VOLUME-9, ISSUE-2, FEBRUARY-2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

EVALUATION OF ANTEPARTUM AND POSTPARTUM LIPID PROFILES IN A SOUTHERN AFRICAN POPULATION

Sara Mosima Pheeha*

School of Pathology, Department of Chemical Pathology, Sefako Makgatho Health Sciences University/ National Health Laboratory Services, Dr George Mukhari Academic Hospital, Pretoria, South Africa.
Division of Epidemiology and Biostatistics, Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa *Corresponding Author

Donald Moshen Tanyanyiwa

School of Pathology, Department of Chemical Pathology, Sefako Makgatho Health Sciences University/ National Health Laboratory Services, Dr George Mukhari Academic Hospital, Pretoria, South Africa.
Division of Chemical Pathology, Department of Pathology, University of Witwatersrand, Johannesburg, South Africa

ABSTRACT

Objective: Pregnancy is associated with changes in metabolic processes that result in increased levels of lipids and lipoproteins. It is important to assess if these changes occur at the same rate and percentage across racial groups. Therefore, the aim of this study was to explore antepartum and postpartum of lipid profiles in a Southern African population.

Methods: This cross-sectional study was conducted in Harare. It included 446 normotensive pregnant African women were aged 16 – 41 years. Lipid tests were analysed on the Roche modular platform. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 25 and level of significance was set at a p-value of ≤ 0.05

Results: There was a significant difference ($p < 0.0001$) between the antepartum and postpartum total cholesterol (TC), Triglycerides (TG), high density lipoprotein-cholesterol (HDL-C) and very low density lipoprotein-cholesterol (VLDL-C). Postpartum TG had a significant difference ($p = 0.05$) in the inter-trimester comparisons. LDL-C had a significant difference ($p = 0.03$) in the intra-trimester age comparisons for the second trimester.

Conclusion: This is a reasonably large study that demonstrated increased lipids during pregnancy and provided the first insight into the marginal intra-trimester age lipid increases and postpartum lipid concentrations in the Southern African population.

KEYWORDS : pregnancy, trimesters, lipid profile, African.

INTRODUCTION

Pregnancy is accompanied by changes and alterations in metabolic processes (1–4). These changes support the demand for metabolic energy for the developing fetus and also result in hormonal changes which contribute to changes in the lipid profile (Mankuta et al., 2010). Changes in the lipid profiles are attributed to the anabolic and catabolic phases antepartum (Barrett, Nitert, McIntyre, & Callaway, 2014; Grimes & Wild, 2000). The initial anabolic phase occurs during the first two trimesters, where there is increased fat synthesis and storage (Barrett et al., 2014), in preparation for the increased energy demand by the fetus (Grimes & Wild, 2000; Phuse, 2018; Wiznitzer et al., 2009).

This phase is supported by increased insulin sensitivity and increased appetite leading to increased food consumption (Bassi, Kaur, & Sharma, 2011; Idonije et al., 2011). However, metabolic changes during the third (3rd) trimester, referred to as catabolic are associated with insulin resistance which enhances the breakdown of stored TG. The increment of lipids and lipoproteins is considered to be normal during pregnancy (Mankuta et al., 2010; Wiznitzer et al., 2009) and it is believed to increase with increasing gestational age (Bassi et al., 2011; Idonije et al., 2011; Jin et al., 2016; Phuse, 2018; Pusukuru et al., 2016). However, the increase may reflect an underlying pathology and therefore should be used as a basis to investigate possible atherogenic alterations later (Mankuta et al., 2010). Elevated maternal TC and TG in early stages of gestation are associated with increased rates of gestational diabetes (Sánchez-Vera et al., 2007; Savvidou et al., 2010), pre-term birth (Vrijkotte et al., 2012), pregnancy-induced hypertension (Vrijkotte et al., 2012; Wiznitzer et al., 2009) and pre-eclampsia (Enquobahrie et al., 2004; Vrijkotte et al., 2012). Moreover, there are reports on children of hypercholesterolemic mothers developing atherosclerosis faster when compared to those with normal mothers (Frantz et al., 2012).

Lipid profiles between trimesters as well comparisons between different age groups are not well described in the African population. The highest rate of unintended pregnancy has been reported among young adult women aged 20–24 years (Finer & Zolna, 2014). Therefore, this study was undertaken to assess lipid profile between trimesters of a normal pregnancy as well as assess age related differences in each trimester.

