Original Article

Lipid Profiles and Its Association with Pre-Eclampsia and Eclampsia in Nulliparous Pregnant Women

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Abstract

Objectives: To access the lipid profiles and their association with pre-eclampsia and eclampsia in nulliparous pregnant women.

Materials and Methods: This cross-sectional study was performed on 234 nulliparous pregnant women with a gestation period of > 20 weeks and aged 15-45 years, at the Institute of Basic Medical Sciences (IBMS), Khyber Medical University (KMU), Peshawar, Pakistan with cooperation from gynecology and obstetrics departments of three tertiary-care hospitals of Peshawar & Khyber Medical College, Peshawar, Khyber Pakhtunkhwa (KP), Pakistan. Subjects were assigned to three groups i.e., group A, group B, and group C. For performing biochemical assays and lipid profiling, through ELISA, blood samples were collected from already subjects both with the disease and the controls.

Results: Both subjects having pre-eclampsia and eclampsia showed significantly elevated levels ($p < 0.001$) for low-density lipoproteins cholesterols (LDL-c), high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC)/HDL-c and LDL-c/HDL-c ratio. But TC of pre-eclampsia subjects was found significantly elevated ($p < 0.001$) in relation to controls. LDL-c/HDL-c and TC/HDL-c also revealed an elevated significant change ($p < 0.001$) both for pre-eclamptic and eclamptic subjects. On the other hand, only TG/HDL-c in pre-eclamptic patients was found significantly higher ($p<0.004$) when compared to the control group.

Conclusion: Serum lipid levels were observed higher in pre-eclampsia and eclampsia patients hence an early assessment is necessary to prevent complications in such patients.

Keywords: Pre-eclampsia, Eclampsia, Lipid Profiling, Hypertension, IBMS, RMC.

Introduction

Pregnancy hypertensive disorders are among the vital factors that could cause maternal and fetal morbidity and mortality and accounts for approximately 5-10% of all pregnancies worldwide.[1,2] Several phenomena lead to the wide-ranging manifestations of these diseases that may become an emergency in severe cases.[3] Pre-eclampsia and eclampsia along with their severe features are most significant.[2,3] It can also impose an adverse impact on everybody's organ; with also potential for a long-lasting and significant impact on the mother and baby's health. In other words, pre-eclampsia is characterized as a pregnancy complication by hypertension leading to the signs of organ systems damage, particularly liver and kidneys; whereas eclampsia is a severe complication of pre-eclampsia that leads to further elevated blood pressure, and seizures.[3] It could also cause preterm birth, perinatal demises, and intrauterine growth retardation, especially in developing countries.[4-6] The incidence rate of this life-threatening condition is variable across the countries mainly due to geographical, socio-economic, cultural, and racial alterations,[7] availability and accessibility of prenatal care facilities.[8] Additionally, the incidence of pre-eclampsia increases significantly due to various risk factors such as the previous history of pre-eclampsia, multiple gestations, nulliparity, age >35 years at first pregnancy, Africo-American race, and smoking.[9] In Pakistan, a 9.3% incidence of pregnancy-induced hypertension is reported.[10]

The exact mechanism of how pre-eclampsia occurs is still not clear but previously, elevated serum lipid profiles were well associated with essential hypertension supporting the role of altered lipoprotein in endothelial dysfunction.[11] Nevertheless various hypotheses for causation of pre-eclampsia have been put forth but the most popular one is the involvement of lipid-mediated oxidative damage leading to endothelial dysfunction.[12]

Altered levels of serum lipoproteins in pre-eclampsia and eclampsia is an established phenomenon that has been reported worldwide[13] and can be helpful in the early detection of this dreadful condition. Many studies, showing an association between elevated lipid profiles and pre-eclampsia and eclampsia, have been conducted in western populations, but with very limited contribution from our local community which does not help to establish a relationship between raised lipid levels and pre-eclampsia and eclampsia in our setup. Hence taking the effects of the factors, such as racial, ethnic, social, geographic, etc. on the disease process, into account, this study was designed to weigh up the changes in lipid profiles and evaluate their association with pre-eclampsia and eclampsia subjects in our community.

