Atherogenic Index of Plasma in the Three Trimesters of Pregnancy

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***Abstract*—This study investigates the change that occurs for atherogenic index of plasma (AIP) which is a very good marker for the evaluation of the risk of atherogenicity and cardiometabolic health. This study indicates the logarithm of the triglyceride and high-density lipoprotein cholesterol (log [TG/HDL-c]). The parameters of triglycerides (TG) and high-density lipoprotein cholesterol (HDL-c) are estimated and compared with the control cases. The AIP is calculated for each case during pregnancy in first, second, and third trimesters separately and each is compared with control cases. The study population comprised (80) women aged between (20–40) years distributed to (20) healthy non-pregnant women, (20) in the first trimester, (20) in the second trimester, and (20) in the third trimester in Koya health centers. The results of this study showed a significant increase in the TG level in both the second and third trimesters of pregnancy compared to the control cases. Whereas, in the first trimester of pregnancy, it can be assumed that there is a non-significant decrease of TG level rather than control cases. As well as the serum levels of HDL for all three trimesters of pregnancy displayed non-significant changes when compared to non-pregnant cases. These data illustrate that the AIP levels during both the second and third trimesters of pregnancy are significantly higher, as compared to control cases, whereas the AIP levels in the first trimester are non-significantly elevated, as compared with control cases.**

***Index Terms*—Atherogenicity, Lipoproteins, Plasma, Pregnancy, Trimester.**

1. Introduction

Pregnancy is a significant life experience that influences identities, relationships, and the pregnant mother's capacity to adjust to the growing fetus through substantial physiological and physical transformations. The alterations commence after conception and affect each of the body's organ systems (Chikhaoui, et al., 2023, Adam, et al., 2022). Pregnancy-related physiological changes, for example, alterations in lipid metabolism, promote growth, and prenatal development. During a normal pregnancy, there is an increase in the levels of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-c), and a reduction in high-density lipoprotein cholesterol (HDL-c) (Bartha, et al., 2023). During the pregnancy, the lipoprotein lipid physiology has significant effects on the pregnant woman and her unborn child as well as the developing fetus. High triglyceride levels meet the mother's energy requirements while sparing glucose for the fetus. For a fetus to develop normally, cholesterol and essential fatty acids are not necessary. During pregnancy, many physiological changes take place and affect the healthy and gestating women's lipid profile, that to prepare for the fetal development energy required for the late of pregnancy, for increased lipid synthesis and fat storage initially that is anabolic phase, and as lipid physiology enters to the net catabolic phase and the fat been breakdowns in the third trimester. Overall, during pregnancy, the mother's lipid physiology changed to reflect her increasing insulin resistance and facilitate the provision of adequate nutrients to the fetus (Wild and Feingold, 2023). The physiological adjustments that occur during pregnancy benefit the growing fetus and get the mother ready for birth and delivery. While some of these changes affect biochemical values, which are frequently stable, others could mimic disease symptoms. Distinguishing between typical physiological changes and the pathophysiology of diseases is crucial (Muhammad, Aghatise and Bello, 2023).

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II. Characterization of Pregnancy by Trimesters

Figured from the 1st day of the last menstrual cycle or 256–270 days after ovulation, the normal human pregnancy lasts an average of 280 days, or 40 weeks (Muralidhara, 2023). This is divided into three sections named trimesters, each of which is approximately 3 months long, corresponding to about nine calendar months. These three trimesters are distinguished by particular fetal changes. Infants delivered before the end of 37 weeks are regarded as preterm. A pregnancy is deemed to be full-term at 40 weeks. Premature babies may struggle with breathing and digestive problems, as well as growth and development problems (Hadi, Mahmoodb and Hadi, 2021, Butt and Lim, 2019).

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A. First Trimester of Pregnancy

Pregnancy's first trimester is generally considered to the past weeks 1–13. The first trimester was analyzed and correlated with the normal menstrual cycle and the day of the previous menstrual period. Medical professionals have historically relied on the day of the last menstrual cycle, ovulation, fertilization, implantation, and chemical detection to establish the occurrence of pregnancy, as shown in Fig. 1 (Vinh, 2021). Beginning in the 12th week of pregnancy, TC, TG, LDL-c, HDL-c, and phospholipids all started to rise in pregnant women's serum lipid levels (Zhu, et al., 2021). During the first trimester, lipid levels, including TG, typically decrease, while HDL cholesterol levels may increase. This phenomenon is apparent to be a protective mechanism, ensuring sufficient lipid supply for fetal development. As a result, the AIP may decrease during this period (Wild and Feingold, 2023).

