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RESEARCH ARTICLE
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A COMPARATIVE STUDY TO EVALUATE THE SERUM LIPID LEVELS AND LIPOPROTEIN-(a) WITH PREGNANCY INDUCED HYPERTENSION AND NORMOTENSIVE PREGNANT WOMEN AT A TERTIARY CARE TEACHING HOSPITAL IN TELANGANA.

Deepa Polepaka[1], Narender Sayini[2*], J. Naveena[3].

[1]associate Professor, Department Of Obstetrics And Gynecology, Ggh, Karimnagar.
E-Mail: Polepska7@Gmail.Com
[2*]civil Surgeon, Department Of Pulmonology, Ggh, Karimnagar.
E-Mail: Sayininarender0@Gmail.Com
[3]civil Surgeon, Department Of General Medicine, Ggh, Karimnagar.
E-Mail: Naveena_Naveena2009@Yahoo.Co.In

***Corresponding Author:** Dr. Narender Sayini,
*Md, Department Of Pulmonology. Ggh, Karimnagar, Telangana-509103.
E-Mail: Sayininarender0@Gmail.Com. Mobile Number:7702230202.

ABSTRACT

Background and objectives: Blood pressure of 140/90 mm Hg or higher, without proteinuria and oedema after 20 weeks of pregnancy, is considered pregnancy-induced hypertension. A clinical characteristic of PIH, proteinuria and hypertension, can arise from endothelial dysfunction associated with dyslipidaemias. There is a clear correlation between the rise in plasma triglycerides and plasma cholesterol and the steady increase in mean serum oestradiol concentration from 10 to 35 weeks of pregnancy. Serum lipid concentration and serum Lipoprotein (a) levels may provide a useful marker for screening patients at risk for developing PIH. Therefore, the study aims to assess and compare the serum levels of lipid and lipoprotein (a) in pregnant women with pregnancy-induced hypertension and normotensive pregnant women.

Methods: A case-control observational study was carried out at the Government General Hospital, Karimnagar, over 12 months with 50 cases of Pregnancy-induced hypertension and 50 age-matched controls.

Results: A total of 100 subjects were grouped into cases and controls. Their serum lipid profile and lipoprotein (a) levels were evaluated. The t-test was used as a test of significance for qualitative data. A p-value of <0.05 was considered statistically significant after assuming all the rules of statistical tests. Among cases, the mean total cholesterol was 185.68+ 25.61mg/dl, the mean serum triglycerides were 217.28 + 56.49 mg/dl, the mean HDL levels were 37.34 + 5.95 mg/dl, the mean LDL was 100.04 + 26.22 mg/dl, the mean VLDL was 48.11+ 14.67 mg/dl and the mean Lp(a) was 48.58 + 13.62 mg/dl.

Conclusion: This study concludes that elevated lipid profile and lipoprotein (a) levels were shown to be highly correlated with PIH, indicating that elevated lipids may play a role in the pathophysiology of PIH.

Keywords: Pregnancy-induced Hypertension, Gestational Hypertension, Preeclampsia**,** lipid profile**,** Lipoprotein (a).

INTRODUCTION:

Gestational hypertension and Preeclampsia are two disorders that can cause high blood pressure during pregnancy. Both disorders are classified as pregnancy-induced hypertension (PIH). Most international recommendations classify blood pressure (BP) of 140/90 mm Hg or above during pregnancy as hypertension[1]. After 20 weeks of pregnancy, elevated blood pressure without proteinuria or other preeclamptic symptoms is referred to as gestational hypertension[2]. The second most common cause of maternal mortality globally is hypertensive disorders during pregnancy, and the first is maternal haemorrhage. According to the JNC7 guidelines, the prevalence of hypertension was 7.8%, whereas the 2017 guideline said that it was 16.5%. According to the 2017 guidelines, antihypertensive drugs should include 8.6%, which is comparable to the JNC7 guideline's 8.5% recommendation[3]. Pregnancy complications from hypertensive diseases affect 8-10% of pregnancies worldwide and are a major cause of morbidity and mortality for both the mother and the foetus[1].

Clinically, PIH is defined as the new onset of hypertension (HTN), which is systolic blood pressure (BP) ≥140 mm Hg and/or diastolic BP ≥ 90 mm Hg, or an absolute rise in BP of at least 140/90 mm Hg if the prior BP is unknown, or a rise in systolic blood pressure of at least 30 mm Hg or a rise in diastolic blood pressure of at least 15 mm Hg when proteinuria is absent [4]. Pre-eclampsia is defined as BP ≥140/90 mmHg and proteinuria at or after 20 weeks of gestation in a woman with previously normal BP[5]. Eclampsia is defined as the occurrence of seizure on a background of pre-eclampsia[5].

