

EVALUATION OF LIPID AND THYROID STATUS IN PREGNANCY AND ITS EFFECT ON NEONATAL OUTCOME

GURPREET KAUR GILL*, DIKSHA KAPILA

Department of Medical Lab Sciences, Khalsa College of Pharmacy and Technology, Amritsar, Punjab, India.

*Corresponding author: Gurpreet Kaur Gill; Email: gurpreet_pau25@yahoo.com

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ABSTRACT

Objective: Maternal nutritional status is essential for the achievement of maternal and fetal growth. Blood lipid concentrations have been associated with adverse pregnancy outcomes such as gestational diabetes, pregnancy-induced hypertension, and high birth weight. As blood lipids are not routinely measured during pregnancy, there is limited information on what is considered normal during pregnancy. In early pregnancy, there is an increase in fat buildup associated with increased fat concentration in blood, lipoprotein, and apolipoprotein in plasma increased significantly during pregnancy. This study was aimed at the analysis of lipid profile and thyroid profile in second- and third-trimester pregnant women, with the incidence of hypertension and their possible effect on neonatal outcome.

Methods: Blood samples were collected from the Beri Maternity Hospital, Amritsar, and were analyzed for biochemical investigation, namely lipid profile and thyroid profile.

Results: The levels of total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very LDL have been significantly increased in third-trimester pregnant women as compared to second-trimester pregnant women. However, the level of HDL diminished in the third trimester as compared to the second trimester. Thyroid-stimulating hormone (TSH) levels increased in third-trimester pregnant women.

Conclusion: Our findings highlighted the importance of maternal lipid metabolism in preventing pregnancy complications and adverse birth outcomes as human gestation is associated with an "atherogenic" lipid profile which could act as a potential risk factor for pre-eclampsia and endothelial cell dysfunction if further enhanced than the normal limits. Increased blood lipid concentrations during pregnancy are altered by maternal body mass index. This study will help in understanding baseline lipid parameters in the second and third trimesters among pregnant women. Excessive dietary nutrition intake and inadequate physical activity during pregnancy may be important contributors of dyslipidemia which can lead to complications.

Keywords: Cholesterol, Pregnancy, Maternal, Blood Pressure, Body Mass Index.

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INTRODUCTION

Metabolic functioning is altered in pregnancy which leads to lipid profile changes to accommodate the developing fetus. Blood lipid profile has been associated with adverse pregnancy outcomes such as gestational diabetes, pregnancy-induced hypertension, and high birth weight although these changes are physiologically necessary [1]. Maternal nutritional status is essential for the achievement of maternal and fetal growth. As blood lipids are not routinely measured during pregnancy, there is limited information on what is considered normal during pregnancy. In the first trimester, the maternal metabolic environment gets modified due to a rise in serum levels of estrogen, and progesterone by pancreatic beta-cell hyperplasia leading to an increase in insulin secretion. The component of the metabolic syndrome associated with insulin resistance, i.e., dyslipidemia is a well-known cardiovascular risk factor. The most common method used to know the nutritional status of a person is by calculating the Body Mass Index (BMI). BMI is defined as a person's weight in kilograms (kg) divided by the square of the person's height in meters (kg/m²).

In pregnancy, there is an increase in fat buildup and its concentration in blood, lipoprotein, and apolipoprotein in plasma increases significantly during pregnancy leading to accumulation [2]. Lipid accumulation can cause endothelial dysfunction causing pre-eclampsia, lipid profiles include total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and very LDL (VLDL). It is suspected that there is an association between pre-eclampsia with elevated total cholesterol, triglycerides, LDL, and VLDL. Elevated plasma triglycerides and LDL during pregnancy can be used to identify women who will

experience atherogenic changes in later life [3]. Birth weight can be used to measure the health, nutrition, and socioeconomic status of the population. Several factors such as mothers' genetic characteristics, sociocultural, demographic, behavioral factors, high BMI, and gestational weight gain among others contribute to birth weight. A low maternal BMI and suboptimal weight gain during pregnancy are long recognized risk factors for delivery of infants too small for gestational age, low birth weight as well as to increase the risk of subsequent obesity and hypertension in the offspring. However, high maternal BMI is also related to adverse neonatal outcomes including pre-term delivery, macrosomia, congenital anomalies, neonatal asphyxia, neonatal death, hypoglycemia, hyperbilirubinemia, increased requirement for neonatal intensive care, and a longer duration of hospital stay [4].