B. Second Trimester of Pregnancy

The pregnancy in the second trimester is known as weeks 13–26. During this time, most women report feeling more energized and start to gain weight as the morning sickness symptoms gradually become better. After 14 weeks: Gender can be determined and at about 16–20 weeks: Pregnant women usually feel the movements of the fetus. Women who have had previous pregnancies usually feel movement about 2 weeks earlier than women who are pregnant for the first time. The pineal gland appears and the female reproductive tract appears (Shah, et al., 2023).

In the second trimester, lipid levels start to rise gradually due to increased energy demands for both the mother and the growing fetus. TG may increase, while HDL cholesterol levels could remain stable or show slight changes. The AIP may increase slightly during this period but is still likely to be lower than pre-pregnancy values (Wild and Feingold, 2023, Musa, 2023).

C. Third Trimester of Pregnancy

The third trimester of pregnancy is well-known as weeks 26–40. Fetal lungs mature between 30 and 34 weeks with each passing week spent in the womb. However, the kicks and fetal movements are stronger than ever. Approximately 38 weeks of development the average weight of a fetus is 3250 g for females and 3300 g for male. The face is distinctly appearance and nearly all muscles appear in adult form. Due to the fetus's downward turn as it prepares to birth, the woman's abdomen will change shape and drop (Shah, et al., 2023).

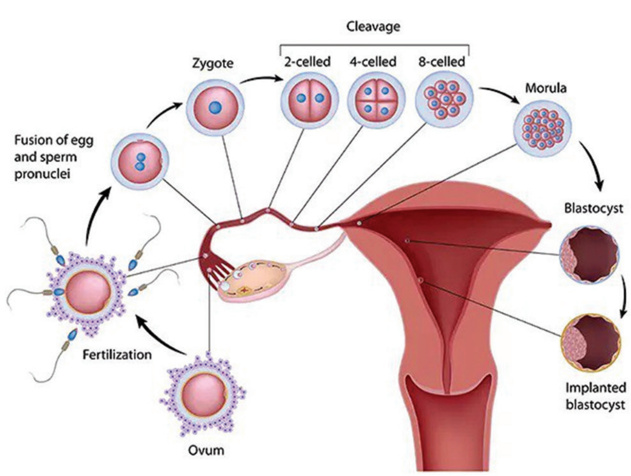

Fig. 1. Fertilization steps and development of blastocyst and implantation (Shah, et al., 2023).

During the third trimester, there is a further increase in lipid levels, particularly TG. This rise is partly attributed to increased insulin resistance in late pregnancy. HDL cholesterol may also increase, but it might not keep pace with the rise in TG. As a result, the AIP may increase during this trimester, indicating a relatively higher risk of atherogenicity (Wild and Feingold, 2023).

III. Lipid Profiles

The serum lipid profile is determined, prediction of cardiovascular risk and present nearly in common tests (Mora, et al., 2019). Most importantly, cardiac risk assessments can help in determining whether a person may have experienced a coronary event because of blood vessel obstruction or arteriosclerosis (Ireshanavar, et al., 2019). It is ordinarily done in fasting blood specimens. Fasting is 12–14 h complete overnight diet with exceptional water and medicine. It may be true there are two main reasons: Postprandial TG remained boosted for several hours (Galal, et al., 2020, Zhang, et al., 2023) and the majority of serum lipid reference values has been determined using fasting blood samples. A shift to a catabolic state promotes the use of maternal tissue lipids as the source of energy, preventing the fetus from consuming glucose and amino acids. Moreover, fetus utilization of maternal lipids, including cholesterol, is accessible for the development of cell membranes as well as for use for the precursor to bile acids, and steroid hormones (Sobik, et al., 2023). Dobiasová showed that the atherogenic index of the plasma (AIP), calculated as the logarithm ratio of TG to HDL cholesterol, is connected with lipoprotein particle size (Paleari, et al., 2023) and may function as a plasma atherogenicity measure (Chen, et al., 2023, Chen, et al., 2020).

