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Biochemical changes in the serum of pregnant women in the third trimester

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Abstract

The current study was designed to verify the implication of pregnancy in the induction of serum lipid and lipoprotein changes in pregnant women . To achieve this aim ,50 pregnants and 50 age matched healthy non pregnant women (control group) were enrolled. Serum Iron, Hb, cholesterol , TIBC ,triglyceride, HDL – cholesterol , LDL- cholesterol ,VLDL- triglyceride concentration were measured in all subjects. Significant (P<0.0) increases were found in the levels of serum TIBC, cholesterol, triglyceride, LDL and VLDL in the pregnant women of third trimesters when compared with those of the control group. HDL levels were found to be significantly (P<0.0) elevated in pergnants of the third trimesters with those of the control group. Significant (P<0.0) decreases were found in the levels of serum iron and Hb in the pregnant women when compared with control group.

التغيرات الكيميائية الحياتية في مصل النساء المرحلة الثالثة من الحمل

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المستخلص

تم تصميم الدراسة الحالية للتحقق من دور الحمل في حث تغيرات مستويات Hb, TIBC, Iron والبروتينات الدهنية المصلية لدى نساء المرحلة الثالثة من الحمل شملت الدراسة 50 امرأة حامل و50 امرأة طبيعية ليست حاملا وبأعمار مقاربة للنساء الحوامل ,استعملت بوصفها مجموعة سيطرة . تم تقدير تراكيز Iron, Hb, cholesterol , TIBC ,triglyceride, HDL – cholesterol , LDL- cholesterol ,VLDL- triglyceride في امصال النساء الحوامل ومجموعة السيطرة . ولوحظت زيادة معنوية (P<0.0) في تراكيز المصلية TIBC ,الكوليستيرول والكلسريدات الثلاثية ,البروتينات الدهنية ذات الكثافة الواطئة وذات الواطئة جدا, لدى الحوامل في ثلثي الحمل , عند مقارنتها مع مثيلاتها في مجموعة السيطرة , بينما بينت مستويات البروتينات الدهنية ذات الكثافة العالية زيادة معنوية (P<0.0) لدى الحوامل في ثلث مدة الحمل. أشارت الدراسة إلى نقصان معنوي(P<0.0) لمستويات الحديد وTIBC في النساء الحوامل مقارنتا مع مجموعة السيطرة.

Introduction

The anatomical, physiological , and biochemical adaptation to pregnancy are profound. Many of these changes begin soon after fertilization and continue through gestation(1). Most of these remarkable adaptations occur in response to physiological stimuli provided by the fetus (2). In addition , maternal adjustments in pregnancy are designed to support the requirements of fetal homeostasis and growth without unduly jeopardizing maternal well being the sheer physical presence of the enlarging uterus impinges on diverse maternal functions, including , circulation ,respiration(3). The uterus during pregnancy undergoes remarkable growth due to hypertrophy of muscle fibers. Its weight increases from 70 g in the non pregnant state to about 1100 g at term (4). The enormous growth of the myometrium during pregnancy is caused by two factors-hormonal stimulation and distenstion(5). During early pregnancy the embryo dose not fill the uterine cavity and distension has no influence at this stage. An identical uterine enlargement occurs in cases of ectopic pregnancy when the embryo is outside the uterus. The growth is brought about by the action of oestrogen and progesterone. Later on, as the fetus and placenta become larger, the distension of the uterus provides a further stimulus to growth (6). The placental is essentially a fetal organ; it is the only means of transfer of anabolites and catabolites and, as such , is the main interface between the fetus and the outside world. It secretes large amounts of chorionic gonodotrophin, oestrogen and progesterone in large amounts, but also secrets other hormone which play an essential part in the maintenance of the deciduas and the growth of the uterus and breasts(2,7). Maternal metabolism must satisfy the demands of the developing fetus in addition to the energy requirements of the mother . There are many changes in lipid metabolism during pregnancy; The total lipid requirements being 3.5 Kg , Fat is a major nutrient for fetal growth and energy. It has been shown that storage of fat occurs primarily during mid pregnancy . This fat is deposited mostly in central rather than peripheral sites (7) During the third half of pregnancy , however, probably as a result of rising human placental lactogen , lipolysisis augmented , and the plasma concentration of free fatty acids after an overnight fast is elevated. The free fatty acids act as substrates for maternal energy metabolism , whereas glucose and amino acids cross the placenta to the fetus. In the humoral milieu of the third half of the pregnancy , the increased free fatty acids lead to keton body formation . Pregnancy is thus associated with an increased risk of ketoacidosis , especially after prolonged fasting.(8,9).The latter is thought to be a storage pool of metabolic fuel to sustain the fetus during periods of starvation or inadequate nutrition (10). As a consequence, the maternal lipid metabolism is specifically altered during pregnancy. Cholesterol increase moderately, whereas serum triglycerides levels rise markedly(11,12). Most of the cholesterol in the pregnant is synthesized by the body and some has dietary origin(13). Cholesterol plays a central role in many biochemical processes. During pregnancy cholesterol level is generally increases (13,14).Cholesterol is required to build and maintain membranes ; function of cholesterol is explain by Olson , it regulates membrane fluidity over a wide range of temperatures The hydroxyl group on cholesterol interacts with the phosphate head of the membrane , while the bulky steroid and the hydrocarbon chain is embedded in the membrane .(15) Triglyceride plays an important role in metabolism as energy sources and transporters of dietary fat, they contain more than twice as much energy (9 kcal/gm) as carbohydrates and proteins ,during pregnancy as expected, significant increases in total Triglyceride were observed with advancing gestation (14,15). This could further escalate the cycle by increasing