Hypertension in pregnancy is a complication found in 5–10% of all pregnancies and has an increased risk of poor pregnancy outcomes. The risk of poor outcome of pregnancy in hypertension is commonly found related to the diagnosis of pre-eclampsia [5]. Hypertensive disorders in pregnancy may cause maternal and fetal morbidity, and they remain a leading source of maternal mortality. The exact etiology of gestational hypertension remains elusive, there are, however, several factors that may probably contribute to the rise in blood pressure during pregnancy. These factors include an expansion in total plasma volume of up to 40%, an increase in the red cell mass of about 25%, and 25% increase in the glomerular filtration rate, and an increase in the synthesis of thyroid hormones.

During normal pregnancy, changes in thyroid function are also well documented, but information about thyroid function in complicated

pregnancy is scanty. During pregnancy, there is an increased thyroid demand and increased iodine uptake and synthesis of thyroid hormones. Estrogen induces a rise in serum thyroxine-binding globulin (TBG) and the placenta releases several thyroid stimulatory factors in excess [6]. Thyroid dysfunction without any primary thyroid disease may result in various qualitative changes in triglycerides, phospholipids, cholesterol, and other lipoproteins [7].

METHODS

A comparative study of thyroid and serum lipid profiles was done among pregnant women in the third trimester, second trimester, and non-pregnant healthy controls in the reproductive age frame of 20–35 years. The control group included pregnant women at the same gestation with normal blood pressure, no proteinuria, and any other systemic or endocrine disorders. Inclusion criteria involved pregnant women in the second trimester and third trimesters without any ongoing complications. Exclusion criteria included the cases having hypertension diagnosed before the onset of gestation, diabetes mellitus, multiple pregnancies, history of chronic hypertension, any renal disease, any metabolic disorder, or medication known to affect thyroid function. Pregnant women with age above 40, any physical and mental disability, and women who had a miscarriage or stillbirth during the recruitment process were excluded. Informed consent was taken from the patients and the study protocol was approved by the Institutional Ethical Committee. Samples of patients and controls were collected at the Beri Maternity Hospital, Amritsar, and distributed in three groups, namely Group-I: Non-pregnant healthy women, Group-II: Second-trimester pregnant women, and Group-III: Third-trimester pregnant women. Serum samples were separated by centrifugation at 1500 rpm for 15 min, and preserved for further analysis. Thyroid-stimulating hormone (TSH) was analyzed by immunoenzymometric assay method using ERBA THYROKIT. The level of cholesterol was determined by the CHOD-PAP method. Triglycerides were analyzed by the GPO/POD method. HDL cholesterol was determined by the CHOD-PAP method after precipitation with phosphotungstic acid. The level of VLDL and LDL was calculated by the Friedwald formula. Analysis was performed on a semi-autoanalyzer and data were recorded. Descriptive statistics were used to analyze the data for the values of mean and standard deviation.

RESULTS

The mean age of the pregnant women included in the study was almost comparable to each other. The mean age of third-trimester pregnant women, second-trimester pregnant women, and controls included in the study was 28.1±3.31 years, 26.7±2.62 years, and 27.8±4.33 years, respectively. The mean weight of third-trimester pregnant women, second-trimester pregnant women, and controls was 61.3±6.53 kg, 59.08±4.66 kg, and 53.06±5.47 kg. The mean height of third-trimester pregnant women, second-trimester pregnant women, and controls was 1.54±0.07 m, 1.56±0.05 m, and 1.55±0.07 m, respectively. The mean BMI of third-trimester pregnant women was 25.53±2.53 kg/m², and second-trimester pregnant women were 24.33±2.34 kg/m². The controls included in the study had of mean BMI of 21.99±2.20 kg/m² (Table 1).

The body of pregnant women requires more oxygen and the oxygen-carrying capacity of the blood is proportional to the circulating hemoglobin concentration. In the present study, the hemoglobin content of third- and second-trimester pregnant women was found to be 11.17±1.35 g/dL and 10.89±1.28 g/dL, respectively. The level of hemoglobin was found to be 10.74±1.28 g/dL in non-pregnant healthy women. The level of hemoglobin developing to 10.5 g/dL is quite normal in the pregnancy. This is because the blood volume increases by 50% in the pregnancy for providing essential nutrients for developing baby. The increase in blood plasma is higher, when compared to increased RBC volume.