To assess the risk to the cardiovascular system, National Cholesterol Education Programme (NCEP) and Europe Guidelines also propose lipid profiling fasting blood tests. These recommendations do permit TC and HDL, though. There is little variation in cholesterol levels between fed samples and non-fed samples of these lipids. In addition, panel III's non-HDL cholesterol (TC minus HDL cholesterol) can be used in the non-fasting state as a secondary target treatment for adults (Nordestgaard and Varbo, 2021, Marou, 2021). The lipid profile serum includes the measurements of the following tests: TC, TG, HDL-c, and low-density lipoprotein (LDL-c) (Bailey and Mohiuddin, 2022). Lipids such as cholesterol and TG can be carried through the bloodstream via lipoproteins (Liu, et al., 2022).

LDL-c is frequently used to calculate how much LDL-c drives certain medical outcomes advancement of atherosclerosis. The assessment of the risk of cardiovascular disease (CVD) sometimes involves comparing the ratio of TC to HDL-c (Castañer, et al., 2020, Rajab, 2012).

A. TC

The TC level of the patient is determined by measuring all of the lipoproteins (Brown, 2007). High cholesterol can cause atherosclerosis due to the excessive buildup of cholesterol and other deposits on the walls of the arteries. There are no symptoms associated with elevated cholesterol, but these deposits (plaques) might decrease blood flow through your arteries. Moreover, the only way to know if you have it is the blood test. Levels below 5 mmol/L = 200 mg/dl were confirmed by both the European Society of Cardiologists and the American NCEP (Bartels and O'Donoghue, 2011).

B. TG

TG, a specific type of fat, are carried by the blood. Your body either makes TG on its own or gets them from food. For optimal health, the body requires some TG (Wang, et al., 2013). Elevated blood TG levels do not cause any symptoms. However, if left unmanaged, they can increase the risk of significant problems including stroke and coronary heart disease (Jadhav and Annapure, 2023). Triglyceride levels can be assessed when not fasting or while doing so, and levels between 2 and 10 mmol/L are linked to a higher risk of CVD (Yildiz, et al., 2023), levels ≥150 mg/dl were linked to relating non-coronary atherosclerosis (Hao, et al., 2022) and concentrations exceeding 10 mmol/L may induce CVD and an increased risk of acute pancreatitis (Yildiz, et al., 2023).

C. HDL–c

One of the main classes of plasma lipoproteins, HDL-c, is referred to as the "good cholesterol" because the main role of HDL-c is to carry and absorb the amount the Cholesterol in the blood and carry it back to the liver, and HDL removed the excess cholesterol from tissues (it cleans blood) (Jomard and Osto, 2020, Bailey and Mohiuddin, 2022). A high level of (HDL-c), in the presence of hypertriglyceridemia, increases hepatic lipase (HL) activity, and increased HDL-c catabolism (degradation of HDL-c). For every 1 mg of HDL-c lost, the risk of coronary artery disease (CAD) increases by 2% (Rajab, 2012). Normal values are more than 50 mg/dI for women and 40 mg/dI for men (Karizi, et al., 2023).

D. LDL-c

Law-density lipoprotein contains less protein and more cholesterol and indicated the "bad" cholesterol, also well-known as LDL-c, which moves cholesterol metabolites from the liver throughout the body. The accumulation of LDL cholesterol can cause narrowing and hardening of arteries which leads to the development of atherosclerotic lesions. Accurate LDL-c assessment is crucial for medications that target lipid reduction to slow or stop the development of atherosclerosis and prevent plaque. Normal values: <70 mg/dl (Pownall, et al., 2021).

IV. Atherogenic Index of Plasma

TG and HDL-c make up the AIP, a new marker for evaluating atherogenicity risk and cardiometabolic health. Among patients with type 2 diabetes mellitus and high cardiovascular (CV) disease risk, there is a correlation between AIP and a higher frequency of major adverse cardiovascular events (MACEs). In just a few studies has the connection between AIP and CV risk in general populations been examined (Kim, et al., 2022). To investigate the association with the AIP, researchers examine the logarithm of the molar ratio of TG/HDL-c. A measure of plasma atherogenesis, (AIP) is established with lipoprotein particle size (Chen, et al., 2020). Several factors have been used to predict the risk of CVD. In the early 1990s, the ratio of LDL/HDL and TC/HDL were the best-correlated predictor of future CVD. The latest indicator of atherogenicity is the AIP, which is directly associated with the risk of developing atherosclerosis (Castañer, et al., 2020, Rajab, 2012).