MATERIALS AND METHODS

This was a cross-sectional study conducted in Harare at two busy urban polyclinics, Mbare and Mabvuku between January 2002 and December 2002. Mbare Polyclinic is located in the oldest high-density suburb in the Southwest of the city of Harare. Mabvuku Polyclinic is located in a high-density suburb east of Harare. The recruitment was divided into four stages, with the fourth stage being six weeks postpartum. Four hundred and forty-six (446) participants aged 16 – 42 years with lipid profile antepartum and 6 weeks postpartum were enrolled. The participants were divided into three groups (trimesters) based on the gestation on presentation. Each group was further divided into two age dependent groups i) young (16-30 years) and ii) older (31 to 45 years).

All normotensive pregnant women attending the two polyclinics for antenatal consultation at any gestational age determined by last menstrual period were included in the present study. Those with diseases or conditions that cause secondary dyslipidemia like (malaria, leprosy, tuberculosis,

renal, thyroid disease and alcohol consumption) were excluded. Anti-retroviral drugs were not available in the public health institutions and none of the participating subjects could afford these drugs in the private sector.

Two fasting venous blood samples were collected into Ethylene-diamine tetra-acetic acid (EDTA) tubes from each participant; first during antepartum and then postpartum. TC, TG, LDL-C, and HDL-C measurements were analysed on the Roche Modular diagnostic platform. The analysis employs published methods. Low Density Lipoprotein Cholesterol (LDL-C) was calculated using the Friedewald Equation (LDL-C = (TC – HDL-C– (TG/2.22) mmol/L (Friedewald, Levy, & Fredrickson, 1972) and very low density lipoprotein cholesterol (VLDL) was determined by dividing triglycerides with 2.2. The performance targets for all the analytes were within the acceptable CV for Roche Modular.

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 25 (IBM, Armonk, NY, USA). All continuous data was tested for Normality using Shapiro Wilks test, with significance set at $p < 0.05$. Data was presented using descriptive statistics (median, interquartile range (IQR), range, minimum (min) and maximum (max) values) and figures (Box and whisker plots). Comparison between antepartum and postpartum lipid levels was done using the Wilcoxon signed rank test. The Mann-Whitney U test was used to compare lipid concentrations between second and third trimesters and between age groups intra-trimesters. For all statistical analysis, level of significance was set at $p \leq 0.05$.

Ethical approval for the study was sought from and granted by the University of Cape Town Human Ethics Research Committee (REC REF No104/2002) and the Medical Research Council (MRC) of Zimbabwe. All participants signed a written informed consent before taking part in the study.

RESULTS

690 subjects were recruited in phase one, but 483 (70%) participated in the postnatal (minimum six weeks postpartum) follow-up. Only those whose samples were adequate for both antenatal and postnatal full investigations had paired analysis done. In order to keep within 15 weeks after delivery, home visits were conducted and this resulted in 446 (65%) final enrolment. The median age of patients was 24 years and the range was 16 to 41 years. The median and interquartile range of the age for both the 2nd and 3rd trimesters was 24 (8), with the youngest being 16 in both trimesters and the oldest being 41 and 40 years in the 2nd and 3rd trimester respectively (Table 1).

Table 1: Descriptive statistics of the age and gestation in the two trimesters

Trimester	(n)	Age median (IQR)	Age range (years)	Median (IQR) of gestation (weeks)	Gestation range (weeks)
2nd trimester	136	24 (8)	16 – 41	25 (3)	13- 27
3rd trimester	304	24 (8)	16 – 40	31 (4)	28- 38

Table 2 below shows comparison of plasma lipid concentrations between antepartum and postpartum in the 2nd and 3rd trimesters.