Blood pressure readings above 140/90 mmHg in pregnancy indicate high blood pressure/hypertension. In the present study, the mean

systolic blood pressure of third-trimester pregnant women was observed as 145.83±20.72 mmHg, whereas the mean systolic blood pressure of second-trimester pregnant women was found to be 117.73±8.80 mmHg, and it was found to be normal and almost similar to the systolic blood pressure of non-pregnant healthy women. Diastolic blood pressure was found to be 89.3±13.88 mmHg in the third trimester when measured at 32 weeks of gestation in pregnant women, whereas it was found to be 75.06±6.31 mmHg and 72.56±6.18 mmHg in second-trimester pregnant women and controls, respectively (Table 2).

The level of various lipids, namely cholesterol, triglyceride, HDL, LDL, and VLDL has been estimated in pregnant females with 28–40 weeks of gestation. It was found that maximum levels of lipids were found in third-trimester pregnant women as compared to second-trimester pregnant women and non-pregnant healthy control group. In third-trimester pregnant women, cholesterol and triglycerides were found higher as compared to second-trimester pregnant women and non-pregnant control (Table 3).

In pregnancy, the production of thyroid hormones T₃ and T₄ increases by about 50%. As a result, the normal TSH level during pregnancy is lower than the normal non-pregnant level. However, in the current study, it has been observed that TSH levels in third-trimester pregnant women were found to be 3.80±2.08 mIU/L. Whereas, the TSH levels in second-trimester pregnant women and non-pregnant women were 2.61±1.01 mIU/L and 2.34±0.93 mIU/L, respectively (Table 4).

The mean level of lipids viz cholesterol, triglycerides, LDL and VLDL were high in women who delivered with C-section pertaining to their high blood pressure (140/80 mm Hg) (Table 5) as compared to women who delivered vaginally. It has also been observed that women with different maternal lipid profiles have been associated with variations in birth weight (Table 6).

DISCUSSION

Maternal atherogenic lipid profile in pregnancy is one of the main causal factors responsible for adverse pregnancy outcomes. A high level of triglycerides is likely to be deposited in predisposed vessels and contributes to endothelial dysfunction, through the generation of LDL, due to which vasoconstriction takes place resulting in increase in blood pressure in pregnancy. Furthermore, estrogen induces hepatic biosynthesis of endogenous triglycerides, which are carried by VLDL [8]. Thus, VLDL increased in the circulation due to hypertriglyceridemia as they carried endogenous triglycerides into circulation. It has also been found that enhanced LDL in pre-eclamptic patients might be due to enhanced lipid peroxidation in the foam cell formation of decidua in the pathogenesis of toxemia in pregnancy [9]. Dyslipidemia leads to the activation of endothelial cells, resulting in the formation of placental-derived endothelial disturbing factors such as lipid peroxides. These could be regarded as possible contributors to the pathogenesis of pregnancy-induced hypertension [10]. Too much increase in lipid levels may also be due to maternal weight gain and dietary modifications. High dietary fibers can decrease TG concentration and reduce pre-eclampsia risk [11]. The association of abnormal lipid values in the promotion of hypertension in pregnant women helps to investigate the underlying pathological process of hypertension in pregnancy. Hypertriglyceridemia may be modulated by hyperinsulinism found in pregnancy [12]. Triglyceride, HDL, LDL, total lipid, cholesterol, and VLDL values are increased during pre-eclampsia [13]. The rise in triglyceride-rich VLDL particles during pregnancy is dependent more on an increased rate of synthesis caused by estrogen than on a decrease in the rate of removal [14]. Significantly higher total cholesterol, triglyceride, and LDL cholesterol in the third trimester than in the second-trimester patients in the present study is in corroboration with earlier studies [15].

Elevated insulin levels or enhanced insulin sensitivity in pregnancy and increased activity of adipose tissue lipoprotein lipase (LPL) contribute to lipogenesis and hyperlipidemia. Too fast plasma lipid elevation

Table 1: Mean age, height, weight, and BMI of second- and third-trimester pregnant women and control group under study

S. No	Group	No. of patients (n)	Age (years)	Weight (kgs)	Height (m)	BMI (kg/m ²)
1.	Controls	30	27.8±4.33	53.06±5.47	1.55±0.07	21.99±2.20
2.	Second-trimester pregnant women	30	26.7±2.62	59.08±4.66	1.56±0.05	24.33±2.34
3.	Third-trimester pregnant women	30	28.1±3.31	61.3±6.53	1.54±0.07	25.53±2.53

