Original Research Article

Role of lipids, ionized calcium, and alkaline phosphatase in progress of pregnancy induced hypertension - A prospective study in Kolkata

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Abstract

Background: Pregnancy induced hypertension may complicate to preeclampsia and eclampsia. The pathophysiology of the former is still confusing, many authors suggested different opinions, and indicated different parameters for the prognosis of this.
Aim: To evaluate serum HDL and LDL cholesterol, alkaline phosphatase, ionized calcium in pregnancy induced hypertension patients.
Materials and methods: We had selected normal non-pregnant females (Group 0), pregnant normotensive females (Group I) and pregnancy induced hypertensive females (Group II). All the above mentioned parameters were estimated in them. Statistical analysis was done by SPSS 17 software; ANOVA and post hoc Bonferroni analysis were used to compare them**.**
Results: Significant increase of LDL and alkaline phosphatase as well as significant decrease of HDL and ionized calcium were found in Group II females.
Conclusion: HDL and LDL cholesterol, alkaline phosphatase, ionized calcium can indicate the severity of gestational hypertension. Normalization of those parameters can prevent the complications like preeclampsia and eclampsia.

Key words

Pregnancy induced hypertension, Lipids, Alkaline phosphatase, Ionized calcium.

Introduction

Hypertensive diseases contribute 5 to 10% of all pregnancies, when associated with hemorrhage and infection leading to maternal mortality and morbidity [1]. Hypertension appears after 20 weeks of pregnancy and resolve within 10 days of postpartum, in a previously normotensive women, without other features of pre eclampsia is called pregnancy induced hypertension (PIH) [2, 3, 4]. This PIH or gestational hypertension, affecting 2-5% of women and can progress to pre-eclampsia and eclampsia which can end in a grave consequence like maternal and perinatal mortality [5].

The pathophysiology of gestational hypertension is still unclear, but different studies postulated that metabolic abnormalities like dyslipidemias and insulin resistance may contribute to it [6]. Lipids may accumulate at the arterial intimal cells leads to endothelial dysfunction and altered lipid profile causes lowering in prostaglandin thromboxane ratio which is a significant pathway for development of PIH [7].

Epidemiological evidences suggested that the women with PIH are at risk of cardiovascular diseases (CVD), hypertension, stroke and death from ischemic heart diseases in later life [5].

Different authors highlighted on different parameters which can prevent the progression of PIH but still there is a scarcity of a reliable predictor.

Placental synthesis of alkaline phosphatase (ALP) during pregnancy has a role in division of normal and transformed cells. This enzyme is responsible for active transport of phosphate [8]. Lowering of serum ALP in pregnancy may be an indicator of intra uterine growth retardation (IUGR) ALP was also noticed to be increased in pre-eclampsia [9].

Epidemiological studies also documented that calcium intake is negatively correlated with PIH.A recent study found that calcium supplementation decreases the risk of hypertension in pregnancy [10]. Altered lipid metabolism, during pregnancy ensures the continuous supply of nutrients to the growing fetus [11].

The aim of the present study was to analyze the serum calcium, ALP, and lipid parameters between normal women without pregnancy, pregnant mothers with PIH, and pregnant mothers without PIH, and to find out whether any significant alteration exists between the groups.

Material and methods

The present study was undertaken in the Department of Biochemistry, Calcutta National Medical College, Calcutta. It was a case control, observational study and the study period extended from 01.06.2014 to 31.05.2015.

Selection of cases and controls

Total 101 pregnant women of 20-35 years old were selected and grouped as follows.

Group 0: Non pregnant women with normal blood pressure (<120/80 mmHg) (n=34)

Group I: Women having normal uncomplicated pregnancy without hypertension (<120/80 mmHg) (n=35)

Group II: Women with pregnancy-induced hypertension (PIH) ($\geq$140/90 mmHg) (n=32)

Inclusion criteria

Gestational age ranges from 24 weeks to term. All the subjects in the group were in the third trimester of pregnancy.