Materials and Methods

After obtaining the ethical approval from the ethical board, this cross-sectional study was conducted at the Institute of Basic Medical Sciences (IBMS), Khyber Medical University (KMU), Peshawar, Pakistan with cooperation from the Gynaecology and obstetrics departments of three tertiary care hospitals of Khyber Pakhtunkhwa, Pakistan. After explaining the aims and objectives of the study and taking a well-informed consent from all subjects; a total of 234 nulliparous pregnant women with a gestation period of >20 weeks, aged 15-45 years were recruited. The subjects were characterized into three main study groups as given below.

Group A comprised 86 pre-eclamptic pregnant women according to American College of Obstetricians and Gynecologists (ACOG) criteria [Blood pressure (BP) > 140/90mm of Hg; Proteinuria > 2+ (on dipstick testing)].[14] Group B comprised 74 pregnant women diagnosed with "eclampsia" according to ACOG criteria (signs of pre-eclampsia along with seizures and/or comma of unexplained nature).[15] And group C comprised 74 healthy normotensive women with normal pregnancies. All the control subjects were age, BMI, and socioeconomic status matched with respect to the cases.

A detailed history was every subject was taken followed by a comprehensive general physical examination. Subject information like maternal age, age at marriage, parity, gravidity, gestational age, and socio-demographic characters at the time of screening were recorded on a pre-designed proforma. In addition to that, each participant went through measurement of their arterial BP, height (H), and weight (W) using standard protocols. Peripheral blood samples from a vein, 5cc each, were withdrawn from each patient and controlled in a fasting state under strict aseptic conditions in EDTA tubes. Lipid profiling was determined by the enzymatic colorimetric method of Roche diagnostics using an automated chemistry analyzer (Modular P-800, Cobas by Roche). The lipoprotein biochemical analysis included total cholesterol (TC), and triglycerides (TG), low-density lipoproteins cholesterols (LDL-c), high-density lipoprotein cholesterols (HDL-c), TC/HDL-c and LDL-

c/HDL-c rations. The diagnosis of dyslipidemia was determined as per guidelines of the American Association of Clinical Endocrinologists (ACCE).[16]

Statistical analysis was carried out with the help of the Statistical Package for Social Sciences (SPSS) (Version 21.0, Chicago, USA). Reproductive and demographic characteristics were analyzed by the Mean ± SD test. The relation between general and socio-demographic characteristics was determined by the student t-test. Biochemical assays data and ELISA data were analyzed by ANOVA test. Furthermore, to determine the linkage between lipoproteins with respect to systolic pressure all subjects were characterized into two main sub-groups i.e., subjects with systolic BP less than 120 mmHg and subjects with systolic BP greater than 120 mmHg, and significance was found out by ANOVA test. The coefficient of correlation "r" was determined between hypertension and the lipid profile of the subjects by using Pearson product-moment correlation. The student t-test was used for any significant value.

Results

This study was conducted on 234 nulliparous pregnant women with a gestation period of > 20 weeks. The age of the participants varied from 15-45 years with the mean age for eclampsia (29.18 ± 8.72 years) slightly lower than the mean age for pre-eclampsia (32.2 ± 8.00 years). Most of the participants were socio-economically poor. The ethnicity data shows that the Pashtuns were the most affected group affected by pre-eclampsia (%) and eclampsia (%) (Table 1). Other reproductive and demographic characteristics and the comparison of all the studied groups are shown in Table 2. It was observed that no significant relationship existed between age at the time of marriage, and the number of children patients alive in comparison to healthy women. However, an inverse relation was observed in parity, systolic BP, and Diastolic blood BP of patients i.e., highly significant ($p < 0.000$) in comparison to the control group.

