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Relation between maternal lipid profile and pregnancy complications and perinatal outcomes.

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ABSTRACT

Background: Pregnant experiences physiological changes in maternal lipid metabolism to support fetal growth and development. In some cases a maladaptation occurs and exceeds the physiological range and dyslipidemia is recognized, some pregnancies pacing without associated pregnancy alterations and in pregnancies pacing with pathologies.
Aim of the study: determine the relationship between maternal lipid profile and pregnancy and perinatal complications. Besides, determine the cut - of value of each lipid profile components for predicting maternal compilations.
Patient and Methods: 164 pregnant who attended the Obstetrics and Gynecology department in Suez Canal Authority Hospital in Ismailia city, throughout the period May 2018 – October 2019. Pregnant were assessed clinically, obstetrically, and tested for lipid profile during 2nd and 3rd Trimester, for detecting any maternal or neonatal complications.
Results: 28 pregnant developed maternal complications [GHTN (3.66%), Preeclampsia (2.44%), GDM (3.05%), IHCP (1.83%), PTL (4.27%), PTB (3.05%) and ROM (4.78 %)]. Lipid profile in complicated cases during 2nd/3rd trimester for TC, TG, LDL, and HDL were 189.3 ± 4.8/243.2 ± 4.8 mg/dl, 271.0 ± 8.4/251.2 ± 8. 4 mg/dl, 110. 8 ± 5.6/114.2 ± 5.6 mg/dl) and 60.4 ± 1.8/61.2 ± 1.9 mg/dl). We observed every mg/dl elevation in maternal 3rd-trimester TG concentration was associated with an increased risk of GDM, GHTN, preeclampsia, and IHCP. Every mg/dl increase in 3rd-trimester TG concentration was associated with an increased risk for SGA, LGA, and macrosomia.
Conclusion: maternal dyslipidemia is a risk factor and associated with the development and occurrence of maternal complications during pregnancy and affects neonatal outcomes.

Keywords: *dyslipidemia; gestational hypertension; gestational diabetes; cholestasis; macrosomia.*

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INTRODUCTION

Pregnant experiences physiological changes in maternal lipid metabolism to support fetal growth and development.[1] Maternal lipid metabolism varied during pregnancy and this condition was characterized by being progressive, increased with weeks of gestation.[2] There is adipose tissue expansion, and hepatic lipid synthesis increases and this physiological adaptation is associated with changes in Lipid profile during pregnancy.[3]

During normal pregnancy, there are increases in the blood concentration of TC, TG, LDL-C, and decreases in HDL-C.[4] Accumulation of lipids in maternal tissues and the development of maternal hyperlipidemia occur. In some cases, a maladaptation occurs and these levels increase over a physiological range, and dyslipidemia is recognized. This condition occurs in some pregnancies pacing without associated pregnancy alterations and in pregnancies pacing with pathologies as preeclampsia (PE) and GDM. [5]

Our goal was to find if there is a relationship between maternal lipid profile and pregnancy complications and perinatal outcomes.

PATIENT AND METHODS

A Prospective Observational Study was conducted on 164 pregnant who attended regular prenatal health care visits in the obstetrics clinic in Suez Canal Authority Hospital in Ismailia city, during the period May 2018 – October 2019.

Singleton pregnancy with gestational weeks 21–37 of 18 – 40 years old pregnant who naturally conceived was participated in this study. Pregnant with multiple pregnancies, had metabolic diseases or inherited diseases before pregnancy, Infection during early pregnancy, or conceived with ART were excluded.

All participated were requested to complete an extensive medical history and physical examination. Then, each Pregnant was assessed clinically, obstetrically, and tested for lipid profile during the period 21–24 weeks and repeated during the period 33–37 weeks.

All participants were antenatally followed-up from recruitment to delivery. Her medical status and occurrence of complication with pregnancy were collected from medical records .

In the present study, we tested an association between maternal lipid profile status of the pregnant mother and the possibility of complications for her or her fetus, or the occurrence of problems during or after childbirth. For maternal complications, GDM, GHTN, preeclampsia, ICP, PTB, and ROM were selected. For fetal conditions, SGA, LGA, and macrosomia were recorded. Regarding maternal outcome [delivery mode, Obstetric trauma (as Perineal injury (2nd -4th degree) or cervical injury], Obstructed labor and shifted to perfume CS delivery and occurrence of PPH. Information of newborn sex, birth weight, Apgar scores, and perinatal outcomes were recorded upon delivery .

