IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB)
ISSN: 2455-264X, Volume 2, Issue 4 (May. – Jun. 2016), PP 16-21
www.iosrjournals.org

Serum Lipid Profile and Fasting Insulin Levels in Second Trimester of Pregnancy As Predictors of Pregnancy Induced Hypertension

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I. Introduction

Pregnancy is a physiological process in women but it may be associated with certain risks to the health and life of both the mother and child. Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infection that results in maternal and perinatal morbidity and mortality in both under developed and developed countries[1].Hypertension after 20 weeks pregnancy in a woman with edema and proteinuria without previous history of hypertension is called pregnancy induced hypertension. When associated with proteinuria, the disorder is termed preeclamptic- eclampsia/toxemia, and when present without protein in urine it is called transient hypertension or gestational hypertension. One way to reduce the impact of arterial hypertension on maternal mortality is to establish the correct diagnosis of hypertensive disorders of pregnancy, and to proceed with an early intervention when it is diagnosed. The clinical signs are considered to be a late manifestation of a disease that has been present since the first trimester of gestation due to "diagnostic delay". The atherogenesis may be initiated by hypertriglyceridemia. Monocytes first adhere to endothelial cells and then transmigrate into the vascular intima[2-6]. These adhesion molecules are significantly increased in the serum of patients with severe hypertriglyceridemia. Since Triglyceride related vasculopathy may be one of the etiologic factors and positively correlated with the development of pre eclampsia and also may influence a future pregnancy as well as a woman's long term risk of cardiovascular disease. It is worthwhile to explore the metabolism and transport of various sub fractions of lipoproteins in pregnant women from 20 weeks of gestation who have developed increase in blood pressure. Dyslipidemia due to deregulation of lipoprotein lipase may damage trophoblast invasion thus contributing to a cascade of pathophysiologic events that proceed to the progress of pregnancy induced hypertension[7-10].There is direct and indirect evidence of hyperinsulinemia playing a role in the pathogenesis of pre eclampsia and indicates that higher fasting insulin levels in the pregnancy are markers for risk of PIH. Elevated concentrations of insulin can cause insulin resistance by down regulating insulin receptors and desensitizing post receptor path ways. Pre-eclamptic women have an associated hyperinsulinemia as reflected by the higher levels of insulin as compared to women with normal pregnancy and so it was hypothesized that hyperinsulinemia contributes to pathogenesis of disease by its effects on the urinary sodium excretion, glomerular filtration rate, renal blood flow and plasma aldosterone concentration. and hence therapeutic approaches that improve insulin sensitivity adds a potential role in reducing the risk of PIH. Higher fasting insulin levels were seen in the women of pregnancy which was associated with increased risk of pregnancy induced hypertension. Several previous studies have concluded that insulin resistance is an important factor in the pathogenesis of hypertension in pregnancy and hence therapeutic approaches that improve insulin sensitivity adds a potential role in reducing the risk of PIH[11,12].

II. Materials and Methods

This study was carried out in the Department of Biochemistry from May 2015 to April 2016 in Sri Venkata Sai Medical College and Hospital, Yenugonda, Mahaboobnagar district,Telangana. The study was conducted on 60 subjects among which the study group contains 30 women with pregnancy induced hypertension (with BP > 140/90 mmHg around 20 weeks of gestation) and the control group with 30 normotensive pregnant women who were in their second trimester. For both the groups, age of the women was between 20 to 45 years and the gestational age of all the women in both the groups was between 12-20 weeks