Table 2: Plasma lipid median concentrations during 2nd and 3rd trimesters and postpartum

TC	Median & IQR (mmol/L)	Range of lipid values (mmol/L)	Min & max values (mmol/L)	P-value
2nd trimester:	4.1 (1.3)	4.5	2.5- 7.0	0.000
Postpartum	3.5 (0.9)	4.2	1.9- 6.1	
3rd trimester	4.1 (1.1)	5.4	2.3- 7.7	0.000
Postpartum	3.5 (1.0)	4.7	1.0- 5.7	
TG				
2nd trimester	1.5 (1.2)	3.4	0.4- 3.8	0.000
Postpartum:	0.7 (0.4)	1.4	0.4- 1.8	
3rd trimester	1.5 (1.1)	3.9	0.4- 4.3	0.00
Postpartum	0.6 (0.3)	1.8	0.1- 1.9	
LDL-C				
2nd trimester	2.0 (0.9)	4.5	0.5- 5.0	0.898
Postpartum	2.0 (0.9)	3.5	0.9- 4.4	
3rd trimester	2.1 (0.9)	4.0	0.4- 4.4	0.231
Postpartum	2.0 (0.8)	3.8	0.4- 4.2	
HDL-C				
2nd trimester	1.4 (0.6)	2.7	0.4- 3.1	0.000
Postpartum	1.1 (0.4)	2.1	0.1- 2.2	
3rd trimester	1.3 (0.6)	3.1	0.2- 3.3	0.000
Postpartum	1.2 (0.4)	2.2	0.1- 2.3	
VLDL-C				
2nd trimester	0.7 (0.5)	1.5	0.2- 1.7	0.000
Postpartum				
3rd trimester	0.7 (0.5)	1.8	0.2- 2.0	0.000
Postpartum				

There was a significant difference ($p < 0.0001$) between the baseline antepartum trimester concentrations and the postpartum concentration for; TC, TG, HDL-C and VLDL-C. However, LDL-C remained constant between antepartum and postpartum. TG concentrations were more than 2-fold in pregnancy, compared to postpartum levels. TC and HDL-C were significantly higher antepartum but LDL-C concentration remained constant during pregnancy and postpartum.

Comparison of lipid levels in the 2nd and 3rd trimester and postpartum are shown in figures 1A to 1E below.

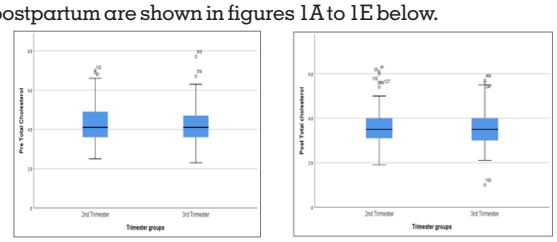

Figure 1A: Comparison of TC

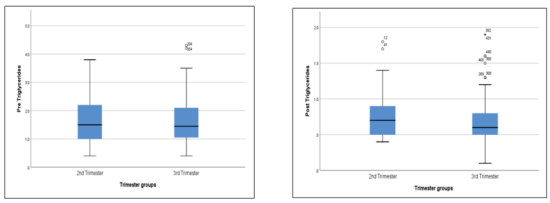

Figure 1B: Comparison of TG

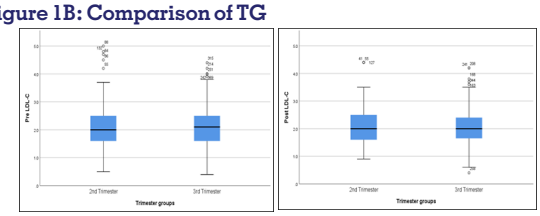

Figure 1C: Comparison of LDL-C

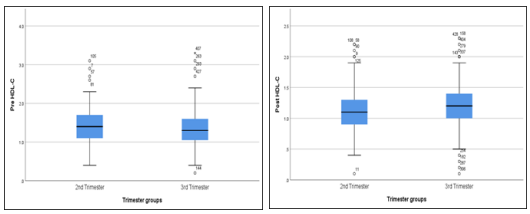

Figure 1D: Comparison of HDL-C

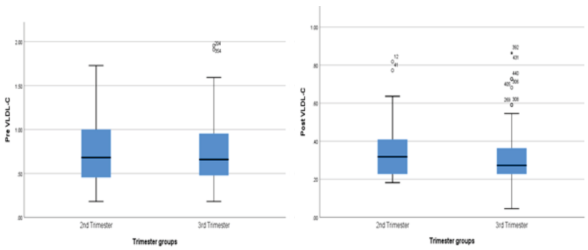

Figure 1E: Comparison of VLDL-C

Table 3 shows the difference between lipid levels in each trimester and postpartum respectively. There was a significant difference (p = 0.05) between the postpartum trimester two and three. VLDL-C also has a significant difference (p = 0.023) between the postpartum trimester two and three. HDL-C has an interesting non-significant but marginal increase in antepartum trimester two of 1.4 mmol/L compared to 1.3 mmol/L for trimester three. During postpartum, the picture changes trimester three with 1.2 mmol/L and trimester two with 1.1 mmol/L. The other parameters did not show any significant or interesting patterns.