Venous blood samples were taken from participants after overnight fasting. The blood samples were collected in a 3.5 ml plan tube for serum preparation. One ml aliquots of serum sample were obtained by centrifugation (3500 rpm for 10 min at 25 - 27 °C) and were store at - 20 °C until analysis. All the lipid measurements were performed on an automatic biochemical analyzer ILab Aries .®

Statistical analysis was performed using Microsoft Excel v2016 and SPSS v21. Qualitative data presented as number and percentage while quantitative data presented as Mean ± sd. The student's t-test was used for quantitative variables and chi - square used for qualitative variables. Correlation coefficients and regression analysis used when appropriate. P-value of <0.05 considered as statistically significant.

RESULTS

In table 1, the average Weight gain of the pregnant in 2nd-trimester, was 3.7 ± 0.65 kg, while in 3rd-trimester it was 4.68 ± 0.57 kg. During the 2nd-trimester assessment, 5 women developed maternal complications. In the 3rd-trimester assessment, 33 more women developed maternal complications as presented.

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		2nd-trimester		3rd-trimester	
		Range	Mean ± sd	Range	Mean ± sd
	Gestational age	26 - 28	26 ± 1.32	32 - 35	33 ± 1.68
	Maternal Weight	68 - 91	70 ± 1.87	73 - 105	79 ± 2.41
	Weight gain	3 - 4	3.7 ± 0.65	4.5 - 6	4.68 ± 0.57
		Freq.	%	Freq.	%
Complications	GHTN	1	0.61%	6	3.66%
	Pre-eclampsia	0	0.00%	4	2.44%
	GDM	2	1.22%	5	3.05%
	IHCP	1	0.61%	3	1.83%
	PTL	1	0.61%	7	4.27%
	PTB	0	0.00%	5	3.05%
	ROM	0	0.00%	8	4.78 %

Table 1. Clinical data of the participants.

In Table 2, the average TC level during 3rd-trimester was highest in GHTN than in other complications. We observed that the level of HDL-C was decreased in patient s with IHCP. There are statistically significant difference between values of each lipid profile between 2nd and 3rd-trimester v occurrence of GHTN, GDM, IHCP, and PTL (P= 0.00, 0.00, 0.02, and 0.00 respectively)).

In Table 3, Multivariate analysis shows that every mg/dl increase in 3rd-trimester TG concentration was associated with an increased risk for SGA (AOR= 1.12), LGA (AOR= 1.21), and macrosomia (AOR= 1.21). On contrary, every mg/dl increase in 3rd-trimester TG concentration was associated with decreased risk for the Low Apgar score (AOR= 0.523).

Table 4 shows a significant association between the level of maternal TG and occurrence of SGA, LGA, Macrosomia Low Apgar score (P= 0.046, 0.025, 0.024 and 0.091 respectively).

In table 5, TG had a strong predictive power for GHNT/PE and SGA at a cut-off point of 309.21 mg/dl. Also, the cut-off point of 291.45 and 254.32 for TC had higher sensitivity for predicting GDM and GHTN respectively. On the other side, the optimal cut-off

points for 3rd-trimester HDL-C in identifying IHCP and SGA was 52.42 mg/dl and 88.2 mg/dl respectively. The optimal cut-off point 113.12 mg/dl for LDL-C has a sensitivity of 73.3% for predicting LGA.

		GHTN	PE	GDM	IHCP	PTL/PTB	ROM
2nd- trimester	TC	201.6		232.52 ±4.4	182.3	232.52	
	TG	225.1		216.99 ±3.3	188.5	216.9	
	LDL-C	97.5		95.13 ± 1.9	89.4	95.13	
	HDL-C	60.5		64.58 ± 2.5	55.3	64.58	
3rd-trimester	TC	211.3 ± 5.3	189.9 ± 3.43	191.82 ± 4.9	187.6 ± 3.6	181.24 ± 3.7	179.82 ± 4.9
	TG	242.2 ± 6.2	260.4 ± 5.27	271.02 ± 7.7	211.3 ± 4.1	171.02 ± 4.8	187.42 ± 6.9
	LDL-C	101.2 ± 3.5	109.3 ± 4.21	110.98 ± 5.4	98.6 ± 3.1	110.98 ± 5.8	110.98 ± 5.6
	HDL-C	57.6 ± 2.7	60.42 ± 1.84	63.60 ± 1.7	51.3 ± 2.3	58.60 ± 1.4	57.68 ± 1.7
P-value		0.00*		0.00*	0.02*	0.00*	

Table 2. Lipid profile parameters in complicated pregnancies.