circulating peroxide levels(10,11).High amounts of triglycerides are not only found in the very low density lipoprotein (VLDL) fraction , but in all lipoprotein fractions. (LDL and HDL) during the gestation (16). The abundance of VLDL triglycerides drives an accelerated transfer of triglycerides to lipoproteins of higher density by the cholesteryl ester transfer protein (CETP)(17). LDL particles during gestation become enriched in triglycerides as well . However, in contrast to HDL particles , LDL particles have been reported to become smaller and denser (18). Siedel and Gomez (18) , cited some evidence that progesterone may act to reset a lipostat in the Hypothalamus , and at the end of pregnancy the lipostat returns to its previous non pregnant level and the added fat is lost. After delivery, the concentration of the these lipids, lipoproteins, and apolipoproteins decrease at different rates. Lactation increases the rate of decrease of many of these compounds(17,18). Iron is an essential component of hemoglobin, the oxygen-carrying pigment in the blood. Iron is normally obtained through the food diet and by recycling iron from old red blood cells and in the absence of the required iron blood concentrations, blood cannot carry oxygen effectively and hence normal functioning of every cell in the body will be affected. It is estimated that a median amount of 840-1210 mg of iron needs to be absorbed over the course of the pregnancy.1 The greatest need for increased iron in take occurs in the second half of pregnancy. When the iron needs of pregnancy are not met, maternal hemoglobin falls below 11 g/dL. When the hemoglobin level is below 10 mg/dl (hematocrit under 33%), iron deficiency is suspected.2 Many women begin pregnancy in a slightly anemic state. In pregnancy, mild anemia can rapidly become more severe; therefore, it needs immediate treatment. Iron deficiency anemia is the most common medical complication of pregnancy, primarily because of expansion of serum volume without normal expansion of maternal hemoglobin mass.3 Women with poor diet histories, frequent conceptions, or records of prior iron depletion are particularly at risk. Woman's nutritional status prior to and during pregnancy can significantly influence her own health and that of her unborn child(19). The study include measurements of the biochemical changes in, Iron, TIBC, Cholesterol ,TG,LDL,HDL,VLDL ,in serum and Hb of pregnant women at third trimester and non- pregnant.

