Role of cholesterol in the body health essay

Health & Medicine

Cholesterol is a lipid composed of a hydroxyl group, tetracycline rings and a hydrocarbon chain (1). Cholesterol is a precursor in the synthesis of Vitamin D and steroid hormones – cortisol, aldesterone, progesterone, oestrogen and their derivatives (2, 3). It is a structural component of the plasma cell membranes; regulating membrane fluidity over a wide range of temperature. The hydroxyl group on the cholesterol molecule interacts with the phosphate groups of the membrane phospholipids, while the carboxyl groups interact with the carboxyl groups of the phospholipids (4). This increases membrane packing at the same time reducing membrane fluidity. Cholesterol reduces the permeability of the membrane to neutral solutes, protons and sodium ions (5). In the cell membrane, cholesterol is important for clathrin-dependent endocytosis (6). This is particularly important in phagocytosis by cells of the immune system. Cholesterol is also important in cell signaling by aiding in the formation of lipid rafts. Lipid rafts bring receptor proteins into close contact with high concentrations of secondary messenger molecules such as cyclic adenosine monophosphate (cAMP). This makes cholesterol important in the propagation of signaling cascades (7-9). Cholesterol is important in the activation and propagation of hedgehog signaling (10). Sonic hedgehog (SHH) is responsible for development and patterning of the central nervous system (CNS) (11). This is particularly important in a foetus for development of the brain and spinal cord.

1. 2 Biosynthesis

Cholesterol is synthesised from acetyl-coA and this occurs mostly in hepatic cells of the liver although all cells of the body are capable of synthesizing it. Biosynthesis is regulated by homeostatic mechanisms which involve

enzymes such as sterol regulatory element binding protein (SREBP) and 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) (12, 13). SREBP responds to low intracellular cholesterol levels by up-regulating expression of lipogenic proteins such as HMGCR and low density lipoprotein receptor (LDLR) which promotes uptake of cholesterol into cells (13).

1. 3 Metabolism

Cholesterol is oxidized in the liver and conjugated to glycine, glucoronic acid and sulfate to form bile salts; a component of bile (14, 15). Bile is important for emulsification of dietary fats before digestion by lipases. If cholesterol is highly concentrated in the bile it leads to the formation of gall stones (16).

1. 4Plasma transportation

Cholesterol is not soluble in blood hence the need for it to be coupled to lipoproteins for transportation (1). There are six major sub-fractions of lipoproteins which are: chylomicrons, very low density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) (17-22). The different lipoproteins contain apolipoproteins which serve as ligands for cell receptors. Chylomicrons are the least dense of all the lipoproteins. They carry cholesterol from the gut to the muscles and other tissues that use fatty acids as a source of energy or for fat production. Chylomicrons not utilized by the muscle are absorbed by the liver. VLDL are synthesized by the liver and contains cholesterol not required for bile salts production (17-22). IDL are taken up by the LDL receptors on the liver surfaces or continue to lose triacylglycerols in the blood circulation until they form LDL (18; 19). LDL transport cholesterol from the liver to other cells of the body that have need of extracellular amounts.

High levels of LDL result in deposition of cholesterol in arteries (atherosclerosis) which can result in coronary heart disease (19). HDL is responsible for reverse cholesterol transport (RCT) that is transport of excess cholesterol from the cells and circulation to back to the liver (20-22). High levels of HDL correlate with good cardiac health (17-22). HDL and LDL are the two major fractions of lipoprotein cholesterol.

1. 5 Cholesterol and pregnancy

During pregnancy, maternal physiological and hormonal changes occur that are concerned primarily with the nutrition of the growing foetus (23). One of the changes is the increase in the levels of total cholesterol in the blood (24). Maternal LDL cholesterol is important for the synthesis of placental progesterone (25). Structural cholesterol in plasma membranes plays a critical role in implantation and the formation of blood vessels in the utero-placental area (25-27). Placental cholesterol levels changes affect transportation of molecules across the placenta and this varies with the gestational period (25-27). HDL cholesterol is involved in maintaining a balance in the placental cholesterol levels (20-27). Maternal cholesterol is thought to be transported to the foetus for development of fetal and placental tissue (25-27). Studies have established that total cholesterol levels rise with increasing gestational age (20-28). This hypercholesteromia (high blood cholesterol levels) has been attributed to the hormonal effects of progesterone and oestrogen (17; 18; 23). The daily production of progesterone increases thirtyfold, while that of oestrogen increases tenfold during pregnancy (29). Progesterone increases plasma levels of LDL cholesterol and total cholesterol while lowering HDL-cholesterol but