Criteria for making a diagnosis of gestational hypertension

The diagnosis of gestational hypertension was based on two consecutive measurements of systolic and diastolic blood pressure $\geq$140/90 mmHg 6 hours apart, one measurement of diastolic blood pressure of 110 mmHg or more or a rise of 30 mmHg or 15 mmHg above the normal pre-pregnancy systolic and diastolic blood pressures after the 20th week of pregnancy

[5] while Urinalysis was done using COMBI-URISCREEN reagent strips. Persistent elevation of the blood pressure on two occasions without proteinuria was used to make a diagnosis of gestational hypertension.

Exclusion criteria

Exclusion criteria was preexisting hypertension, ischemic heart disease (IHD), chronic renal failure (CRF), diabetes mellitus (DM), patient under treatment with drugs which can interfere lipid profile. The pre-eclampsia patients were diagnosed by the presence of persistent hypertension (more than 140/90 mmHg) gross proteinuria (tested by heat test of urine) and pathological edema.

Sample analysis for test parameters

Blood samples were drawn from all the subjects following a fast of 12 hours and analyzed for serum HDL and LDL cholesterol by enzymatic end point method with the help of kits on ERBA chem-5 semi-auto analyzer.

(S) LDL by Direct method [12] (Erba Lachema, diagnostics).

(S) HDL by PEG/CHOD-PAP method [13] (Crest Biosystems).

Serum Alkaline phosphatase determined by kinetic assay (Pnpp-AMP method) [14] and Serum ionized calcium was analysed by 9180 Electrolyte Analyser [15]. Principle based on Ion Selective Electrode (Roche Diagnostics GmbH MannheimGermany).

Statistical analysis

It was done by using SPSS 17 Software. To see the differences in between the groups, one way analysis of variance (ANOVA) procedure using the Statistical Package for the Social Science (SPSS) program (SPSS Statistics 22.0) was applied. The differences between the individual pairs were done by post hoc Bonferroni Correction. The P values were given at appropriate places. A statistically significant difference was considered at $p < 0.05$.

Results

ANOVA showed significant of difference between different groups in various parameters as per **Table – 1**. Post hoc Bonferroni analysis showed significance between various groups was as per **Table – 2.** Significant increase of LDL and alkaline phosphatase as well as significant decrease of HDL and ionized calcium was found in Group II females.

Table - 1: ANOVA showing significance of difference between different groups in various parameters.

	Non-pregnant (GROUP-00) n=34	**Pregnancy without complications (GROUP-I) n=35**	**Pregnancy induced hypertension (PIH) (GROUP-II) n=32**	**Levels of significance between groups**
Serum HDL in mg/dl (mean±SD)	47.03±1.42	47.14±1.47	40.84±1.73	F= 178.309 p<0.0001
Serum LDL in mg/dl (mean±SD)	142.40±6.96	116.19±4.88	131.66±12.7	F= 225.498 p<0.0001
Serum alkaline phosphatase in IU (mean±SD)	136.25±3.07	288.06±11.25	402.39±21.07	F= 3160.924 p<0.0001
Serum Ionized Calcium in mmol/l (mean±SD)	1.2±0.09	1.1±0.08	0.92±0.11	F= 63.200 p<0.0001

ANOVA performed with SPSS version 17 .0 for windows to show the significance between different groups at 95% confidence interval

Table - 2: Post hoc Bonferroni analysis showing significance between various groups.

	(I) GROUP H1	(J) GROUP H1	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
HDL	.00	1.00	-.10756	.37262	1.000	-1.0152	.8001
		2.00	6.19467*	.38113	.000	5.2663	7.1230
	1.00	.00	.10756	.37262	1.000	-.8001	1.0152
		2.00	6.30223*	.37848	.000	5.3803	7.2241
	2.00	.00	-6.19467*	.38113	.000	-7.1230	-5.2663
		1.00	-6.30223*	.37848	.000	-7.2241	-5.3803

	(I) GROUP L1	(J) GROUP L1	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
LDL	.00	1.00	26.20696*	1.30585	.000	23.0262	29.3877
		2.00	5.23790*	1.33567	.000	1.9845	8.4913
	1.00	.00	-26.20696*	1.30585	.000	-29.3877	-23.0262
		2.00	-20.96905*	1.32639	.000	-24.1998	-17.7383
	2.00	.00	-5.23790*	1.33567	.000	-8.4913	-1.9845
		1.00	20.96905*	1.32639	.000	17.7383	24.1998