Materials and Methods

This study was conducted at the Tikrit teaching hospital .All measurement were during the period (2/2/2010 to 16/5/2010). This study was conducted on 50 pregnant women at third trimester fasting for 12 hours and 50 non-pregnant as control group. Some of blood used directly before separated to measured hemoglobin and the other parts were placed in plane tube (no anti coagulant) left for (15min) at room temperature, then centrifuged (at 2500 round /min for 10 min)to get the serum ,which is stored at(-20^0c)unless used immediately. Iron and TIBC colorimeter method was done to assess using kit TI 1010 of randox companyU.K. Iron, bound to Transferrin, is released in an acidic medium and the Ferric ions are reduced to Ferrous ions. The Fe (II) ions react with Ferrozine to form a violet coloured complex. Intensity of the complex formed is directly proportional to the amount of Iron present in the sample. For TIBC, the serum is treated with excess of Fe (II) to saturate the iron binding sites on transferrin. The excess Fe (II) is adsorbed and precipitated and the Iron content in the supernatant is measured to give the TIBC(18). Hemoglobin (Hb) was measured by using capillary tube and instrument (MICRO- HAEMATOCRIT CENTRIFUGE, HAWKSLEI., ENGLAND). Cholesterol was measured by (cholesterol Enzymatic colorimetric method kit –LOT (12328E), LiNEAR Chemical

,SPAIN. Cholesterol esterase ,cholesterol oxidase and peroxidase in the presence of the former the mixture of phenol and 4-aminoantipyrine are condensed by hydrogen peroxide to form a red- violet quinoneimine dye as indicator. Triglyceride was measured by(Triglyceride Enzymatic colorimetric method kit –LOT(12328E) , LiNEAR Chemical ,SPAIN. Triglyceride hydrolysis to glycerol and fatty acids ,the glycerol is phosphorylated by adinosintriphosphate (ATP) in presence of glycerolkinase to form (G-3-P) and (ADP) . G-3-P is oxidized by glycerophosphate oxidase to form dihydroxyacetone phosphate and hydrogen peroxide red chromogen is produced by the peroxidase. Statistical analysis Students ,tests were performed in the statistical package computer program for social sciences(Spss computer program).All results are expressed in the form of mean values ± standard deviation (SD), with statistical significance differences at probability less than ($P<0.05$).

- LDL,VLDL and chylomicron fraction were precipitated quantitatively by the addition of phophotungestic acid in the presence of magnesium ion.

VLDL-triglyceride concentration was determined by dividing triglycerides value on 5.

VIDL-triglyceride=triglyceride concentration/5
LDL cholesterol –total cholesterol –(VLDL triglyceride + HDL- cholesterol).

Instruments

- spectrophotometer (ECCIL-CF1011).
- centrifuge (Beckman) UK.
- Bathroom (memmert)USA.

Results and Discussions

Table (1) indicateds that there is a significant decrease in both Hb and iron levels during third trimester of pregnancy compared with the control group this is agreement with (19,20,21).The reason for that is the case of anemia which occurred in pregnant women who need excess of iron to fill full the requirements of fetus, moreover , the production of erythrocytes increases the availability of essential nutrients that the fetus need (22). The volume of pregnant blood increases by 50%compared to non-pregnant women because of these change during pregnancy .(23) This leads of dilute the blood which decreases the Concentration of Hb during the 25th week and 30th week of pregnancy (24-26). Table(1) also shows a significant increase ($P<0.05$) of TIBC of pregnant compared to non- pregnant women (Piechota) proposes that the rise in TIBC of serum serves the useful purpose of enhancing mobilization of iron from maternal stores thus enabling easier transport of iron to the fetus. This study showed also a significant increases of cholesterol compared to control ,this is in agreement with (27-29). During the course of normal pregnancy, serum triglyceride and cholesterol concentrations rise and as pregnancy progresses both become normal. Hormonal variations during pregnancy affect lipid metabolism.(8) The endogenous female sex hormones have significant effect on serum lipids.(13,24) During pregnancy, there is an increase in the hepatic lipase activity and decrease in lipoprotein lipase activity.(5,22) Hepatic lipase is responsible for the increased synthesis of the triglycerides at the hepatic level, whereas the decreased activity of lipoprotein lipase is responsible for the decreased catabolism at the adipose tissue level, the net effect of which will be an increase in circulating triglycerides and the second step of uptake of the remnant chylomicrons by the liver is delayed so it leads to accumulation of triglycerides in plasma as observed during present study shown in Table (1). The data of all pregnant and control women were evaluated for the difference of serum cholesterol , triglycerides, VLDL ,HDL-cholesterol, and LDL- cholesterol levels by using the student (r) test. Significant ($P<0.05$)increase was found in the levels of