oestrogen has an opposite effect (20-29). Various studies have shown the attribute of diet to this hypercholesteromia during pregnancy to be insignificant (27-29). Some studies have documented changes in maternal total and the fractions of cholesterol (20-28). HDL cholesterol increases from the second semester of pregnancy and remains high throughout the rest of pregnancy in response to oestrogen levels. Maternal LDL and total cholesterol increase progressively from the second semester of pregnancy and even remains high after delivery (24-28). In the first trimester of pregnancy, cholesterol levels are thought not to change but several studies have shown that they actually fall when compared to pre-pregnancy levels (17; 18; 23). Total cholesterol levels rise in the second and peak in the third trimester (24-28). The placenta is an anatomical barrier that prevents contact of the maternal and fetal blood and is composed mainly of multinucleated trophoblast (25). It is thought that maternal cholesterol is able to cross the placenta and enter fetal circulation and is taken up in the form of lipoproteins by the trophoblast on the maternal side by both receptor mediated and receptor independent mechanisms (26; 27). Studies using animal models have shown that there is a direct association between maternal and fetal total cholesterol levels (26). According to the National Health Institution of the United Kingdom, the optimum total cholesterol levels should be less than 5. 2 milli moles per liter irrespective of sex and age. The USA National Institute of Health's National Human Genome Research came up with reference ranges of total cholesterol levels for pregnant women. It proposed less than 4 mmol/liter as low, moderate levels to be between 4 and 6. 8 mmol/liter and high levels to be above 6. 8 mmol/liter (30). However differences in maternal total cholesterol levels have

been linked with age, sex, race and ethnicity (23; 29; 30). This makes it difficult to recommend optimal maternal levels. It is because of this reason that most physicians do not recommend testing for cholesterol in pregnant women (23).

1. 6 Conditions associated with maternal total cholesterol levels

There are several disease states that can lead to either low or high levels of cholesterol during pregnancy. Women that have abetaproteinaemia or hypobetaprotenaemia and those that have a moderate to extreme low cholesterol diet usually have low cholesterol levels- the former due to lack of transport proteins (31; 32). Hypercholesterolemia usually occurs in pregnancy in the third trimester as a result of hormones (24-28). It also occurs in connection with familial hypercholesterolaemia type 2, obesity and gestational diabetes (33). The Barker thrifty phenotype hypothesis postulates that if during pregnancy a woman experiences nutritional deficiencies, the lack of adequate nutrients experienced by the fetus in the uterus programs it for survival in a nutrient poor environment even if after birth it is exposed to these nutrients (34). This hypothesis is now known as in utero programming (34; 35). Recent studies have shown the hypothesis to be true for high levels of nutrients as well; in this case hypercholesterolemia (25). Studies have shown that both low and high maternal cholesterol levels are associated with premature delivery. According to the USA National Institute of Health and Human Genome Research Institute (USA-NIH-GRI) women with high total cholesterol levels were more likely to give birth prematurely before 34 weeks of gestation than those with moderate levels

(36). Other studies have shown that there is a strong association between maternal total cholesterol levels and infant birth weight in women that carry their pregnancies full term. In one study women with low maternal total cholesterol gave birth to infants with a significantly lower birth weight than those with moderate levels (37). Various studies have shown that there is a direct association between maternal cholesterol levels and the risk of developing a fatty streak in the aorta of the fetus. Aortic lesions that develop in the fetus persist in childhood into adulthood and increase the risk of one developing cardiovascular diseases (CVD) (22; 25; 28; 33). Various studies have shown that hypercholesteroleamia in pregnancy leads to increased susceptibility to artherosclerosis (a stage of arteriosclerosis involving deposition of cholesterol and other fatty deposits on the endothelial cells, narrowing the arteries) of the infant later in life and of the woman as well. The risk is there even if the hypercholesterolemia is limited to pregnancy (22; 25; 28; 33). This deposition affects vascular response to chemical mediators of inflammation (25).