Table 3: Comparison of lipid levels between the 2nd and 3rd trimester (Inter-Trimester)

TC	Median and IQR) (mmol/L)	Range of lipid values (mmol/L)	Min & max values (mmol/L)	P-value
2nd Trimester-antepartum	4.1 (1.3)	4.5	2.5- 7.0	0.392
3rd trimester-antepartum	4.1 (1.1)	5.4	2.3- 7.7	
2nd Trimester-postpartum	3.5 (0.9)	4.2	1.9-6.1	0.445
3rd trimester-postpartum	3.5 (1.0)	4.7	1.0- 5.7	
TG				
2nd trimester-antepartum	1.5 (1.2)	3.4	0.4- 3.8	0.646
3rd trimester-antepartum	1.5 (1.1)	3.9	0.4-4.3	
2nd trimester- postpartum	0.7 (0.4)	1.4	0.4-1.8	0.051*
3rd trimester- postpartum	0.6 (0.3)	1.8	0.1- 1.9	
LDL-C				
2nd trimester-antepartum	2.0 (0.9)	4.5	0.5- 5.0	0.966
3rd trimester-antepartum	2.1 (0.9)	4.0	0.4-4.4	
2nd trimester-postpartum	2.0 (0.9)	3.5	0.9- 4.4	0.469
3rd trimester-postpartum	2.0 (0.8)	3.8	0.4- 4.2	
HDL-C				
2nd trimester-antepartum	1.4 (0.6)	2.7	0.4- 3.1	0.228
3rd trimester-antepartum	1.3 (0.6)	3.1	0.2-3.3	
2nd trimester-postpartum	1.1 (0.4)	2.1	0.1- 2.2	0.252
3rd trimester-postpartum	1.2 (0.4)	2.2	0.1- 2.3	
VLDL-C				
2nd trimester-antepartum	0.7 (0.5)	1.5	0.2- 1.7	0.294
3rd trimester-antepartum	0.7 (0.5)	1.8	0.2-2.0	
2nd trimester-postpartum	0.3 (0.2)	0.6	0.2- 0.8	0.023*
3rd trimester-postpartum	0.3 (0.1)	0.8	0.05- 0.9	

* = Significant difference

Comparison of lipids between different age groups in each trimester is shown in Table 4 below.

Table 4: Comparison of age difference lipid levels within each trimester (Intra-trimester)

	Second trimester			Third trimester		
Parameter (mmol/L)	16-30 years	31-41 years	P-value	16-30 years	31-40 years	P-value
TC	4.1 (1.1)	4.4 (1.2)	0.12	4.1 (1.1)	4.2 (0.9)	0.61
TG	1.5 (1.3)	1.8 (1.3)	0.32	1.5 (1.1)	1.5 (1.1)	0.31
LDL-C	2.0 (0.9)	2.3 (1.1)	0.03*	2.0 (0.9)	2.2 (0.9)	0.43
HDL-C	1.4 (0.6)	1.3 (0.6)	0.66	1.3 (0.5)	1.2 (0.6)	0.70
VLDL-C	0.7 (0.6)	0.8 (0.6)	0.15	0.7 (0.5)	0.7 (0.5)	0.14

* = Significant difference

The younger participants had general lower lipid level and higher HDL-C. LDL-C was significantly (p-value= 0.03) lower in the younger (16-30 years) compared to the older 31-41-year group.

DISCUSSION

The study aimed to look at lipid profiles between trimesters in normal pregnancy as well as to assess if there are any age related differences within trimesters. There was a significant difference between the younger and older group in LDL-C levels within the second trimester (Table 4).

Participants in the first trimester were not available and this seem to be a challenge for some researchers as shown in Table 5. When participants were asked why they did not consult earlier, the major reason for non-consultation was that despite the presence of signs and symptoms individuals and couples wait until a period or two is missed and then a pregnancy test is done. After confirmation of pregnancy, the first antenatal consultation "Clinic Booking" is sought to prepare for delivery because most of them said "pregnancy is not a disease". By then, it will be the second or third trimester. Those (<5%) seeking antenatal consultation in the 1st trimester do it because of severe signs and symptoms, or because they might have underlying chronic conditions like diabetes or hypertension.