of pregnancy (second trimester).Pregnant women with other systemic disorders like gestational diabetes, gestational age less than 12 weeks or more than 20 weeks, pregnant women with any maternal or fetal complications and disorders involving any other organs like hepatic or renal disease were excluded. The aim was to estimate serum lipid profile and fasting serum insulin levels in normal pregnant women and in women with pregnancy induced hypertension to find out any alterations and compare the above parameters biochemical between the test group and control group. A fasting (12 hours) venous blood sample (5ml) was drawn from the patients and controls into a sterile disposable syringe which was transferred into centrifuge tubes and was allowed to clot for 30 minutes. The sample was centrifuged at 3000 rotations per minute for 10 minutes and the serum was separated and collected from the centrifuge tubes and analyzed within one hour as follows. Serum Triglycerides were estimated by CHOD-PAP method(Including LCF-lipemic clearing factor),Total Cholesterol and HDL-Cholesterol by CHOD-PAP method, LDL and VLDL- Cholesterol by calculation(Freidewald's fourmula). LDL-C = Total cholesterol – (HDL –C + VLDL –C). VLDL-C = Triglyceride/5.Fasting serum insulin levels were estimated by Chemiluminescence immunoassay (CLIA) with Lumax CLIA strip reader instrument.The data was expressed as mean and standard deviation values.

III. Statistics

The data between the groups was analysed by using unpaired t-test . P value less than 0.001 was considered to be significant.

IV. Results and Discussion

Table 1 shows the control population and Table 2 shows the test population charecteristics like blood pressure, gravida, serum total cholesterol, serum triglyceride, serum HDL-cholesterol, serum VLDL-cholesterol, serum LDL-cholesterol and fasting serum insulin levels of the pregnant women attending the out patient department. Mean and standard deviation values were calculated .Unpaired t test was applied and p values were calculated.

Figure 1 compaired the mean value of lipid profile.

In our study the Total cholesterol levels were significantly high in the test group in comparission to that of the control.The mean and S.D of Total cholesterol levels in controls is 198.1 ± 13.10 which is lower when compared to that of cases where the mean and S.D of Total cholesterol levels are found to be 225.066 ± 13.480. This difference was statistically significant ($p < 0.001$) However even other studies have found significant increase in serum total cholesterol levels [13,14].Some previous studies showed Hypertriglyceridemia in pre eclamptic pregnant women [15-17]. In our study also this observation holds true. The mean and S.D of Triglyceride levels in controls is160.53 ± 16.86 and that in cases is187.2 ± 22.75. The test group showed an increase in the triglyceride levels (hypertriglyceridemia) when compared with that of the control group.The difference was statistically significant($p<0.0001$).

The principle modulator of this hypertriglyceridemia is oestrogen as pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL. This process may be modulated by hyperinsulinism found in pregnancy [13]. Increased TG, found in pregnancy induced hypertension, is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL[18]. Moreover, this hypertriglyceridemia may be associated with hypercoagulability .

In our study the levels of HDL-C was almost equal in both control and tests groups. The mean and S.D of HDL-C levels of controls is 41.8333 ± 5.59 as compare to cases is 42.30 ± 6.550.The HDL-C levels is almost equal in test and in control groups. Oestrogen is responsible for induction of TG and HDL and suppression of serum LDL and oestrogen level falls in preeclampsia[1,19]. The low level of HDL-C in pregnancy induced hypertension is however not only because of hypo-oestrogenemia but also due to insulin resistance[20].In our study the mean and S.D of VLDL-C levels of controls is 32.786 ± 3.115 and that of cases is 37.44 ± 4.551. The test group showed a rise in VLDL-C levels when compaired with that of the control group. The difference was statistically significant which is perhaps due to hypertriglyceridemia leading to enhanced entry of VLDL that carries endogenous triglyceride into circulationVLDL level further increase in PIH as evidenced in the present study in corroboration with those of other workers [18].

In our study all the subjects(test group) showed a significant increase in the LDL-C levels when compared with that of the control group.The mean and S.D of LDL-C levels of controls is 123.360 ± 12.673 as compare to cases is 175.263 ± 13.596. This difference is statistically highly significant ($p < 0.001$).

may be attributed to hyperestrogenaemia, while LDL-C level increases significantly in PIH. Hypooestrogenaemia,

predominance of smaller and denser serum LDL particles and significant concentration of soluble vascular cell adhesion molecule-1 (VCAM-1) are supposed to be important contributors for endothelial dysfunction in PIH [1,14,18].