There is physiological hyperlipidaemia during pregnancy[6]. The concentration of cholesterol and plasma triglycerides increases by 25-50% and 200-400%, respectively, during a normal pregnancy[7]. There is a clear correlation between the rise in plasma triglycerides and plasma cholesterol and the steady increase in mean serum oestradiol concentration from 10 to 35 weeks of pregnancy[7]. Serum lipid concentration and serum Lipoprotein (a) levels may provide a useful marker for screening patients at risk for developing PIH. Null parity, extreme ages, obesity, a family history of hypertension, and insufficient antenatal care are some of the risk factors for PIH[5].

It is well recognized that an abnormal lipid profile directly affects endothelial functioning and is closely linked to atherosclerotic cardiovascular disorders [7,8]. Elevated serum levels of Lp (a) may contribute to the vascular changes seen in hypertensive disorders during pregnancy, making it an area of interest for comparative studies between PIH and normotensive pregnant women. Several studies have examined the variations in serum lipid profiles (TC, TG, LDL-C, HDL-C, and VLDL-C) in pre-eclamptic women compared to normotensive pregnant women [9,10]. However, only a few studies have compared serum lipid concentration and lipoprotein (a) levels. Therefore, this study aimed to investigate and compare serum lipid levels (including total cholesterol, triglycerides, low-density lipoprotein cholesterol [LDL-C], and high-density lipoprotein cholesterol [HDL-C]) and Lp(a) levels in pregnant women diagnosed with PIH and those who are normotensive.

OBJECTIVE:

The study aims to assess and compare the serum levels of lipid and lipoprotein (a) in pregnant women with pregnancy-induced hypertension and normotensive pregnant women.

METHODOLOGY:

Study design:

This study was a case-control study after obtaining informed consent from the study subjects.

Study setting:

The study was conducted at the Government General Hospital, Karimnagar, a tertiary care teaching hospital, in Telangana. The study was conducted over a period of 12 months. During this period, the

patients who attended the OPD with symptoms and signs of pregnancy-induced hypertension were studied.

Study duration:
The duration of the study was 12 months.

Study subjects:
Pregnant women with symptoms and signs of pregnancy-induced hypertension were compared with normotensive pregnant women.

Study tool:
Pregnancy-induced hypertensive patients were evaluated based on their serum cholesterol, triglycerides, HDL, LDL, VLDL, and Lipoprotein (a). The collected data was analysed statistically to obtain the results in patients with PIH.

Inclusion criteria:
Pregnant women with pregnancy-induced hypertension presenting with abnormal lipid profiles and lipoprotein (a) levels, who were willing to give informed consent to participate, were included in the study.

Exclusion criteria:
Patients with Diabetes Mellitus, Renal disorders, Hepatic disorders, Patients in labour, Patients on anti-hypertensive drugs before pregnancy, Blood disorder, Epilepsy, Chronic drug intake, and those who are not willing to give informed consent to participate in the study.

Sample size: 100 subjects (50 cases and 50 controls).

