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# Case study of biomarkers and risk stratification in Cardiovascular diseases during pregnancy

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## ABSTRACT

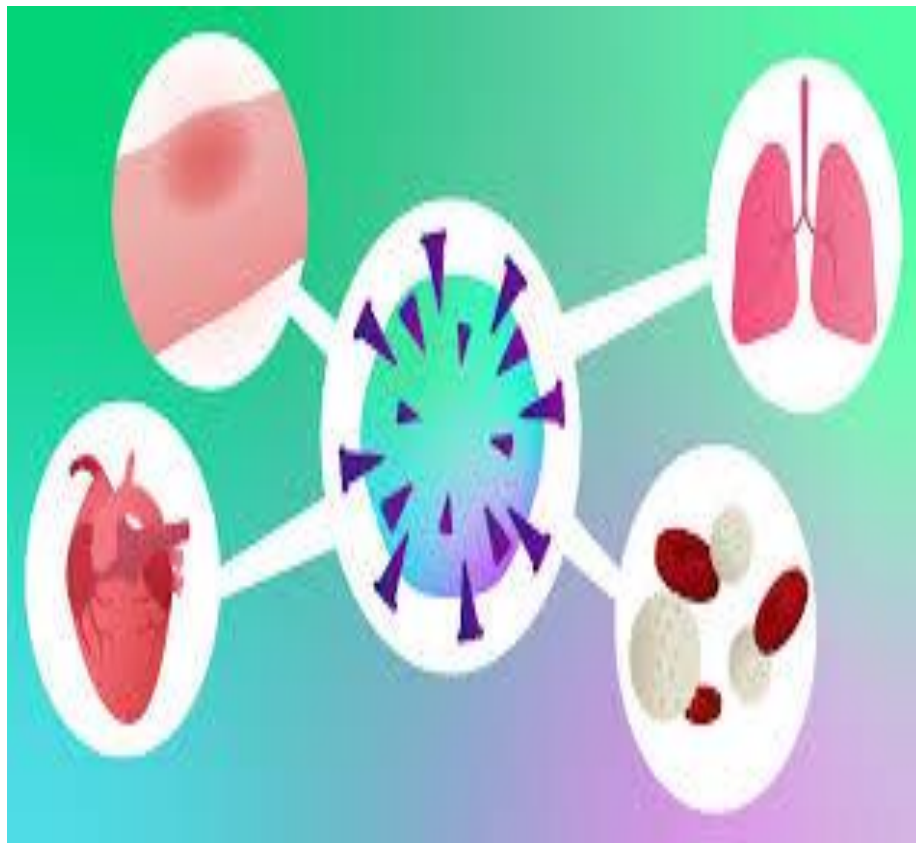
To improve the quality of care and optimise management, new and older biomarkers in analysis and risk stratification for women with cardiovascular diseases (CVD) are required. The role of cardiac biomarkers during pregnancy is still a hot topic that needs to be investigated further with a larger sample size study. The phrase "biological marker" was coined in the 1950s. Older hypertensive disorders (HDP) gestational hypertension & preeclampsia increase CVD risk throughout pregnancy, hence biomarkers are employed to prevent CVD and predict older outcomes related to cardiac events. Fasting blood measures of glycemia [glucose, insulin, homeostatic model assessment of insulin resistance (HOMA-IR, percent haemoglobin)] and lipids [total high density lipoprotein (HDL), low density lipoprotein (LDL), cholesterol, and triglycerides after 4-5 and 6-8 years of delivery] are some of the maternal metabolic health biomarkers. The disease's cause is unknown, but recent research has found that it appears to originate in the placenta and is characterised by widespread maternal endothelial dysfunction. According to a recent study presented at COVID-19, biomarkers have a significant role in the diagnosis and therapy of multisystem inflammatory syndrome in children (MIS-C). MMR ratios are highest in the United States and lowest in Finland. The most common cause of death during or after pregnancy is cardiovascular disease.

**Key Words:-** Pregnancy, CVD, Biomarker, Disease, Diagnosis.

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## HISTORY

Biomarkers are defined as "biochemical, cellular, physiological, or behavioural alterations that can be evaluated in body fluids or tissues at the level of organisms that open up the exposure or effects of one or more chemical contaminants," according to Depledge in 1994. In 1996, Van Gestel and Van Brummelen redefined biomarkers to clearly distinguish a biomarker from a bioindicator. According to Van Gestel and van Brummelen, the term "biomarker" should only be used to indicate sublethal biochemical changes caused by individual xenobiotic exposure. The National Institutes of Health (NIH) described biomarkers as "a characteristic that is objectively analysed and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic treatment" by the National Institutes of Health (NIH) in 1998. To begin, in an 1848 study, the cancer biomarker was found in 75% of leukaemia patients who had light chain immunoglobulin in their urine. Clinicians are still working on tests for these biomarkers.