Figure 2 showed the mean and S.D of Insulin levels of controls is 20.883 ± 13.456 and that of cases is 48.773 ± 19.738.This difference is statistically significant ($p < 0.001$). The test group showed a significant increase in the Insulin levels (Hyperinsulinemia) when compared with that of the control group. Some studies have shown that hypertensive subjects were more hyper insulinimic i.e more insulin resistance than normotensive patients[13,20]. Kaplan reported that hyperinsulinemia and insulin resistance has a central role to play in the pathogenesis of pregnancy induced hypertension[21].Hyper insulinemia per se has been proposed to cause insulin resistance. Elevated concentrations of insulin can cause insulin resistance by down regulating insulin receptors and desensitizing post receptor path ways.

V. Figures and Tables

Table 1 Control group

SI	B.P MmHg	TC mg/dl	TG mg/dl	HDL mg/dl	VLDL mg/dl	LDL mg/dl	INSULIN μU/ml	GRAVIDA
1	100/70	183	164	45	32.8	105.2	17.2	Primi
2	102/74	203	152	36	30.4	136.6	37.7	Primi
2	110/78	208	184	42	36.8	129.2	16.7	Primi
4	120/80	214	174	51	34.8	128.2	38.0	Primi
5	120/76	201	152	42	30.4	128	6.0	Multi
6	106/68	195	146	34	29.2	131.8	18.5	Primi
7	138/80	198	151	38	30.2	126.8	6.1	Primi
8	110/78	196	149	47	29.8	119.2	7.8	Primi
9	118/80	167	159	38	31.8	97.2	15.9	Mul;ti
10	120/84	201	162	48	32.4	120.6	7.2	Multi
11	118/72	208	158	44	31.6	132.4	28.4	Primi
12	120/80	212	172	51	34.8	126.2	18.1	Primi
13	116/78	199	158	38	31.6	129.4	7.5	Primi
14	100/70	211	178	47	35.6	128.4	6.9	Primi
15	100/76	187	149	45	29.8	112.2	26.3	Primi
16	118/76	198	168	40	33.6	124.4	17.2	Primi
17	126/74	206	184	42	36.8	127.2	7.8	Primi
18	106/78	166	139	31	27.8	107.2	46.2	Primi
19	124/82	200	160	44	32	124	5.8	Multi
20	100/74	229	106	31	41.2	156.8	37.4	Primi
21	128/88	179	158	44	31.6	103.4	18.3	Primi
22	124/82	197	189	42	37.8	117.2	46.2	Multi
23	128/76	202	174	52	34.8	115.2	28.2	Primi
24	118/78	196	151	40	30.2	125.8	16.7	Multi
25	116/70	199	159	38	31.8	129.2	28.7	Primi
26	118/74	174	159	47	31.8	95.2	6.1	Primi
27	126/84	200	160	34	32	134	10.2	Multi
28	110/70	218	193	45	38.6	134.4	16.4	Multi
29	124/80	198	149	41	29.8	127.2	45.9	Primi
30	126/74	198	159	38	31.8	128.2	37.1	Multi
TOTAL		**5943**	**4816**	**1255**	**983.6**	**3700.8**	**626.5**	
MEAN		**198.1**	**160.5333**	**41.8333**	**32.7866**	**123.360**	**20.883**	
SD		**13.10**	**16.86**	**5.59**	**3.115**	**12.673**	**13.456**	

Table 2 Test group

SI	B.P MmHg	TC mg/dl	TG mg/dl	HDL mg/dl	VLDL mg/dl	LDL mg/dl	INSULIN μU/ml	GRAVIDA
1	152/106	262	220	38	44	180	62.0	Primi
2	160/106	263	182	40	36.4	186.2	32.8	Primi
3	168/112	247	165	32	33	182	55.6	Multi
4	144/104	231	162	55	32.4	143.6	76.1	Primi
5	142/98	265	219	30	43.8	191.2	49.6	Primi
6	170/120	285	189	44	37.8	203.7	14.8	Primi
7	150/110	268	149	50	29.8	186.2	59.2	Primi
8	152/110	252	209	49	41.8	161.2	68.2	Multi
9	144/100	251	184	43	36.8	171.2	34.9	Multi
10	164/118	250	172	45	34.4	170.6	23.0	Primi
11	150/106	242	192	38	38.4	165.6	51.6	Primi
12	148/112	262	179	44	35.8	182.2	31.2	Primi
13	150/112	251	220	39	44	168	65.2	Primi
14	144/96	263	180	50	36	177	28.4	Primi