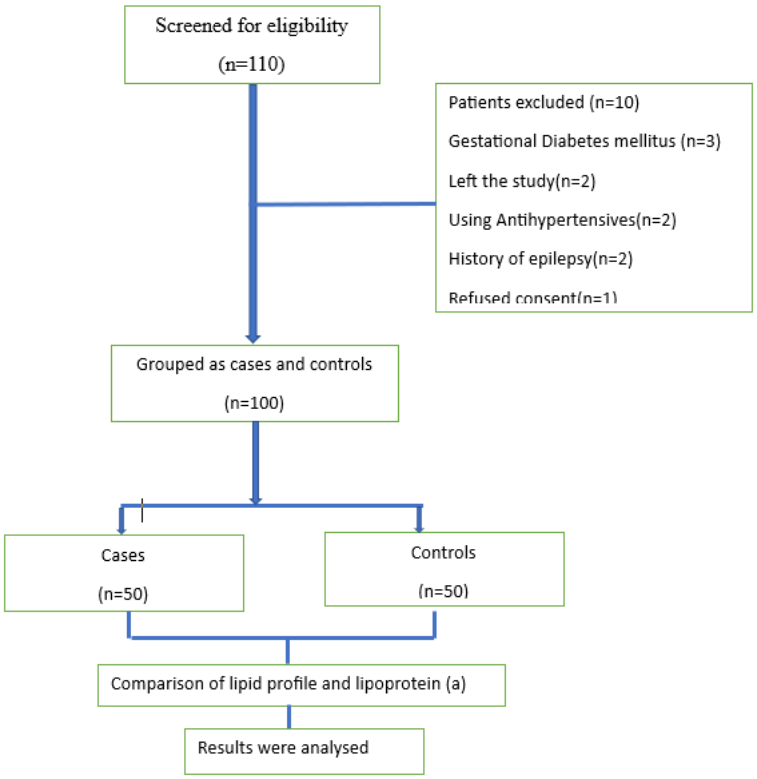
Materials and Methodology:
A case-control study was conducted at the Government General Hospital, Karimnagar. A total of 110 Pregnant women were evaluated. Out of them, 100 subjects were included in the study. 10 were excluded from the study. Of those 2 individuals had Gestational Diabetes mellitus, 3 had antihypertensive treatment, 2 had a history of epilepsy, 2 had quit the trial by not showing up to the hospital for an unspecified reason, and one had refused to give informed consent while the study was underway.

A detailed history including the present, past, family, diet, and drug history was taken, and a thorough general physical and systemic examination was done. Then the individuals who met the inclusion criteria were grouped into 2 groups (Cases & Controls).

Cases
50 cases with signs and symptoms of pregnancy-induced hypertension were included in this group.

Controls
50 age-matched controls without pregnancy-induced hypertension were included in this group.
A detailed evaluation of the Lipid profile (Total Cholesterol, Sr. Triglycerides, HDL, LDL, VLDL) and lipoprotein(a) levels of cases was performed. These were compared with the controls, and the results were analysed using SPSS software version 26.

Figure -1. Methodology of the study



Statistical Analysis:
Data was entered into a Microsoft Excel data sheet and was analyzed using SPSS 26 software. Categorical data was represented in the form of Frequencies and proportions. **The t-test** was used as a test of significance for qualitative data.
Graphical representation of data: MS Excel and MS Word were used to obtain various types of graphs, such as bar diagrams. A **p-value** of <0.05 was considered statistically significant after assuming all the rules of statistical tests.

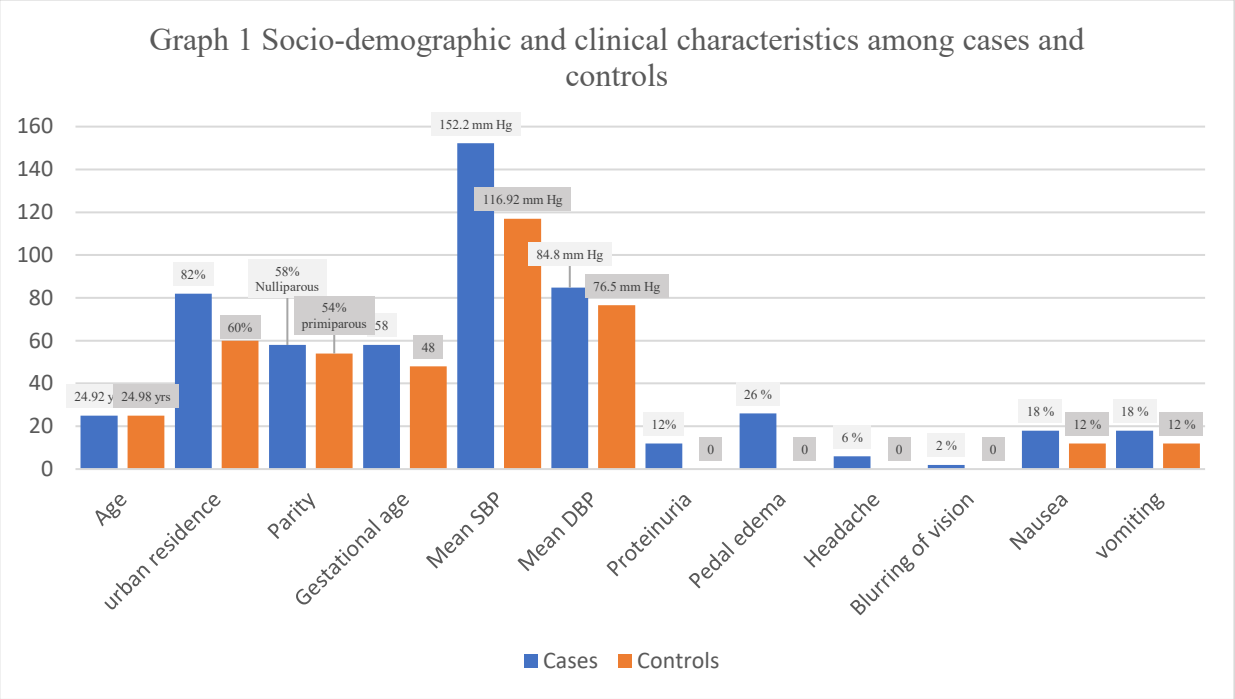
Outcome Measures:
Total cholesterol, Triglycerides, High-Density Lipoprotein, low-density lipoprotein, and very low-density lipoprotein levels, and Lipoprotein (a) were the primary endpoints, whereas the systolic and diastolic blood pressure, proteinuria, headache, pedal oedema, nausea, and vomiting were the secondary end points used to evaluate the outcome of the study.