V. Materials and Methods

A. Chemicals and Procedures

The biochemical parameters of TG and HDL-C were measured by enzymatic colorimetric assay by the (Fuji dry-chem slide TG-Piii) and (Fuji dry-chem slide HDL-C-piii) respectively, with a company of Fuji film and Japanese origin. As well as, the common instrument and model of (Fujifilm dri-chem NX500) with Japan origin and also the (800-1 centrifuge) with China origin used for this study (Nakamura, et al., 2011).

B. Study Population

Participants in the study were (80) healthy pregnant women and (20) healthy non-pregnant women, the ages between (20–40 years).

C. Sampling

This study, which was conducted at koya health centers in November 2022, found that (60) pregnant women were between the ages of 20 and 40, were not clearly experiencing any pregnancy-related complications, and were grouped into three groups:

1. (20) in the first trimester of pregnancy (up to 13 weeks).
2. (20) in the second trimester of pregnancy (13–28 weeks).
3. (20) in the third trimester of pregnancy (28–40 weeks).

Twenty healthy, non-pregnant women served as controls in addition. A venous sample of 3 ml was taken from each group being tested. The blood samples were placed in gel tube, and the serum was extracted by centrifuge at 1500 rpm about 10 min. The serum was then separated into small parts and kept frozen until further analysis. As well as the AIP was determined as log (TG/HDl-c) using the Czech online atherogenic risk calculator.

D. Statistical Analysis

The GraphPad prism with version 9 (Graphpad Software, Inc.,) was used to conduct the statistical analysis. As well as,

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the student t-test was used to analyze the differences between the groups. The data results represented as mean and standard error of mean (mean ± standard error of the mean [SEM]), p value ($p < 0.05$), was regarded as statistically significant, while if ($p > 0.05$) represented as no significant (N.S) and the results represented as median.

VI. Results and Discussion

A. Serum TG Level Results

The results of this study reveal that the value of TG in sera of healthy pregnant women in three trimesters and non-pregnant women (control cases) from the Table I, Figs. 2 and 3. The (mean ± SEM) of TG is (148.7 ± 4.820) for control case, however, the (Mean ± SEM) of the second and third trimesters are (236.7 ± 27.84 and 259.9± 24.78) respectively. On the other hand, the median for the first trimester is (142.0).

As well as, from Table I it can be seen that the TG level in first trimester has recorded the lowest level but the decrease is non-significant difference if compared to control cases, inversely we can notice that there is a significant increase in TG level for both second and third trimester of pregnant cases if compared with control cases, and this may be according to the biochemical, hormonal, and physiological changes that occur during these two trimesters of pregnancy and growth of the fetus inside the womb.

TABLE I
Serum Level of TG for Both Pregnant Women (in Each Trimester) and Non- Pregnant Women

Groups	N	Serum level of TG (mg/dl)	p
Control	20	148.7±4.82	-
First trimester	20	142.0	0.7603 (N.S)
Second trimester	20	236.7±27.84	0.0042 (S)
Third trimester	20	259.9±24.78	0.0001 (S)

*The values expressed as (mean±SEM) for significant value and (median) for non-significant value