Table 2 depicts the comparison of biochemical analysis of the lipid profile variables between pre-eclamptic, eclampsia, and control groups. It was observed as a result that all studied lipid parameters were highly significant ($p < 0.005$) as compared to controls. The subjects having pre-eclampsia and eclampsia showed significantly elevated levels ($p < 0.001$) for HDL-c, LDL-c, TC: HDL-c ratio, LDL-c: HDL ratio but only total cholesterol of pre-eclampsia patients was found to significantly higher ($p < 0.001$) as compared to controls. TC: HDL-c and LDL-c: HDL-c ratio revealed a highly significant change ($p < 0.001$) for both the eclampsia and pre-eclampsia patients whereas, only TG: HDL-c ratio was found significantly higher ($p < 0.004$) in pre-eclampsia patients to control group.

It was observed as a result of biochemical analysis (Table 3) that majority of the study parameters were significantly high ($p < 0.005$) except for TGs and TC ($p > 0.05$). As a result of the linkage between lipoproteins and systolic blood pressure, it was observed that noted that total of 166 subjects had SBP greater than 120 mmHg while the remaining 68 subjects were having SBP lower than 120 mmHg. The remaining parameters were also significantly higher ($p < 0.001$) except for TC and TG (Table 4).

The comparison of lipoprotein concentration of overall patients and controls with diastolic BP $\leq$ 80 mmHg and > 80 mmHg was determined and it was observed that subjects with diastolic BP with > 80 mmHg revealed significantly higher levels ($p<0.001$) for LDLC, HDLC, LDLC/HDLC, and TC/HDL-c ratios, after comparing with DBP > 80 mmHg. Moreover, the subjects with DBP > 80 mmHg outclass those with DBP $\leq$ 80 mmHg and were 175 in number (Table 5). As a result of the correlation coefficient between hypertension and lipid profiles; a significant difference has been observed between cholesterol and systolic BP and diastolic BP in group C ($p < 0.05$), respectively. In addition to that, HDL-c levels were also found significantly related to diastolic BP in Group C ($p < 0.05$) (Table 6). However, no other parameter showed any significant association in any other group.

Table 1: Distribution of Study Population-based on Ethnicity

Variables	Group A (Pre-eclamptics) N=86 (%)	Group B (Eclamptics) N=74 (%)	Group C (Controls) N=74 (%)
Nationality			
Pakistani	73 (84.88)	58 (78.37)	63 (85.13)
Afghani	13 (15.12)	16 (21.63)	11 (14.87)
Residence			
Urban	30 (34.89)	29 (39.19)	27 (36.49)
Rural	56 (65.12)	45 (60.81)	47 (63.51)
Ethnicity			
Pasthun	51(59.3)	40 (54.05)	48 (64.86)
Hinkoon	22(25.58)	18 (24.32)	15 (20.27)
Muhajir	13 (15.12)	16 (21.63)	11 (14.87)

Table 2: Sociodemographic and Reproductive Data and Comparison of the Disease with Controls of the Study Population

Variables	*Group A (N=86)*	*Group B (N=74)*	*Group A+B (N=150)*	*Group C (N=74)*	*p - value*
Age (Years)	32.2±8.04	29.1±8.72	30.80±8.48	30.9±7.54	0.081
Marriage age (Yrs)	15.8±2.38	14.9±2.41	15.4±2.42	15.5±2.21	0.370
Gestation Age (Wk)	34.5±3.26	34.9±2.96	34.6±3.12	35.6±3.88	0.023
Parity (n)	03.0±2.61	01.7±1.20	02.4±2.17	02.0±1.15	0.001
Alive offsprings (n)	1.8±1.87	1.0±1.12	1.4±1.62	1.7±1.04	0.153
SBP (mm Hg)	159.7±24.10	158.9±19.83	159.3±22.16	106.8±11.33	0.000
DBP (mm Hg)	107.7±14.98	105.5±9.95	106.7±12.91	68.5±9.60	0.000
Monthly Income (/PKR)	8033.7±6003.24	7050.0±6254.58	7578.7±6121.16	11831.0±5235.72	0.000