15	164/112	268	209	41	41.8	185.2	44.5	Primi
16	156/106	242	130	48	26	168	31.0	Primi
17	146/98	253	219	34	43.8	175.2	77.5	Primi
18	160/102	240	169	42	33.8	164.2	26.6	Multi
19	152/118	241	184	48	36.8	156.2	45.9	Multi
20	148/104	267	213	32	42.6	192.4	60.2	Primi
21	156/120	264	198	52	39.6	172.4	26.4	Multi
22	158/118	271	201	45	40.2	185.8	75.6	Multi
23	148/110	244	169	38	33.8	172.2	36.7	Primi
24	160/108	273	209	41	41.8	190.2	70.6	Primi
25	158/106	265	182	35	36.4	193.6	26.5	Primi
26	154/102	255	201	45	40.2	169.8	57.3	Multi
27	148/100	247	162	54	32.4	160.6	24.1	Primi
28	152/104	226	163	39	32.6	154.4	50.8	Primi
29	148/100	264	191	40	38.2	185.8	78.2	Primi
30	150/116	240	194	38	38.8	163.2	78.7	Multi
TOTAL		7652	5616	1269	1123.2	5257.9	1463.2	
MEAN		255.066	187.2	42.3	37.44	175.263	48.773	
SD		13.480	22.75	6.550	4.551	13.596	19.738	
t-test		16.1159	5.1577	0.2968	4.6213	15.295	6.3947	
p-value		0.0001	0.0001	0.7677	0.0001	0.0001	0.0001	

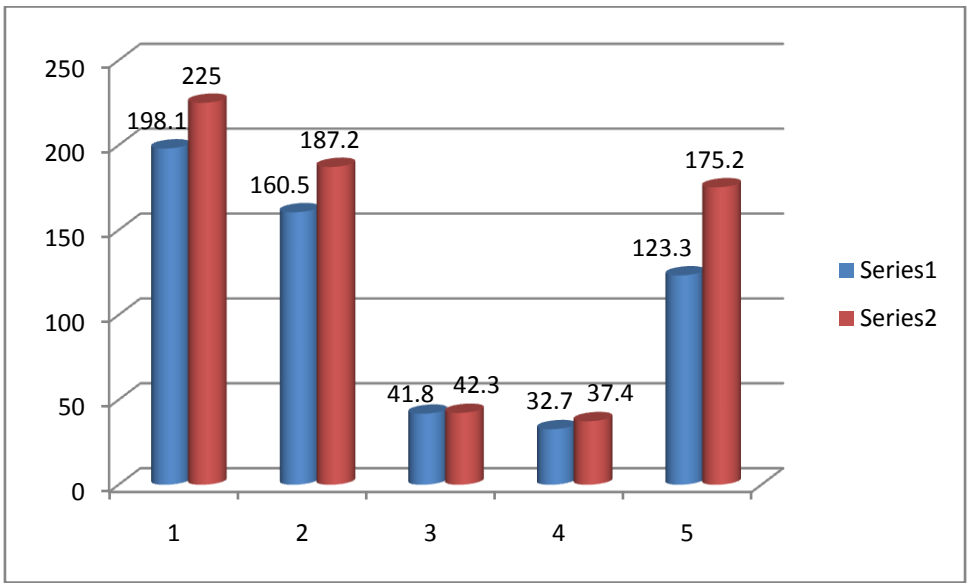

Fig 1 Comparision of mean values of lipid profile (gms/dl)