		Maternal complications					
		GDM	GHTN	PE	IHCP	PTL	ROM
TC	AOR	0.84	1.17	0.99	1.20	1.37	0.52
	CI	0.68 - 1.04	1.04 - 1.61	0.64 - 1.54	0.97 - 1.49	1.06 - 1.42	0.13 - 0.58
	P-value	0.009	0.00	0001	0.096	0.142	0.131
TG	AOR	1.37	1.10	1.50	1.28	0.52	0.84
	CI	1.181 - .58	0.89 - 1.52	1.16 - 1.93	1.09 - 1.51	0.71 - 1.63	0.67 - 1.48
	P-value	0.00	0.00	0.002	0.002	0.085	0.071
HDL-C	AOR	0.52	0.62	0.65	0.59	0.48	1.37
	CI	0.38 - 1.72	0.31 - 1.28	0.33 - 1.31	0.64 - 1.16	1.27 - 1.89	0.99 - 1.32
	P-value	0.00	0.00	0.228	0.003	0.061	0.058
LDL-C	AOR	1.27	1.22	0.48	0.56	1.37	1.37
	CI	0.73 - 1.58	0.57 - 1.61	0.10 - 2.26	0.25 - 1.22	0.76 - 1.23	0.68 - 1.04
	P-value	0.001	0.00	0.352	0.141	0.103	0.121

Table 3. Associations between maternal 3rd-trimester lipid profile and maternal complications.

		Neonatal outcome					
		PTB	SGA	LGA	Macrosomia	Low Apgar score	NICU admission
TC	AOR	0.80	1.12	1.21	0.99	0.523	0.427
	CI	0.57 - 1.11	0.80 - 1.56	0.86 - 1.32	0.81 - 1.21	0.433 - 0.62	0.77 - 1.38
	P-value	0.18	0.062	0.051	0.103	0.324	0.105
TG	AOR	1.04	0.63	1.13	1.19	0.79	0.46
	CI	0.77 - 1.38	0.40 - 0.99	1.02 - 1.26	1.02 - 1.39	0.71 - 1.89	0.57 - 1.11
	P-value	0.218	0.046	0.025	0.024	0.091	0.081
HDL-C	AOR	0.83	1.16	0.93	0.93	1.12	3.15
	CI	0.52 - 1.32	0.71 - 1.89	0.78 - 1.11	0.69 - 1.25	0.77 - 1.38	0.73 - 1.89
	P-value	0.43	0.565	0.418	0.621	0.281	0.068
LDL-C	AOR	1.05	3.15	0.79	0.46	0.99	1.04
	CI	0.37 - 3.00	1.15 - 8.65	0.52 - 1.21	0.22 - 0.94	0.57 - 1.11	0.87 - 1.38
	P-value	0.131	0.026	0.281	0.034	0.112	0.221

Table 4. Associations between maternal 3rd-trimester lipid profile and neonatal outcome.

Outcomes	Cut-off point (mg/dl)	AUC	Confidence interval 95 %		Sensitivity (%)	Specificity (%)
			Min	Max		
TC						
GHNT/PE	254.32	0.713	0.538	0.788	82.3	64.2
SGA	164.23	0.684	0.557	0.715	78.4	68.3
TG						
GDM	242.85	0.708	0.572	0.742	62.1	47.8
GHNT/PE	259.21	0.713	0.538	0.788	82.3	64.2
LGA	261.21	0.713	0.538	0.788	82.3	64.2
HDL-C						
GHNT/PE	72.54	0.795	0.532	0.645	74.3	65.4
IHCP	52.42	0.842	0.677	0.911	88.2	74.4
SGA	60.45	0.647	0.531	0.798	62.1	73.1
LDL-C						
GHNT/PE	109.76	0.778	0.584	0.765	64.2	65.4
LGA	113.12	0.737	0.517	0.684	73.3	54.3

Table 5. Optimal cut-off points of maternal 3rd-trimester lipids for predicting pregnancy complications and perinatal outcomes.