Values are expressed as Mean±SD
Group A = Pre-eclamptics; Group B = Eclamptics; Group C = Controls; Wk = Weeks

Table 3: Distribution of Lipid Profile and Comparison among the Study Population

Lipid Profile	*Group A (N=86)*	*Group B (N=74)*	*Group C (N=74)*	*p - Value Group A & C*	*p - Value Group B & C*
Total Cholesterol (TC) (mg/dL)	182.33±45.34	208.11±62.69	180.09±36.76	0.736	0.001
Triglycerides (mg/dL)	188.76±83.40	203.64±103.92	187.31±84.82	0.914	0.297
HDL-C (mg/dL)	44.91±12.56	45.77±9.20	54.35±6.87	0.000	0.000
LDL-c (mg/dL)	99.66±42.07	121.611±59.80	88.281±39.740	0.082	0.000
LDLC/HDL-C	2.56±1.69	2.943±2.23	1.701±0.99	0.000	0.000
TC/HDL-C	4.49±1.99	4.948±2.84	3.412±1.10	0.000	0.000
TG/HDL-C	4.61±2.53	5.028±4.78	3.558±1.90	0.004	0.015

Values are expressed as Means±Standard Deviations (SD).
Group A = Pre-eclamptics; Group B = Eclamptics; Group C = Controls

Table 4: Comparison between Lipoprotein of Disease Groups (Pre-eclamptic+Eclamptic) and Controls with Systolic BP ≤ 120 mm of Hg and ≥ 120 mm of Hg

Lipoprotein Concentration	*BP Systolic ≥ 120 mmHg Mean±SD (N=166)*	*BP Systolic ≤ 120 mmHg Mean±SD (N=68)*	*p – Value*
Total Cholesterol (mg/dL)	193.31±54.93	181.15±37.03	0.095
HDL-C (mg/dL)	45.64±11.03	54.32±7.25	0.000
LDL-C (mg/dL)	108.73±51.69	89.01±40.47	0.005
Triglyceride (mg/dL)	194.63±92.07	189.03±87.83	0.669
TC/HDL-C	04.63±2.39	03.45±1.20	0.000
LDL-C/HDL-C	02.69±1.94	01.73±1.04	0.000
TG/HDL-C	04.73±3.67	03.62±2.06	0.020

Table 5: Comparison between Lipoprotein Concentration of Disease Groups (Pre-eclamptic+Eclamptic) and Controls with Diastolic BP ≤ 80 mm of Hg and ≥ 80 mmHg

Lipoprotein Concentration	*Diastolic BP ≥ 80 mmHg Mean±SD (N=175)*	*Diastolic BP ≤ 80 mmHg Mean±SD (N=59)*	*p – value*
Total Cholesterol (mg/dL)	193.00±54.11	180.20±37.18	0.093
HDL-C (mg/dL)	45.74±10.86	55.36±6.70	0.000
LDL-C (mg/dL)	108.51±51.35	86.67±39.30	0.003
Triglyceride (mg/dL)	193.73±91.80	190.85±88.11	0.833
TC/HDL-C	4.60±2.34	3.36±1.18	0.000
LDLC/HDL-C	2.66±1.90	1.65±1.02	0.000
TG/HDL-C	4.69±3.62	3.56±1.97	0.023

Table 6: Correlations between Blood Pressure and Biochemical Parameters Determined in the Study Subjects