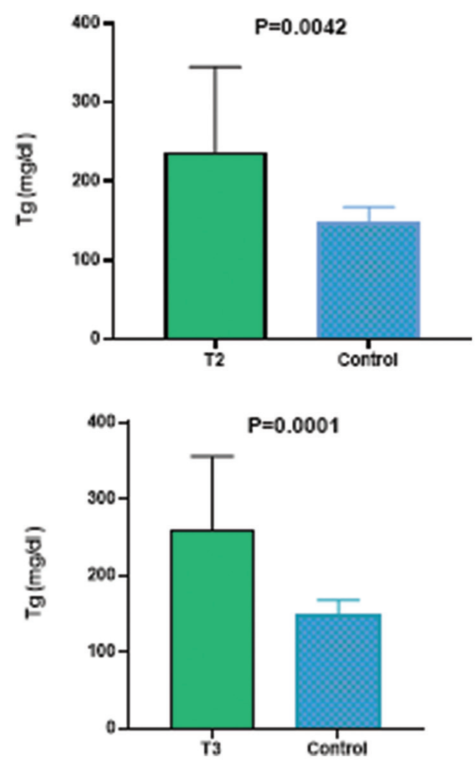

Fig. 2. Serum levels of triglycerides in both second trimester (T2) and third trimester (T3) of pregnancy with non-pregnant women.

B. Serum HDL Level Results

The data from Table II and Fig. 4, that show the serum level of HDL during the three trimesters of pregnancy and healthy non-pregnant women cases. The median HDL level of each trimester and control cases was investigated to be (44.00) for non-pregnant women and (45.00, 53.00, and 51.00) for first, second, and third trimesters, respectively. From the results, it can be assumed that there are no significant differences in serum HDL levels in all three trimesters of pregnancy compared with non-pregnant women.

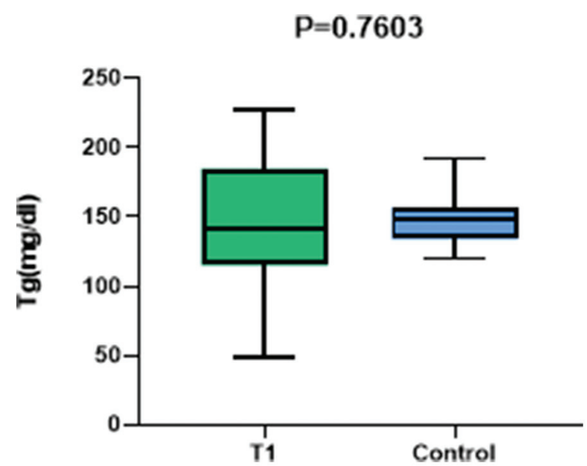

Fig. 3. Serum levels of triglycerides in both first trimester (T1) of pregnancy with non-pregnant women.

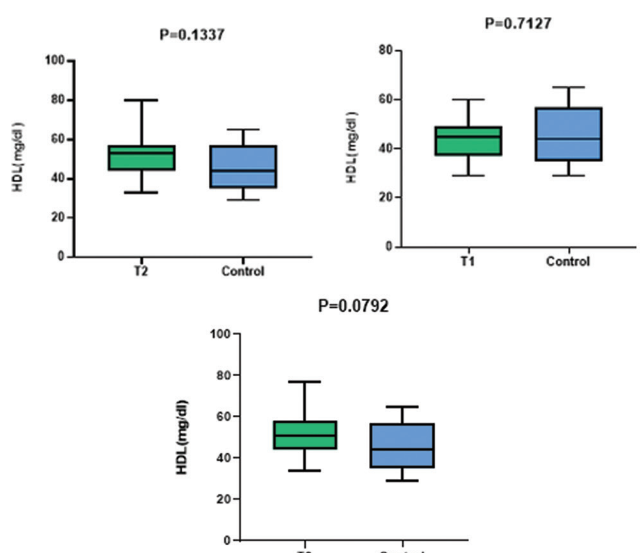

Fig. 4. Serum levels of high density lipoprotein in three trimesters of pregnancy with non-pregnant women.

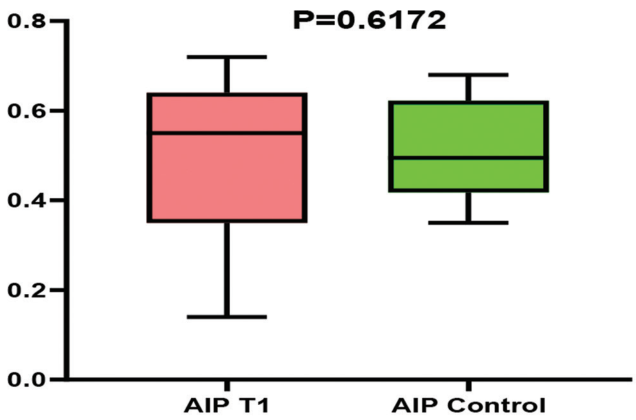

Fig. 5. Calculated atherogenic index of plasma for first trimester (T1) and non-pregnant women.