*Data represented as mean±SD

Table 2: Hb and blood pressure of pregnant women and controls under study

S. No	Group	No. of patients	Hb (g/dL)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mm Hg)
1.	Controls	30	10.74±1.28	118.43±6.17	72.56±6.18
2.	Second-trimester pregnant women	30	10.89±1.28	117.73±8.80	75.06±6.31
3.	Third-trimester pregnant women	30	11.17±1.35	145.83±20.72	89.3±13.88

Hb: Hemoglobin, *Data represented as mean±SD

Table 3: Lipid profile of second- and third-trimester pregnant women and controls under study

S. No	Group	No. of Patients	Cholesterol (mg/dL)	TG (mg/dL)	HDLc (mg/dL)	LDLc (mg/dL)	VLDLc (mg/dL)
1.	Controls	30	175.16±35.19	111.86±19.68	46.53±6.44	106.33±27.11	22.35±3.79
2.	Second-trimester pregnant women	30	211.5±28.54	120.63±35.10	58.13±9.48	143.02±24.64	24.10±7.54
3.	Third-trimester pregnant women	30	237.23±24.26	145.7±42.08	44.30±7.64	153.76±16.45	28.3±7.11

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very Low-density lipoprotein, *Data represented as mean±SD

Table 4: Levels of thyroid stimulating hormone in pregnant women and controls under study

S. No	Group	No. of patients	TSH (mIU/L)
1.	Healthy control	30	2.34±0.93
2.	Second-trimester pregnant women	30	2.61±1.01
3.	Third-trimester pregnant women	30	3.80±2.08

*Data represented as mean±SD

may induce endothelial dysfunction secondary to oxidative stress. Dysregulation of LPL resulted in a dyslipidemic lipid profile. In the present study, levels of HDL were found to be diminished in the third trimester as compared to levels found in the second trimester whereas levels of LDL were found higher in the third trimester. In pregnancy, profound anatomic and physiologic changes take place in almost every organ system. These changes start occurring just after conception has taken place and keep on evolving throughout the pregnancy including the delivery period. These changes occur to facilitate the needs of the mother and fetus. Maternal physiology is highly influenced by the placental hormones, especially in the last trimester of the pregnancy. The variation in hormonal levels generally affects glucose and lipid metabolism and such variations take place to make sure that the fetus receives an ample supply of nutrients for its development [16].

Moreover, the deposition of proteins, fats, and water in the intracellular compartment of the body leads to physiological maternal weight gain. Due to an increase in metabolic requirements during pregnancy, the maternal body responds by switching over to fat utilization from carbohydrates. An increase in insulin resistance and plasma lipolytic hormonal concentration also facilitates it [17]. These changes lead to large variations in insulin and glucose levels in the mother as she oscillates from fed to fasted state. During the fasted state, the glucose is preserved for the fetus whereas alternative sources of fuels are made available to the mother for her metabolic use. The large rise in triglycerides is due to two factors, increased hepatic lipase activity, leading to enhanced hepatic triglyceride synthesis, and reduced LPL activity, resulting in decreased catabolism of adipose tissue [18]. The white adipose tissue is a very active endocrine organ, which also releases a number of endocrine and paracrine factors termed adipokines [19]. Apolipoproteins A-I, A-II, and B also rise across gestation, whereas

HDL-cholesterol concentrations initially increase and then fall in the third trimester [20]. These changes in lipid metabolism help the mother and fetus to adapt. High triglyceride concentrations are thereafter being used for maternal metabolic needs while sparing glucose for the fetus. The placental synthesis of steroids is facilitated by elevated LDL cholesterol levels. In short, the second trimester is characterized by the accumulation of fat, which will be later consumed by the mother in the third trimester. The association between elevated lipid levels during normal pregnancy and the development of atherosclerosis later in life has not been found yet. However, it is seen that the fall in HDL levels in the third trimester of a normal pregnancy could be a potential risk factor for developing atherosclerosis [21]. Studies attempting to correlate the risk of coronary heart disease and the number of pregnancies have produced contradictory results [22].