Elevated (almost 3x) TG levels reported in this study confirms reports from several studies that showed TG levels as high as three folds during pregnancy compared to non-pregnant women (Chiang et al., 1995; Parchwani & Patel, 2011). Conversely, Jamil et al reported that no significant difference was found in TG concentrations between pregnant women and non-pregnant controls (Jamil et al., 2013). The increase in TG's attributed to estrogen increase (Grimes & Wild, 2000; Phuse, 2018; Wiznitzer et al., 2009); increased hepatic lipase activity which leads to enhanced hepatic TG synthesis and the reduction in lipoprotein lipase activity (Kershaw & Flier, 2004). Parchwani and Patel, 2011 finding that lipid fractions decreased six weeks postpartum are similar to the current study except LDL-C concentrations that remained constant (Parchwani & Patel, 2011). However some studies reported increased LDL-C levels antepartum (Alemu, Abebe, Biadgo, Terefe, & Baynes, 2018; Idonije et al., 2011; Jamil et al., 2013; Phuse, 2018).

In contrast to other findings, the present study observed no significant difference between lipid levels in the 2nd and 3rd trimesters. Discordant results may be due to dietary and other lifestyle habits which differ among populations. Interestingly, Mankuta et al., 2010 demonstrated a slight decrease in TC level in the 1st trimester with a significant average increase towards the 2nd trimester, however a further increase between the 2nd and 3rd trimesters was observed (Mankuta et al., 2010).

Table 5 shows other studies that compared lipids between trimesters. The current study is one of the few that looked at both the antepartum and postpartum lipid levels. It also stands out as the largest with 446 number of participants. Table 5 also shows that lipid levels in the current study are generally lower than other groups demonstrating the importance of ethnic related reference ranges.

Table 5: Summary of findings from similar studies

Parameter in mg/dl	Trimester	Present study	Raghuram Pusukuru et al.,(Pusukuru et al., 2016)	Giuseppe Lippi et al.,(Lippi et al., 2007)	Abdelhai AT Jamil et al.,(Jamil et al., 2013)	Idonije O Blessing et al.,(Idonije et al., 2011)	Shital S Phuse et al.,(Phuse, 2018)
N		446	200	57	150	160	75
TC	1st Trimester	Not reported	Not reported	173±18	141.00±21.95	164.3±11.5	180.7
	2nd Trimester	166.28±38.67	214.59±18.16	243.0±53	162.50±24.01	191.4±12.8	255.1
	3rd Trimester	162.41±34.80	242.64±20.43	267.0±30	170.10±26.23	231.4±9.1	270
TG	1st Trimester	Not reported	Not reported	79±27	100.40±5608	180.9±21.1	150.6
	2nd Trimester	141.71±62.0	188.68±20.87	151.0±80	136.80±58.3	217.5±34.5	178.4
	3rd Trimester	141.71±62.0	216.78±20.09	245.0±73	175.90±70.93	211.1±26.3	198.8
HDL-C	1st Trimester	Not reported	Not reported	67±12	44.64±9.49	45.6±4.1	38.6
	2nd Trimester	54.14±19.34	49.12±6.14	83±19	58.84±19.27	44.4±6.4	32.8
	3rd Trimester	50.27±15.47	43.06±4.36	81±17	38.09±13.64	47.9±3.8	27.6
LDL-C	1st Trimester	Not reported	Not reported	90±17	61.79±17.01	82.4±12.9	118.5
	2nd Trimester	81.21±30.94	92.41±18.94	130±46	67.94±23.35	103.5±16.2	170.9
	3rd Trimester	81.21±27.07	137.81±13.45	136±33	76.62±26.95	141.2±8.6	195.7
VLDL-C	1st Trimester	Not reported	Not reported	Not reported	Not reported	Not reported	28.9
	2nd Trimester	28.34±12.40	28.22±7.66	Not reported	Not reported	Not reported	40.2
	3rd Trimester	28.34±12.40	36.27±6.72	Not reported	Not reported	Not reported	45.2

Adapted from (Pusukuru et al., 2016). Results from the current study were converted to mg/dL.