1. 7 Literature review

Studies have proven that total cholesterol levels rise with gestational age and peak in the third trimester (20-28). Some studies have shown that there are ethnic differences in the levels of total cholesterol and these are also found in pregnant women (23). In a case control study carried out by the Department of Physiology, Mymensingh Medical College, Mymensingh, Bangladesh, between July 2006 and July 2007 to investigate the effect of pregnancy on serum total cholesterol, the results showed that the mean total cholesterol was significantly higher in pregnant women of the third

trimester than the second trimester (29). One study that was carried out on Nigerian women in second and third trimesters to determine their serum lipid profiles the total cholesterol levels in this case were significantly higher in the second trimester than in the third trimester of pregnancy. This shows that there are indeed ethnic differences on the maternal total cholesterol levels (19). No published studies are available on how the levels of total cholesterol vary with gestational age in Zimbabwean pregnant women and on the effects of maternal hypo or hypercholesterolaemia on the mother and the infant. Given how the levels of maternal total cholesterol vary with ethnic differences and how they could impact the infant's health in utero and after birth; this study therefore explored the differences in maternal total cholesterol levels in Zimbabwean women during the different trimesters of pregnancies.

1. 8 Statement of the problem

Many obstetricians do not recommend cholesterol testing during pregnancy due to high levels of cholesterol expressed during pregnancy. Maternal total cholesterol levels have however been linked with infant birth weight, risk of developing atherosclerosis and CVD later in life and thus cannot be ignored. This study therefore aims to determine the total cholesterol levels of women between 16 and 40 years of age attending Chitungwiza Central Hospital's Ante-natal Clinic in the second and third trimester of pregnancy.

1. 9 Hypothesis

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1. 10 Aims and objectives

1. 10. 1 Aim

To determine the total cholesterol levels of women in second and third trimester of pregnancy attending Chitungwiza Central Hospital Ante-Natal Clinic.

1. 10. 2 Objectives

1. To determine the total cholesterol levels in the second and third trimester of pregnancy. 2. To compare the differences in the total cholesterol levels in the second and third trimester of pregnancy.

CHAPTER TWO: MATERIALS AND METHODS

2. 1 MATERIALS

Are listed in appendix 1.

2. 2 METHODOLOGY

2. 2. 1 Study design

A cross sectional analytical study

2. 2. 2 Study site

Chitungwiza Central Hospital Ante-Natal Clinic

2. 2. 3 Sample processing

Residual blood collected in red-topped plain tubes collected for routine tests from pregnant women visiting Chitungwiza Central Hospital Ante-Natal Clinic were used for this study. Blood samples were centrifuged at 1500 rounds per minute for 5 minutes. Serum was separated and placed in serum pots which were stored at -20oC until the day of processing. On the day of processing,

samples were thawed at room temperature and analyzed for total cholesterol using the Mindray BS120 after calibration. The standard one tailed proportion Z test was used to test the hypothesis.

2. 2. 4 Principle of the method

The Mindray BS120 chemistry automatic analyzer uses an enzymatic method for the measurement of total cholesterol. About 50 micro liters of patient's serum is mixed with the commercial reagent for total cholesterol. The reagent uses a bacterial cholesteryl ester hydrolase to cleave cholesterol esters. Cholesterol + ester → cholesterol + fatty acidThe 3-OH group of the cholesterol is oxidized to a ketone using cholesterol Oxidase enzyme. Cholesterol +O_2 → Cholestenone + H_2O_2. The hydrogen peroxide is catalyzed to form a colored compound. H_2O_2 + Phenol + 4 aminoantipyrine → quinoneimine + H_2O_2The absorbance of quinoneimine is measured and used to calculate the total cholesterol concentration in the original sample.

2. 3 INCLUSION AND EXCLUSION CRITERIA

2. 3. 1: Inclusion criteria

Pregnant women between 16 and 40 years in the second trimesterPregnant women between 16 and 40 years of age in the third trimester

2. 3. 2: Exclusion criteria

All non-pregnant women. Pregnant women below 16 years of age. Pregnant women above 40 years of age. All pregnant women in the first trimester.

2. 3. 3Sample size determination

See appendix 2

2. 4: Ethical considerations

Residual blood collected in red-topped plain tubes collected for routine tests from pregnant women visiting Chitungwiza Central Hospital Ante-Natal Clinic were used for this study. Permission to use these specimens was sought from the Clinical Director of Chitungwiza Central Hospital, the Sister-in-charge of the Ante-natal Clinic and the Chief Medical Laboratory Scientist heading the Laboratory. Ethical clearance was sought from the Joint Parirenyatwa Hospital – University of Zimbabwe Ethics Committee to carry out the study. Samples were assigned a research number to maintain patient confidentiality.

CHAPTER THREE: RESULTS AND ANALYSIS