**Fig :- History of biomarkers and CVD risk during pregnancy**

## INTRODUCTION

Biomarkers are biological molecules found in blood, other bodily fluids, and tissues that serve as indicators of normal or pathological processes, as well as a condition or disease. Cardiovascular disease (CVD) is the major cause of maternal death, responsible for more than 33% of all pregnancy-related deaths, including cardiomyopathy (10.8%) and other cardiovascular diseases (15.1 percent). coming from poor nations The United States has a high maternal mortality rate. According to the World Health Organization, the Finnish maternal morbidity rate has decreased from 6 per 1000,000 in 1977 to 9 per 1000,000 now. Finland is a country with a low maternal mortality rate. . In India, the maternal mortality rate has decreased by 70%, from 398 per 100,000 in 1997-98 to 99 per 100,000 in 2020. Biomarkers play an important role in the diagnosis of diseases as well as the development of drugs to treat them. Screening, diagnostic, and prognostic biomarkers are the most popular classifications. Preterm preeclampsia (and related preterm delivery and perinatal morbidity) can be prevented with a biomarker that can identify high-risk women early in pregnancy (less than 6 weeks). It is common practise in pregnancies to categorise pregnancies as "low" or "high" risk, depending on the risk of a negative neonatal or maternal outcome. Some metabolic and cardiovascular changes occur during pregnancy. Changes in glucose and lipid metabolism are also required to develop a connection between the foetus and the mother. Increased release of diabetogenic hormones, for example, causes mothers to develop insulin secretion in the second trimester, which peaks in the third trimester before recovering in the postpartum period. During pregnancy, there are significant changes in glucose metabolism, serum cholesterol, including both high (HDP) and low (LDL) density lipoprotein, and triglyceride levels. Almost half of maternal deaths occur on the first day after delivery, and 66% occur within the first week.

## TYPES OF BIOMARKERS

Biomarkers are essential in the diagnosis of diseases as well as the development of therapeutic treatments for sick states. They're also used to figure out how much medicine to take. Biomarkers are now commonly used as a clinical trial's endpoint. Biomarkers are categorised as screening, diagnostic, or prognostic based on their intended application. These are some of the most frequent categories or types of biomarkers. Biomarkers for screening have high specificity, as well as known separate module limits and the ability to add values to traditional risk variables. Biomarkers for prognosis have high specificity and minimal intra-individual variability. They also demonstrate a positive response to therapy. Diagnostic biomarkers are extremely sensitive at a low cost, and they have a high tissue specificity that is related to the severity of the disease. Pharmacodynamic biomarkers or predictive biomarkers are classified based on

their therapeutic effect. Pharmacodynamic biomarkers are the biomarkers that examine how a medicine affects the pathological state. This chapter explains how the targeted organism alters as a result of the sickness and its treatment.