	(I) GROUP C1	(J) GROUP C1	Mean Difference (I-J)	std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Ionized ca	.00	1.00	.08345*	.02421	.003	.0245	.1424
		2.00	.27246*	.02476	.000	.2121	.3328
	1.00	.00	-.08345*	.02421	.003	-.1424	-.0245
		2.00	.18902*	.02459	.000	.1291	.2489
	2.00	.00	-.27246*	.02476	.000	-.3328	-.2121
		1.00	-.18902*	.02459	.000	-.2489	-.1291

	(I) GROUP A1	(J) GROUP A1	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
ALP	.00	1.00	-151.80983*	3.28903	.000	-159.8212	-143.7985
		2.00	-266.13474*	3.36415	.000	-274.3290	-257.9405
	1.00	.00	151.80983*	3.28903	.000	143.7985	159.8212
		2.00	-114.32491*	3.34076	.000	-122.4622	-106.1876
	2.00	.00	266.13474*	3.36415	.000	257.9405	274.3290
		1.00	114.32491*	3.34076	.000	106.1876	122.4622

Discussion

In our study, we didn't find any significant alteration of HDL in normotensive pregnant mothers when compared with non pregnant females. A significant decrease of HDL has been found in PIH mothers when compared with non pregnant females and normotensive pregnant mothers.

The above mentioned findings correlate with the findings of De J, et al. [16] the low levels of HDLC may be due to hyperoestrogenemia and also due to insulin resistance [16, 17, 18].

A significant lowering of LDL was found in normotensive pregnant participants in comparison to non pregnant females in our study. Jayantha C [19] also observed the similar results. They also documented significant rise of LDL in PIH which corroborates our finding.

The rise of LDL in PIH may be contributed by endothelial dysfunction, caused by hypooestrogenemia, predominance of smaller and denser LDL particles [20, 21, 22].

Many authors reported the rise of serum ALP in 2nd and 3rd trimester of pregnancy which coincides with the period of calcification of fetal skeletal growth. Placental ALP (PALP) facilitates the mobilization of calcium ions from mother to fetus. PALP gradually increases with the gestational weeks [21].

Mangal A, et al. [23] observed the rise of PALP activity is directly related to the rise of BP. We also found the same observations. Similar results were also found by Lopez P, et al. [24].

During pregnancy, there is a great demand for calcium for development of fetal skeleton. PALP causes this shift of calcium from mother to fetus. So without adequate intake, the maternal calcium concentration will fall below the normal level which will aggravate during PIH, since PALP increases with hypertension. Furthermore, there is dilution of cations due to expanded extracellular fluid volume and to the normal hypercalciuria of pregnancy [24]. Serum ionized calcium concentration depends on adequate calcium intake [25].

Conclusion

From the above mentioned results, we can assume that the serum HDL and LDL estimation is helpful in the prevention of complications of PIH. High level of ALP in PIH is attributed to increased blood pressure. High PALP activity can be explained by ischemia resulting from maternal hypertension.

Low levels of serum ionized calcium in PIH can be corrected by calcium supplementation, we can hypothesize that maintenance of all these parameters within normal range can control the PIH.

References

1. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouge DJ, Spong CY. Pregnancy Hypertension. In: Williams obstetrics, 23rd edition, New York: McGraw-Hill; 2010, p. 706-56.
2. Reeve J. Calcium Metabolism in Hypertension. In: Chamberlain G. Clinical Physiology in Obstetrics. Oxford UK: Blackwell Scientific Publication; 1980, p. 257-69.
3. Redman CWG. Hypertension in pregnancy A case discussion PIH contribute to 15.6% maternal serum lipid and malondialdehyde levels in primiparous. Journal of Clinical Pathology, 1987; 10: 91-94.
4. Redman CWG. Important role of eicosanoids in pre-eclampsia and placenta. Journal of Clinical Pathology, 1991; 12: 301-308.
5. Irinyenikan TA, Roberts OA, Arowojolu A. Serum lipid levels in pregnant normotensive and gestational hypertensive women in Ibadan, Nijeria. Annals of bio research, 2013; 4(4): 204-208.