cholesterol, triglycerides, VLDL-triglycerides , and LDL- cholesterol in pregnant women of third trimester when compared with those of the control subjects. HDL-cholesterol level was found to be significant ($P<0.05$)elevated in pergnants of third trimester when compared with those of the control group(Table 1).Several metabolic changes are commonly taken place during the period of pregnancy (9).Hyperlipidemia is one of these changes, it has been reported in many investigation(27).These investigation have indicated varied result , Some of them have shown elevation of serum cholesterol and triglyceride levels by approximately 20-25%and 200-300% respectively(28).The mechanism whereby pregnancy induces hyperlipidaemia has not been fully elucidated. The hormonal changes during the course of gestation must be considered as a major directing factor for the disorder of the lipidemic status . During pregnancy serum (E2), progesterone ,human placental lactogen and insulin levels are elevated (29). Some hormone have dual actions in regard to cholesterol and triglyceride levels during period of pregnancy (30).Thus the complementary and opposing actions of the individual gestational hormones would be expected to lead to the pronounced alterations in lipoprotein metabolism as gestation progresses(2,15).Generally , estrogen increases the concentration of HDL- cholesterol through direct stimulation of apolipoprotein AI and AII production and indirectly through the reducing of the catabolism of HDL2 to HDL3 by hepatic lipase . The production of LDL and apolipoprotein B is stimulated by estrogens, but the clearance of LDL is ehanced owing to the enhancement of hepatic LDL receptors (11,31).These aspects may explain the estrogen cadioprotective effects (31). Eestrogen stimulate the hepatic production of very low density lipoprotein and inhibit the hepatic and adipose tissue lipoprotein lipases(12). Thus , they will elevate plasma level of triglycerides. On the other hand estrogen action are complemented and opposed by the other gestational hormones , and in late pregnancy by increasing the insulin resistance(31). Table (2) indicated that there was a correlations between iron and Hb ($r = 0.41$)this was in agreement with (20), Hb and TIBC ($r = 0.72$) and cholesterol and TG (0.49*) this was in agreement with(29,30)

Table (1):- The mean biochemical parameter both in serum women of third trimester pregnant and non-pregnant women.

parameter	Third trimester Mean ±SD	Control Mean ±SD
Hb	9±2.0 g/dl	11.9±1.9 g/dl
Iron	72±11.4 ug/dl	108±21.0 ug/dl
TIBC	300±39.6 ug/dl	287±30.2 ug/dl
Cholesterol	149±20.1 mg/dl	110±19.8 mg/dl
Triglyceride	235±54.2 mg/dl	184±24.9 mg/dl
HDL-C	50±9.1mgl/dl	33±7.3 mg/dl
LDL-C	123±22.0 mg/dl	94±30.0 mg/dl
VLDL-Triglyceride	42±8.5 mg/dl	20±4.9 mg/dl

Table(2):- Correlation between biochemical at the third trimester pregnant women.

	Hb	Iron	TIBC	Cholesterol	Triglyceride	HDL-c	LDL-c	VLDL-Triglyceride
Hb								
Iron	0.41*							
TIBC	0.72**	0.02						
Cholesterol	0.38	0.22	0.09					
Triglyceride	0.163	0.07	0.043	0.49*				
HDL-C	0.22	0.07	0.01	0.32	0.01			
LDL-C	0.03	0.012	0.11	0.41	0.025	0.03		
VLDL-Triglyceride	0.008	0.041	0.09	0.32	0.56	0.007	0.00	0.021

* = strong correlation . ** = correlation .

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