Biochemical Parameters	*Group A (N=86)*				*Group B (N=74)*				*Group C (N=74)*			
	BP Systolic		BP Diastolic		BP Systolic		BP Diastolic		BP Systolic		BP Diastolic	
	r	*p*	*R*	*p*	*R*	*p*	*r*	*p*	*r*	*p*	*R*	*P*
Cholesterol	.123	.295	.198	092	-.030	.782	.034	.755	-.250	.032	-.251	031
TG	.021	.859	.087	.460	-.027	.804	.102	.351	-.092	.437	-.123	.296
HDL-C	.075	.525	.072	.540	.054	.622	.078	.477	-.023	.848	-.241	.039
LDL-C	.111	.348	.166	.158	-.038	.729	-.027	.807	-.188	.108	-.138	.240
TC/HDL-C	.018	.877	.047	.693	-.123	.257	-.030	.785	-.171	.146	-.107	.363
LDL/HDL-C	.020	.868	.049	.680	-.123	.260	-.042	.699	-.157	.181	-.097	.412
HDL/LDL-C	-.088	.454	-.109	.356	.101	.357	.107	326	.086	.467	.010	.933
TG/HDL-C	.009	.941	.025	.835	-.075	.490	.024	.828	-.087	.459	-.061	.607
VLDL-C	.021	.859	.087	.460	-.027	.804	.102	.351	-.092	.437	-.123	.296
HDL/VLDL-C	-.097	.412	-.041	.726	.107	.328	-.122	.264	.003	.977	.002	.988

Discussion

Visfatin was initially known as a growth factor for early B cells also recognized as PBEF; (Pre-B cell colony-enhancing factor.[17] Pre-eclampsia and eclampsia are pregnancy-induced hypertensive disorders along with proteinuria which usually develops after the 20th week of gestation with substantial maternal and perinatal risks. Both pre-eclampsia and specifically eclampsia are among the leading causes of death in underdeveloped countries with limited healthcare access, causing about 60,000 maternal mortality globally per annum.[18] In both pre-eclampsia and eclampsia there is lipid metabolism dysfunction resulting in disturbed lipid profile leading to peroxidation of lipids resulting in endothelial dysfunction and placental hypoxia.

In addition to that, the current study demonstrated that the mean age of the pre-eclampsia cases was 32.2 ± 8.04 and eclampsia was 29.1 ± 8.72 whereas Bonder LM, *et al*.[19] reported that the mean age of pre-eclampsia was 24.00 ± 4.14 years. High TG level is also significantly associated with both diseases' onset which is also reported in another study by Toescu V, *et al*.[20] High triglycerides level also play a key role in decreasing the HDL-cholesterol level.

Moreover, our study also demonstrated the existence of a positive correlation among pre-eclamptic, eclamptic, and lipid profile parameters. Current findings reported that pre-eclampsia and eclampsia patients have significantly high triglycerides levels and low HDL-cholesterol levels in comparison to control subjects. Similar to current findings, Pre-eclampsia was also reported as characteristically linked with increased triglycerides level.[21] In the pipeline of current findings, high triglycerides levels with low HDL-C were also reported by other studies conducted on pre-eclamptic women.[22,23] During regular pregnancy, total cholesterols, and plasma triglycerides levels increase but as pregnancy proceeds, both parameters get back to normal. Metabolism of lipids is also varied during pregnancy.[24] Serum lipids were significantly affected by female sex hormones.[24] Decline in the activity of lipoprotein lipase and increase in activity of the hepatic lipase are responsible for elevated triglycerides synthesis during pregnancy.[25] Whereas as Lipoprotein lipase activity decreases adipose tissue catabolism also decreases ultimately leading to the increase in serum

triglycerides level. In the second step, the liver defers the uptake of the remnant of chylomicrons resulting in the accumulation of the triglycerides in plasma.

The limitations of our study are small sample size, sampling of convenient type, and incomplete adjustment for confounders. So, a well-designed study with a greater number of study samples is mandatory to investigate the actual association between elevated serum concentration of lipids in pre-eclamptic and eclamptic women in our province.

Conclusion

Serum lipid levels were observed to be significantly higher in pre-eclampsia and eclampsia patients hence an early assessment in antenatal care is warranted to prevent obstetrics complications in such cases. Furthermore, it is recommended that such patients be monitored for any cardiac complications during pregnancy and later in life as high lipid profile is a strong risk factor for cardiac problems as well.

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