6. Caruso A, Ferrazzani S, Carolis SD, Lucchese A, Lanzone A, Santis LD. Gestational hypertension but not preeclampsia is associated with insulin resistance syndrome characteristics. Human Reproduction, 1999; 14(1): 219-223.
7. Robson SC. Hypertension and renal disease in pregnancy. In: Edmonds DK (Ed). Dewhurst's Textbook of Obstetrics & Gynaecology for Postgraduates, 6th edition, New York: Blackwell Science; 1999, p. 167-9.
8. Lobel P. Alkaline Phosphatase in fetal Circulation. American Journal of Obstet Gynac., 1969; 83(3): 295-299.
9. Demsey EW, Wislocke GB. Histochemica human alkaline phosphatase. American Journal of Anat., 1945; 76(3): 277-295.
10. Kuber R, De Onis M, Gulmezglu AM, Villar J. Nutritional intervention for the prevention of maternal mobidity. Int. J gynaecol obstet., 1998; 63(3): 231-246.
11. Bradyle R, Crook D. Carbohydrate and lipid metabolism in pregnancy, normal compared with GDM. American Journal of Clinical Nutrition, 2000; 71(5): 205-223.
12. Pisani T, Gebski CP, Leary ET, et al. Accurate direct determination of low density lipoprotein cholesterol assay. Arch Pathol Lab Med., 1995; 119: 1127.
13. Sugiuchi H, Uji Y, Okabe H, Irie T, Uekama K, Kayahara N, et al. Direct measurement of high density lipoprotein cholesterol in serum with polyethylene Glycol-Modified enzymes and Sulfated alpha-cyclodextrin. Clin Chem., 1995; 41: 717-23.
14. Moss DW, Henderson AK. Clinical enzymology. In: Burtis CA, Ashwood ER, Eds WB., editors. Teitz Textbook of Clinical Chemistry. 3rd edition, Philadelphia: Saunders; 1994, p. 617-721.
15. George N, Bowers J, Brassard C, Salvador F. Measurement of Ionized calcium in serum with Ion-Selective Electrodes. A: Mature technology that can meet the daily service needs. Clin Chem., 1986; 32(8): 1437-47.
16. De J, Mukhopadhay AK, Saha PK. Study of serum lipid profile in pregnancy induced hypertension. Ind J of Clin Bioch., 2006; 21(2): 165-168.
17. Nayan S, Meena ML, Hooja N, Fatima A, Singh N. A study of comparison of serum lipid profile of women with pregnancy induced hypertension and normal pregnancy. Schlolars Academic journal of Biosciences, 2014; 2(11): 834-836.
18. Saxena S, Thimmaraju KV, Srivastava PC, Mallik AK, Das B, Sinha N. Role of dyslipidemia and lipid peroxidation in pregnancy induced hypertension. J Clin Sci Res., 2015; 4: 205-212.
19. Jayantha C, Mukhopadhyay AK, Saha PK. Serum lipid profile in pregnancy induced hypertension. Ind j of Clin Bioch., 2006; 21(2): 165-168.
20. Sattar N, Bendomir A, Berry C, Shapherd J, Greer LA, Packard CJ. Lipoprotein subtraction concentration in pre-eclampsia: Pathogenic parallels to atherosclerosis. Obsts & Gynaecol., 1997; 89(3): 403-8.
21. Herret BH, Dakey W. Biochem Test for the Assessment of Feto Placental Function. Annals of Cli. Bio., 1979; 12: 83-107.
22. Hubel CA, Lgcall F, Weiss feld L, Gandlay RE, Roberts JM. Small low-density lipoproteins and vascular cell adhesion molecule-1 are increased in association with hyperlipidemia in pre eclampsia. Metabolim, 1998; 47(10): 1281-8.
23. Mangal A, Shrivastava P, Gaur U, Jain A, Goyal U, Rath G. Analysis of placental alkaline phosphatase in hypertensive disorders complication pregnancy. J Anat Soc. India, 2005; 54(2): 1-9.

24. Lopez P, Narvaes M, Weigel M, Yepez R. Calcium supplementation reduces the risk of pregnancy induced hypertension in an Andean population. British Journal Obstet & Gynecol., 1989; 96: 648-655.

25. Lopez P, Narvaes M, Felix C, Lopez A. Dietary Calcium supplementation and prevention of pregnancy induced hypertension. Lancet, 1990; 335: 293-300.