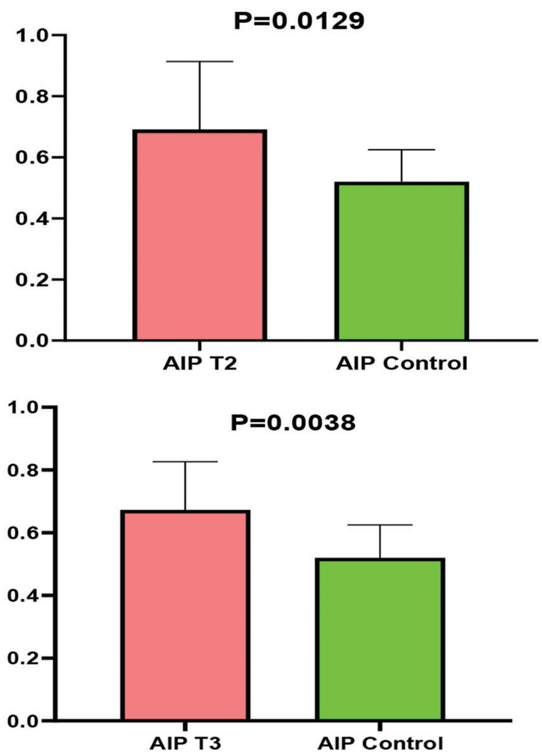

Fig. 6. Calculated atherogenic index of plasma for second trimester (T2) and third trimester (T3) with non-pregnant women.

C. Calculated AIP Level Results

The data from Table III, Figs. 5 and 6, illustrate the values of calculated AIP for all three trimesters of pregnancy and non-pregnant women. The (mean ± SEM) of AIP for non-pregnant women, second and third trimesters are (0.5200 ± 0.02710, 0.6915 ± 0.06168, and 0.6722 ± 0.03984) respectively, while the median of AIP for the first trimester is (0.5500).

From the evaluated results for the first trimester of pregnancy we can conclude that there is a non-significant increase of AIP level compared with control cases, while it can be assumed that there are significant elevates of AIP level in both the second and third trimesters compared with AIP level of non-pregnant women, and this may also relate to the big physiological and biochemical changes in the both second and third trimesters of pregnancy.

TABLE II
Serum Level of HDL for Both Pregnant Women (in Each Trimester) and Non-pregnant Women

Groups	N	Serum level of HDL (mg/dl)	p
Control	20	44.00	-
First trimester	20	45.00	0.7127 (N.S)
Second trimester	20	53.00	0.1337 (N.S)
Third trimester	20	51.00	0.0792 (N.S)

*The values expressed as (median) for non-significant value

TABLE III
Calculated AIP of Both Pregnant Women (in Each Trimester) and Non-Pregnant Women

Groups	N	AIP (Log (TG/HDL))	p
Control	20	0.5200±0.0271	-
First trimester	20	0.5500	0.7603 (N.S)
Second trimester	20	0.6915±0.0616	0.0129 (S)
Third trimester	20	0.6722±0.0398	0.0038 (S)

*The values expressed as (mean±SEM) for significant value and (median) for non-significant value

VII. Conclusion

From the results of this study, we conclude that the TG level is significantly higher in both the second and third trimesters of pregnancy compared with the control cases. While for the first trimester of pregnancy, it can be assumed that there is a non-significant decrease of TG level if compared with the control cases. Non-significant changes were found in the estimation of serum HDL levels for all three trimesters of pregnancy if compared with non-pregnant cases. It can be concluded a significant increase in AIP level during both the second and third trimesters of pregnancy if compared to control cases, while a non-significant increase can be seen in AIP level of the first trimester compared with the control cases.

VIII. Recommendations and Future Work

1. To evaluate some other lipids profile parameters such as TC, LDL-c, and VLDL-c.
2. Study and measured some other Lipid ratios such as: Cardiac risk ratio 1 (TC/HDL-c), and Cardiac risk ratio 2 (LDL-c/HDL-c).
3. Studying if there is association between these factors and the future cardiac complications for the mom and after the baby is born.

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