RESULTS:
A total of 100 subjects were grouped into cases and controls. Their serum lipid profile and lipoprotein (a) levels were evaluated. Pregnant women of age groups ranging from 20 to 35 years were evaluated, and the mean age of the study population was 24.92 and 24.98 years among cases and controls, respectively. Approximately 82% of cases and 60% of controls resided in urban areas, respectively. Most of the cases were nulliparous, accounting for 58%, while the remaining cases were 28% primiparous and 14% comprised other categories. Most of the controls were primiparous, accounting for 54%. About 22% of cases and 18% of controls belonged to 35 weeks of gestation, 58% of cases and 48% of controls belonged to 36 weeks of gestation, and 20% of cases and 34% of controls belonged to 37 weeks of gestation. The mean SBP of cases was 152.2 mm Hg, whereas it was 116.92 mm Hg in controls. The mean DBP of cases was 84.8 mm Hg, and in controls it was 76.56 mm Hg. About 12%, 26%, 6%, 2%, 18%, and 18% of cases had a history of proteinuria, pedal oedema, headache, blurring of vision, nausea, and vomiting, respectively. The socio-demographic and clinical characteristics of the study population are shown in Table -1.

Table 1: Socio-demographic and clinical characteristics.

Factors	Cases	Controls	p- value
Mean Age (20- 35 yrs)	24.92 years	24.98 years	0.94
Urban Dwellings	82%	60%	*0.0006
Most common Parity	58% (nulliparous)	54% (primiparous)	0.65
Common Gestational age	58% (36 weeks)	48% (36 weeks)	0.19
Mean SBP	152.2 mm Hg	116.92 mm Hg	*< 0.00001
Mean DBP	84.8 mm Hg	76.56 mm Hg	*< 0.00001
H/o proteinuria	12%	0%	*0.001
H/o pedal oedema	26%	0%	*0.000074
H/o headache	6%	0%	0.80
H/o blurred vision	2%	0%	0.32
H/o Nausea	18%	12%	0.41
H/o vomiting	18%	12%	0.41

*=P < 0.05 (Significant); an unpaired, equal variance two-tailed t-test was used to compare the means between the groups.