series 1 – controls

series 2 – tests

1 –Total cholesteol , 2 – Triglycerides, 3 – HDL-C, 4 – VLDL, 5- LDL-C

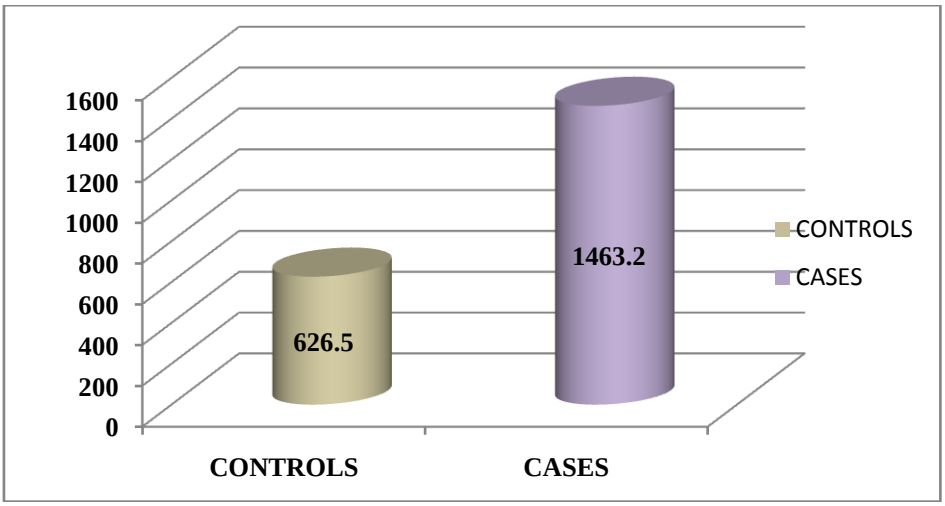

Fig 2 Comparision of Insulin(µU/ml) in controls and cases

VI. Conclusion

A comparative study was done between second trimester normal pregnant women and second trimester hypertensive pregnant women on levels of serum total cholesterol, triglycerides, HDL-C, VLDL-C, LDL-C, Insulin. The patients were clinically diagnosed based upon history, clinical symptoms, signs and levels of blood pressure. In all the blood samples obtained from controls and cases serum total cholesterol, triglycerides ,HDL-C, VLDL-C, LDL-C, Insulin levels were estimated by standard methods. The present study showed that maternal dyslipidemia as well as hyperinsulinemia in second trimester hypertensive pregnant women (test group) are very good noninvasive predictors of PIH. There is a definite relationship between lipid profile and PIH. Moreover the hormonal imbalance is a prime factor for the aetiopathogenesis of PIH and this endocrinal imbalance is well reflected in alteration of serum lipid profile. Dyslipidemia mediated activation of the endothelial cells to the placentally derived endothelial disturbing factors like lipid peroxides and trophoblastic components or combination of placentally derived factors with the lipoproteins could be regarded as possible contributors for pathogenesis of PIH [22]. A clinical trial of life style and dietary modification would help in cases of altered lipid metabolism. Predicting preeclampsia at an early gestational age helps us to monitor the patients closely and detect development of preeclampsia earlier and thereby reducing the maternal and perinatal mortality and morbidity. Dyslipidemia and serum insulin levels seems to be a more efficient marker in predicting PIH at second trimester. It may be concluded that the estimation of maternal lipid profile and fasting insulin levels in early second trimester will bring about early recognition of patients at risk of PIH before the clinical syndrome and complications of PIH (eclampsia, intrauterine growth retardation, HELLP syndrome future cardio vascular risk of the mother, future development of hypertension and stroke) appear for a better feto-maternal outcome . It is not likely that a single marker will prove to be a perfect predictive device for pregnancy induced hypertension; a combination of clinical information concerning history and risk factors along with blood biomarkers or urine in those at risk is more rational. There is clearly a great need for development of predictive means for pregnancy induced hypertension. These developments could well be the solution to improving care for women with this disturbing condition. Thus, our findings may be relevant for the future treatment by lipid modifying regimens of this life-threatening condition.

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