein- Creatinine ratio and to predict proteinuria which is associated with hypertension. They concluded that protein-to-creatinine ratio from a random urine sample provides useful evidence which can rule out the presence of significant proteinuria in patients at risk for preeclampsia [35].

Naturally it can be presumed that there is an association between Gestational hypertension and Urinary protein-Creatinine ratio in spot urine sample. Some authors like Demirci O et al., on 2015 proved necessity of Urinary protein-Creatinine ratio replacing 24 hours urine protein. They concluded that the P/C ratio can be used as a screening test as a good predictor for remarkable proteinuria. The P/C ratio seems to be highly predictive for diagnosis to detect proteinuria over one gram and it could be used as a rapid alternative test in preeclamptic patients not to delay implementation treatment [36].

Young RA et al., on 1996 worked on it and finally concluded that the protein/creatinine ratio of a single voided urine specimen may have a role in the management of complicated Gestational hypertension cases. The main potential benefit of this method is that in institutions where women with suspected complications are hospitalized, women with significant proteinuria may be identified within a matter of hours and their follow-up care handled on an outpatient basis [37].

In a study done by Robert M and his co-workers found that In non-ambulatory hypertensive pregnant patients, there is a strong correlation between random voided protein-creatinine ratios and 24-hour urine protein excretions [38]. Pasternek Y et al., worked on it on 2021 and concluded that UPCR was strongly correlated with various cut off of proteinuria obtained by 24-h urine collection. Though UPCR cut off varied depending on the specific measured outcome. This correlation was not affected by gestational age at examination [39].

Xiao J et al., has done a study most recently i.e., May, 2022 and this study indicated that there was a significant and positive correlation between UPCR and 24-hour urine protein. For neonatal and maternal adverse outcomes, UPCR is an independent predictor of prognosis [40].

In our current study we found that mean urinary protein- Creatinine ratio in spot sample in gestational hypertensive group is 0.26 which is significantly higher than normotensive group that is 0.16. In Mann-Whitney U test p value is found less than 0.0001 which is far below than 0.05.

So, our current study is able to show the association between spot sample of urinary protein- creatinine ratio and Gestational hypertensive cases and side by side it also revealed the positive relation between all components of lipid profile like Total cholesterol, Triglyceride, low density lipoprotein cholesterol (LDL), Very low density lipoprotein cholesterol (VLDL), Total cholesterol- High density lipoprotein ratio and Non- HDL cholesterol with Gestational hypertension cases in comparison to Normotensive pregnant women. This study also showed negative association between HDL cholesterol and Gestational Hypertension.

6. Conclusion

After 18 months study from 1st April, 2021 to 30th September, 2022 on the pregnant mothers in a tertiary care hospital, i.e., in R. G. Kar Medical College & Hospital, Kolkata, we have concluded that there is significant rise of Urinary Protein Creatinine ratio in spot urine sample of Gestational hypertensive women in comparison to normotensive pregnant women. Different analytes like Serum Total cholesterol, Triglyceride, HDL cholesterol, LDL cholesterol, VLDL cholesterol and non-HDL cholesterol as well as some ratios like Total cholesterol: HDL cholesterol, LDL cholesterol: HDL cholesterol and VLDL cholesterol: HDL cholesterol are found to be significantly high in Gestational hypertensive group in comparison to normotensive pregnant women group. Serum HDL cholesterol is found significantly lower in Gestational hypertensive group in comparison to normotensive pregnant women group. From this current study, we can opine that the different components of Serum lipid can be used as the early biomarkers before progression of Gestational hypertension to the graver grades of Pregnancy Induced Hypertension (PIH), i.e., Preeclampsia and Eclampsia. Urinary Protein Creatinine Ratio in spot urine sample may also be used as another biomarker in the Gestational hypertension cases at very early stage to restrict the progression of kidney disease as well as further progression to the complications of PIH, i.e., Preeclampsia, where gross proteinuria is noticed. Hence, we may opine that, measurement of Spot Urinary Protein: Creatinine Ratio as well as Serum Triglyceride, Total Cholesterol, different components of Cholesterol and calculation of their ratios may be used as precautionary steps, to take the necessary actions to prevent the complications of Gestational hypertension, i.e., the graver grades of Pregnancy Induced Hypertension (PIH), namely, Preeclampsia and Eclampsia.

7. Limitations

As the study was done in an urban area, so most of the cases are from urban or sub-urban areas. The study was done within 18 months duration, so, number of samples were not quite high. Samples were taken from only one Tertiary care hospital because of easy and available access of researcher.

Declarations

Source of Funding

The study has not received any funds from any organization.

Competing Interests Statement

The authors have declared no competing interests.

Consent for Publication

The authors declare that they consented to the publication of this study.

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