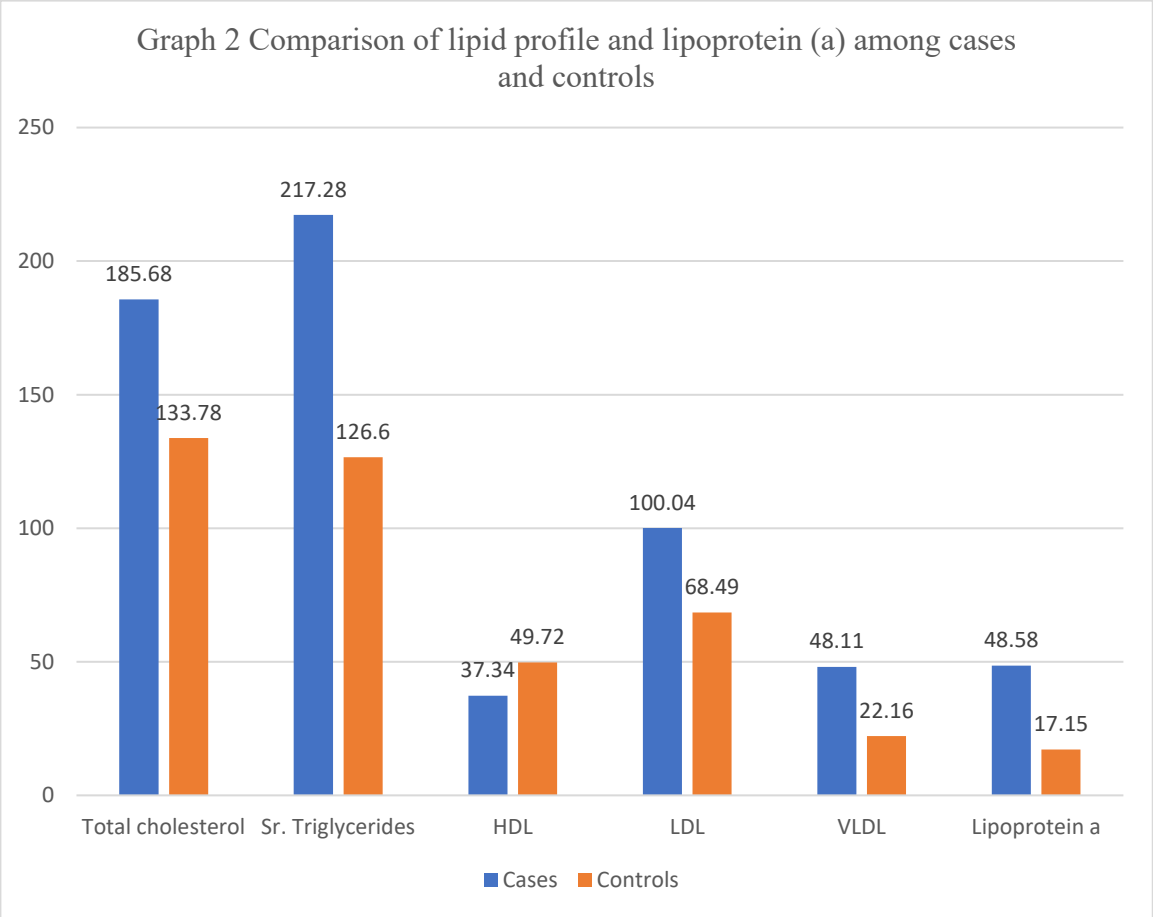


The mean total cholesterol was 185.68 + 25.61 mg/dl in cases and 133.78 + 23.38 mg/dl in controls. The mean serum triglycerides were 217.28 + 56.49 mg/dl among cases. The mean serum triglycerides in controls were 126.6 + 22.20 mg/dl. The mean HDL levels in cases and controls were 37.34 + 5.95 mg/dl and 49.72 + 9.34 mg/dl. The mean LDL was 100.04 + 26.22 mg/dl in cases and 68.49 + 21.18 mg/dl in controls. The mean VLDL among cases was 48.11 + 14.67 mg/dl. The mean VLDL among controls was 22.16 + 5.31 mg/dl. The mean Lp(a) was 48.58 + 13.62 mg/dl among cases. Among controls, the mean Lp(a) was 17.152 + 6.83 mg/dl. Table 2 shows the comparison of serum lipid profile and lipoprotein (a) levels among cases and controls.

Table 2 Lipid profile of cases and controls

Parameters	Cases Mean + SD	Controls Mean+ SD	P value
Total Cholesterol	185.68 + 25.61	133.78 + 23.38	< .00001
Sr. Triglycerides	217.28 + 56.49	126.6 + 22.20	< .00001
HDL	37.34 + 5.95	49.72 + 9.34	< .00001
LDL	100.04 + 26.22	68.49 + 21.18	< .00001
VLDL	48.11 + 14.67	22.16 + 5.31	< .00001
Lipoprotein a	48.58 + 13.62	17.152 + 6.83	< .00001

*=P < 0.05 (Significant); an unpaired, equal variance two-tailed t-test was used to compare the means between the groups.



DISCUSSION:

Blood pressure of 140/90 mm Hg or higher, without proteinuria and oedema after 20 weeks of pregnancy, is considered pregnancy-induced hypertension. A clinical characteristic of PIH, proteinuria and hypertension, can arise from endothelial dysfunction associated with dyslipidaemias. A major contributing factor to the development of gestational hypertensive diseases is improper trophoblast differentiation during endothelial invasion, which is caused by abnormal regulation and/or synthesis of cytokines, adhesion molecules, major histocompatibility complex molecules, and metalloproteinases [11]. Pregnancy causes both qualitative and quantitative alterations in plasma lipid and lipoprotein (a).