It can be inferred from the present study that, high blood pressure leads to an increase in TSH levels which indicates hypothyroidism. The levels of T₄ should be checked to identify overt or subclinical hypothyroidism. The altered levels of T₄ can impair the infants' neurocognitive development. There are also increased risks for premature birth, low birth weight, miscarriage, and lower IQ levels in children. The influence of TSH on lipid profile has been assumed to be mediated indirectly, through its effect on thyroid hormones. In pregnancy, thyroidal activity is increased which leads to an increase in serum TSH. It has also been established that there is a big increase in the concentration of TBG during pregnancy due to the presence of high levels of estrogen circulating in the blood. Increased levels of TBG in the blood lead to the lowering of triiodothyronine (T₃) and tetraiodothyronine (T₄). Decreased levels of T₃ and T₄ provoke the pituitary gland to secrete more TSH. Moreover, increased glomerular filtration in pregnancy leads to an increase in renal clearance of iodine. The iodine loss lowers the circulating level of inorganic iodine and induces a compensatory increase in thyroidal iodine clearance and its entry into the gland. Thus, it can be concluded that the cumulative effect of estrogen, TBG, and renal clearance leads to the hypersecretion of TSH by the gland and its elevated levels present in the blood serum.

Maternal thyroid dysfunction during pregnancy has been associated with the number of adverse outcomes. It has been suggested that there may be an existence of mutual influences between pre-eclampsia and thyroid function [23]. Endothelial dysfunction is an important factor in hypertensive pregnancy leading to a significant increase in TSH levels

Table 5: Mean blood pressure and lipid levels of mothers with vaginal and c-section delivery

S. No.	Mode of delivery	Blood pressure (mg/dL)	Cholesterol (mg/dL)	Triglyceride (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
1.	Vaginal	100/60	232	142	44	149	27
2.	C-section	140/80	243	152	43	158	30

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very Low-density lipoprotein

Table 6: Comparison of neonatal birth weight and lipid profile of third-trimester pregnant women

S. No	Birth weight (kg)	BMI (kg/m ²)	Cholesterol (mg/dL)	Triglyceride (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
1.	2-2.5	24.9	241.8	146.2	44.5	156.2	29.2
2.	2.6-3	26.0	235.6	141.8	43.3	160.6	28.7
3.	3.1-3.5	25.4	236	154.5	41.3	148.1	25.4
4.	3.6-4	25.7	237	142.8	42.8	149	25.7

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very Low-density lipoprotein

in blood serum. It can be explained by the excessive release of anti-angiogenic proteins from the placental to maternal blood. TSH levels should be monitored regularly in the first and second trimester of gestation in hypertensive pregnant women.

Pregnancy complications including pre-eclampsia and perinatal outcomes including pre-term birth and respiratory distress were noted to explore the associations between maternal lipid profile and its possible effects on neonatal outcome. Maternal high cholesterol in late pregnancy was found to be positively associated with increased risk of preterm delivery. Furthermore, respiratory distress was encountered in babies of mothers with relatively higher cholesterol and triglyceride levels. It is noteworthy that disturbed maternal metabolism and atherogenic lipid changes in pregnancy are some of the crucial factors which might be involved in this pathological process. Maternal high triglyceride concentrations and high body mass indices during the second and third trimesters were associated with an increased risk of high birth weight. From the deduced data, it has been observed that 57% of mothers delivered through C-section, had relatively higher levels of lipids as compared to mothers delivered vaginally. It has been observed that relatively higher levels of maternal lipids, namely cholesterol, triglycerides, LDL, and VLDL were associated with high blood pressure levels which lead to complications.

CONCLUSION

Our findings highlighted the importance of maternal lipid metabolism in preventing pregnancy complications and adverse birth outcomes as human gestation is associated with an "atherogenic" lipid profile which could act as a potential risk factor for pre-eclampsia and endothelial cell dysfunction if further enhanced than the normal limits. Increased blood lipid concentrations during pregnancy differ by maternal BMI. This study will help in understanding baseline lipid parameters in the second and third trimesters among pregnant women. Total cholesterol, triglycerides, LDL, and VLDL increased in both the second and third trimesters. The increase is more in the third trimester when compared to the second. HDL is decreased in the third trimester when compared to the second trimester. Excessive dietary nutrition intake and inadequate physical activity during pregnancy may be important contributors of dyslipidemia. Lipid profiling is of utmost importance and should be part of a routine investigation during pregnancy.

AUTHORS CONTRIBUTION

Diksha Kapila collected and analyzed the data. Gurpreet Kaur Gill designed the study and drafted the manuscript. All authors reviewed the results and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors state no conflict of interest.

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