DISCUSSION

During early pregnancy, there is an increase in body fat accumulation, associated with both hyperphagia and increased lipogenesis which is necessary as an energy store to fulfill maternal and fetal metabolic needs.[6]

TG rises disproportionately in comparison to other lipid parameters reaching 2 - 4 times pre-pregnancy levels by the 3rd-trimester, which fall precipitously to pre-pregnancy levels after delivery. [7]

In our study, the serum level of TC, TG and LDL-C increased with increasing gestational age and peaked before delivery, while serum level of HDL-C dropped a little in the 2nd-trimester with more decrease in the 3rd-trimester. Our results of our study are consistent with other studies. [8, 9, 10]

Many hypotheses were built to explain the state of dyslipidemia and changes in the lipids metabolism during pregnancy. The rise in plasma lipids influenced by the placental hormones especially in the 3rd-trimester. [11] Estrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL, while progesterone oppose the action estrogens on lipoprotein metabolism. [4]

During pregnancy the hepatic lipase activity and reduced lipoprotein lipase activity increased resulting in increase in circulating TGs. [12]

In our study, we observe a significant difference in the mean values of the lipid profile between complicated and uncomplicated pregnancies. This makes it sense that a state of dyslipidemia may provoke the occurrence of maternal complications.

In our study, the serum level of maternal TC, TG and LDL-C, were increased in GHNT when compared to normotensive pregnancy, which is statistically significant (P= 0.012, 0.00, 0.00 respectively). Also, the level of HDL-C in women with GHNT was lower than normotensive women. We observe that the serum level of HDL was lower more in cases with PE (P= 0.010).

Our results are in agreement with the study of Shen, [14] White, [15] Vani, [16] Nayan, [17] and Singh, [18] et al.

Previous studies shown that plasma lipids rise significantly in preeclampsia above the levels of normal pregnancies. [19] An association between the atherogenic lipid profile of gestation and the endothelial cell dysfunction during preeclampsia has been described. [20]

We observed every mg/dl elevation in maternal 3rd-trimester TG concentration was associated with an increased risk of GDM, GHTN, preeclampsia, and IHPC. Also, every unit increase in HDL-C was associated with an increased risk of IHCP, GDM and GHNT. Besides, every unit increase in LDL-C reduced the risk of GDM and GHNT. Moreover, every unit increase in TC reduced the risk of GHTN. Our results were in line with the study of Jin et al. [21]

We observed that high levels of TGs during pregnancy were associated with an increased risk of GDM. During 2nd and 3rd trimesters maternal fuel adjustments occur which leads to the sparing of glucose for the fetus leading to GDM. Freinkel had described these changes as “accelerated starvation”, and “facilitated anabolism”. [22]

Women with GDM characterized by a predominant insulin sensitivity defect had significantly higher triglycerides, lower HDL-C, and higher NEFA when compared with women with normal glucose test. [23]

There was a significant association between the level of maternal TG and occurrence of SGA, LGA,

Macrosomia and Low Apgar score. Also, there is a significant association between the level of maternal HDL-C and the occurrence of SGA and Macrosomia. There was no significant association between 3rd-trimester TC and LDL-C with the occurrence of neonatal complications (PTB, SGA, LGA, Macrosomia, Low Apgar score, NICU admission). Jin et al. [20] observed that every unit elevation in 3rd-trimester TG concentration was associated with increased risk for LGA, macrosomia and decreased risk for SGA.

Several previous studies have investigated associations between maternal lipid levels during pregnancy and risk for preterm birth. [24, 25, 26]

Hyperlipidemia is considered as an instigator of inflammation and oxidative stress which are a risk factor for PTB. Previous studies indicated an increased risk of PTB associated with maternal dyslipidemia. [27]

CONCLUSION

Maternal dyslipidemia is a risk factor and associated with the development and occurrence of maternal complications during pregnancy and affects the neonatal outcome. Testing lipid profile during 2nd and 3rd trimesters can early predict certain disorders associated with pregnancy.

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