In the present study, the age group of subjects was 20-35 years. The mean age 24.9 years, and these results were consistent with Jagannath et al study [12]. Most cases and controls resided in urban areas, and these results were consistent with a similar study conducted by Sandhya Kumari et al[13]. In the

present study, PIH was most common in nulliparous pregnant women at 36 weeks of gestation, and these results were consistent with a study conducted by Adewara et al[15]. The mean systolic and diastolic blood pressure were significantly higher in cases than in controls ($p< 0.05$). These results were consistent with Blessy et al study[16]. Proteinuria and pedal oedema were present in less than 15% of cases, which was relatively significant when compared with controls.

A fasting lipid test necessitates a 12-hour fast, with water being the only exception, whereas a non-fasting lipid test can be conducted whenever without fasting [16]. Serum is used to assess cholesterol levels. Total cholesterol should not exceed 200 mg/dl. Values above 240 mg/dl are undesirable, whereas levels between 200 and 239 are regarded as borderline risk[17]. The mean total cholesterol was significantly higher among cases when compared with controls. The p-value was <.00001, which was significant ($p< 0.05$). These results were similar to Patel et al study [17].

The recommended level for serum triglycerides is 150 mg/dl. Borderline risk is defined as levels between 150 and 199 mg/dl, while high risk is defined as levels between 200 and 399 mg/dl. 400 mg/dl and higher are regarded as very high levels. The triglyceride levels were significantly higher among cases than controls. The p-value was <.00001, which was significant ($p< 0.05$). These results were consistent with similar studies conducted by Kondakasseril NR et al[18].

Serum HDL levels below 40 mg/dl were undesirable, those between 40 and 59 were regarded as borderline risk, and those over 60 mg/dl were desirable. There was a significantly low HDL among cases when compared with controls. The p-value was <.00001, which was significant ($p< 0.05$). These results were consistent with a similar study conducted by Dev et al[6].

Serum LDL levels below 100 mg/dl are ideal, those between 100 and 129 were deemed nearly optimal, those between 130 and 159 were considered borderline high, those between 160 and 189 were classified high, and those over 180 were regarded as very high risk. There were significantly high levels of LDL among cases when compared with controls. The p-value was <.00001, which was significant ($p< 0.05$). These results were consistent with a similar study conducted by Jagannath et al[13].

Lipoprotein (Lp) (a) is a subclass of lipoprotein that is made up of apolipoprotein (apo) and low-density lipoprotein (LDL) that are covalently bound by their apolipoprotein B100 component. The metabolism undergoes a significant change during pregnancy in order to support foetal growth[19]. The Lp(a) levels were high among cases when compared to controls. The p-value was <.00001, which was significant ($p< 0.05$). Serum lipoprotein (a) should not exceed 14 mg/dl. Values above 50 mg/dl are high, whereas levels between 14 and 30 are regarded as borderline risk. These results were consistent with Fathima et al and Anupama et al studies[7,8].

LIMITATIONS:

Since the study was conducted over a short period within a small sample size, the results of the present study cannot be generalised. As there was no blinding and the study groups were randomized, there may be a chance of bias, which can be overcome by triple blinding, where the investigator, patient, and the data analyst will not be aware of the treatment details. Multicentric studies in a large group of cases with longer duration are necessary to generalise the results.

CONCLUSION:

The study concludes that when PIH patients were compared to normotensive pregnant women, their serum lipid and lipoprotein (a) levels were abnormal. Elevated lipid profile levels were shown to be highly correlated with PIH, indicating that elevated lipids may play a role in the pathophysiology of PIH. These investigations help to detect associated cardiovascular disorders. Potential contributors to the pathophysiology of PIH may include dyslipidemia-mediated stimulation of endothelial cells

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AUTHORS CONTRIBUTION:
Dr. Deepa Polepaka planned and designed the concept of the manuscript, contributed to drafting the manuscript, and reviewed the manuscript. Dr. Narender Sayini supported in designing and drafting the manuscript, and literature search and review. Dr. J. Naveena contributed for designing the final version to be published.

CONFLICTS OF INTERESTS:
Declared none.

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