In conclusion, lipid concentrations increase during pregnancy across all ethnic groups with the Southern African population exhibiting the lowest increase. However, baseline concentrations are important to determine the rate and percentage increase. Older pregnant females demonstrated marginal increases. This requires further studies especially in African populations where multiparty is common. The study also demonstrated that consultation in the first trimester is not common.

Strength and Limitations of the study are as follows:

i) This is the largest study compared to others that looked at pregnancy related dyslipidemia.
ii) It is one of the few studies that compared antepartum and postpartum lipids in the same individuals.
iii) The only limitation is the absence of participants in the first trimester.

Several studies on pregnancy related dyslipidemia have demonstrated a general increase in both TC and TG. The increased levels of TC and TG in both normal and abnormal pregnancies require long term risk assessment especially in Africa where multiparty is common. We recommend that lipid and lipoprotein levels be offered as a baseline if possible before or early in pregnancy to facilitate determination of the percentage or acceleration rate increase. First trimester tests should be offered to patients with positive pregnancy tests whenever the request is made.

Author contributions

DM Tanyanyiwa was responsible for data collection and SM Pheeha was responsible for data analysis. Both authors were responsible for the concept and design of the study, along with writing the final article and its final approval.

Acknowledgement

We would like to thank Prof AD Marais of University of Cape Town Lipid clinic for his introduction to the study of lipids.

Conflict of Interest

The authors declare that they have no competing interests.

REFERENCES

1. Alemu, A., Abebe, M., Biadgo, B., Terefe, B., & Baynes, H. W. (2018). Biochemical Profiles of Pregnant and Non-pregnant Women Attending at the University of Gondar Hospital, Northwest Ethiopia: A Comparative Cross-sectional Study. Ethiopian Journal of Health Sciences, 28(3), 331–340. https://doi.org/10.4314/ejhs.v28i3.11
2. Barrett, H. L., Nitert, M. D., McIntyre, H. D., & Callaway, L. K. (2014). Normalizing metabolism in diabetic pregnancy: Is it time to target lipids? Diabetes Care, 37(5), 1484–1493. https://doi.org/10.2337/dc13-1934
3. Bassi, R., Kaur, M., & Sharma, S. (2011). Study of changes in lipid profile, lipid peroxidation and superoxide dismutase during normal pregnancy. Indian J Fundam Appl Life Sci, 1(3), 249–254. Retrieved from https://win4.fastwebhost.com:8443/sitepreview/http/cibtech.org/J LIFE SCIENCES/Vol 1 No 3/42 MS JLS-01-03-060 Roopam ...Changes....Lipid Profile.....pdf
4. Chiang, A.-N., Yang, M.-L., Hung, J.-H., Chou, P., Shyn, S.-K., & Ng, H.-T. (1995). Alterations of serum lipid levels and their biological relevances during and after pregnancy. Life Sciences, 56(26), 2367–2375. https://doi.org/10.1016/0024-3205(95)00230-4
5. Diareme, M., Karkalousos, P., Theodoropoulos, G., Strouzas, S., & Lazanas, N. (2009). Lipid profile of healthy women during normal pregnancy. Journal of Medical Biochemistry, 28(3), 152–160. https://doi.org/10.2478/v10011-009-0011-1
6. Enquobahrie, D. A., Williams, M. A., Butler, C. L., Frederick, I. O., Miller, R. S., & Luthy, D. A. (2004). Maternal plasma lipid concentrations in early pregnancy and risk of preeclampsia. American Journal of Hypertension, 17(7), 574–581. https://doi.org/10.1016/j.amjhyper.2004.03.666
7. Finer, L. B., & Zolna, M. R. (2014). Shifts in intended and unintended pregnancies in the United States, 2001-2008. American Journal of Public Health, 104(SUPPL. 1), 43–48. https://doi.org/10.2105/AJPH.2013.301416
8. Frantz, E., Menezes, H. S., Lange, K. C., Abegg, M. P., Correa, C. A., Zangalli, L., … Zettler, C. G. (2012). The effect of maternal hypercholesterolemia on the placenta and fetal arteries in rabbits. Acta Cirurgica Brasileira, 27(1), 7–12. https://doi.org/10.1590/s0102-86502012000100002
9. Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma,Without Use of the Preparative Ultracentrifuge. Clinical Chemistry, 18(6), 499–502. https://doi.org/10.1093/ajw/kwx146
10. Grimes, S. B., & Wild, R. (2000). Effect of Pregnancy on Lipid Metabolism and Lipoprotein Levels. Endotext. Retrieved from http:// www. ncbi. nlm.nih.gov/pubmed/29714937
11. Idonije, O. B., Festus, O. O., Eseigbe, A. M., Okhiai, O., Unuabonah, F., & Dike, M. (2011). Comparative study of lipid profile of normal pregnant women in the different trimesters Arch. Appl. SCi.Res, 3(3)(3), 528–532.
12. Jamil, A. A. T., Elsoni, B., Zaki, H. Y., Eldaim, N., Elbadawi, E., Ahmed, E. G., … Modawe, G. A. (2013). Assessment of Lipid Profile in Sudanese Pregnant Women, 1(1), 4–15. Retrieved from https://www.uniassignment.com/essay-samples/health/assessment-of-lipid-profile-in-sudanese-pregnant-women-health-essay.php
13. Jin, W. Y., Lin, S. L., Hou, R. L., Chen, X. Y., Han, T., Jin, Y., … Zhao, Z. Y. (2016). Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: A population-based study from China. BMC Pregnancy and Childbirth, 16(1), 1–9. https://doi.org/10.1186/s12884-016-0852-9
14. Kershaw, E. E., & Flier, J. S. (2004). Adipose tissue as an endocrine organ. In Journal of Clinical Endocrinology and Metabolism (Vol. 89, pp. 2548–2556). https://doi.org/10.1210/jc.2004-0395
15. Lippi, G., Albiero, A., Montagnana, M., Salvagno, G. L., Scevarolli, S., Franchi, M., & Guidi, G. C. (2007). Lipid and lipoprotein profile in physiological pregnancy. Clinical Laboratory, 53(3–4), 173–177.
16. Mankuta, D., Elami-Suzin, M., Elhayani, A., & Vinker, S. (2010). Lipid profile in consecutive pregnancies. Lipids in Health and Disease, 9, 9–12. https://doi.org/10.1186/1476-511X-9-58
17. Parchwani, D., & Patel, D. (2011). Status of lipid profile in pregnancy. National Journal of Medical Research, 1(1), 10–12. Retrieved from http://njmr.in/uploads/1-1_10-12.pdf
18. Phuse, S. S. (2018). Effective Study of Lipid Profile during Pregnancy. International Journal of Applied Biotechnology and Biochemistry, 2(4), 381–386.
19. Pusukuru, R., Shenoi, A. S., Kyada, P. K., Ghodke, B., Mehta, V., Bhuta, K., & Bhatia, A. (2016). Evaluation of lipid profile in second and third trimester of pregnancy. Journal of Clinical and Diagnostic Research, 10(3), QC12–QC16.

https://doi.org/10.7860/JCDR/2016/17598.7436
20. Sánchez-Vera, I., Bonet, B., Viana, M., Quintanar, A., Martín, M. D., Blanco, P., … Albi, M. (2007). Changes in plasma lipids and increased low-density lipoprotein susceptibility to oxidation in pregnancies complicated by gestational diabetes: consequences of obesity. Metabolism: Clinical and Experimental, 56(11), 1527–1533. https://doi.org/10.1016/ j.metabol. 2007.06.020
21. Savvidou, M., Nelson, S. M., Makgoba, M., Messow, C. M., Sattar, N., & Nicolaides, K. (2010). First-trimester prediction of gestational diabetes mellitus: Examining the potential of combining maternal characteristics and laboratory measures. Diabetes, 59(12), 3017–3022. https://doi.org/ 10.2337/db10-0688
22. Vrijkotte, T. G. M., Krukziener, N., Hutten, B. A., Vollebregt, K. C., Van Eijsden, M., & Twickler, M. B. (2012). Maternal lipid profile during early pregnancy and pregnancy complications and outcomes: The ABCD study. Journal of Clinical Endocrinology and Metabolism, 97(11), 3917–3925. https://doi.org/10.1210/ jc.2012-1295
23. Wiznitzer, A., Mayer, A., Novack, V., Sheiner, E., Gilutz, H., Malhotra, A., & Novack, L. (2009). Association of lipid levels during gestation with preeclampsia and gestational diabetes mellitus: a population-based study. American Journal of Obstetrics and Gynecology, 201(5), 482.e1-482.e8. https://doi.org/10.1016/j.ajog.2009.05.032