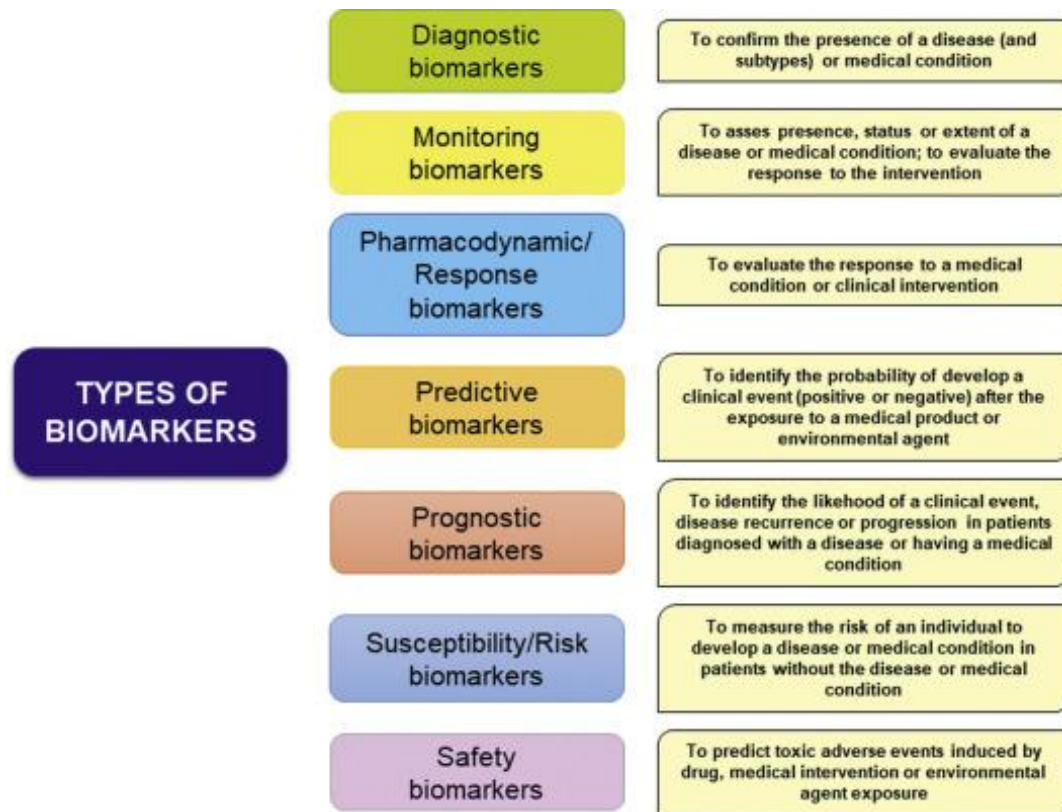


Fig :- Types of biomarkers with their introduction

#### CARDIOVESCUAL DISEASE RISK STRATIFICATION DURING PREGNANCY:

- 1) congenital heart diseases
- 2) Hypertension
- 3) Pre-eclampsia
- 4) A myocardial infarction
- 5) Myocarditis

#### CONGENITAL HEART DISEASES

While pregnant, many patients with congenital cardiac problems require further specific care. It is necessary to report on the effect of various congenital cardiac problems on the foetus, including the possibility of inheritance. Congenital heart illness in women should result in echocardiography, while congenital heart disease in a foetus or neonate should result in parental congenital heart disease screening. Congenital heart disorders are actually recommended during the pregnancy, especially in women who have complex cardiac diseases. Congenital heart diseases are not closely linked to gestation and are not research has indicated for cardiac conditions during pregnancy. During pregnancy, the amount of BNP (B-type or brain natriuretic peptides) remains low in healthy women, peaking at 35pg/ml, whereas in pregnant women with hereditary cardiac disorders, the level of BNP is significantly greater throughout all trimesters, peaking at 79pg/ml.

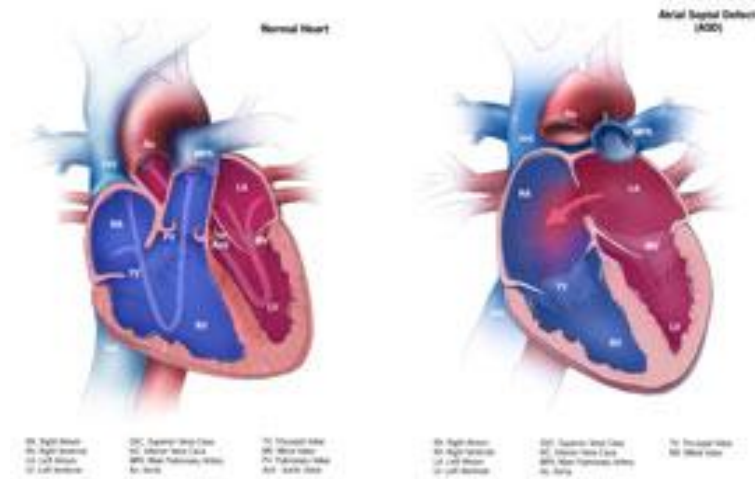


Fig :- Congenital heart diseases during pregnancy

### PRE-ECLAMPSIA

Preeclampsia is a type of pregnancy-related cardiovascular disease that affects 3% to 5% of all pregnancies. High blood pressure (hypertension) is a defining feature, and endothelial dysfunction leads to extensive end-organ destruction. The liver, kidneys, brain, and placenta are all included. Preeclampsia is a major cause of maternal morbidity around the world. Preeclampsia contributes considerably to preterm, neonatal morbidity, and perinatal mortality, with delivery being the only current remedy. Preventing preterm preeclampsia (and related preterm birth and perinatal morbidity) through low-dose prophylaxis with aspirin has clinical efficacy in preventing preterm preeclampsia (and associated preterm birth and perinatal morbidity) with intake of the low-dose prophylaxis with aspirin. The PHOENIX experiment demonstrated the benefit of knowing patients at higher risk of preeclampsia in late pregnancy (allowing for increased surveillance and on-time delivery). The national federation of gynaecology and obstetrics recommends using biomarkers, in addition to other clinical factors, to predict patients who are at risk of developing preeclampsia, resulting in increased close monitoring of the patient and early intervention to reduce the incidence of preeclampsia in high-risk patients. It was also mentioned in 2018 ESC guidelines that preeclampsia can be excluded with sf if it develops in the next week High blood pressure is a symptom of pre-eclampsia, a potentially serious pregnancy condition. It is an uncommon condition that affects less than 1 million people in India each year. Per-eclampsia is managed with oral or intravenous drugs until the baby is ready to be delivered. This frequently necessitates a trade-off between the risk of an early birth and the risk of continuing pre-eclampsia symptoms. Women over the age of 40 are at a higher risk. Multiple gestation is when a woman is pregnant with more than one foetus at the same time. Preeclampsia is a condition that affects the arteries that supply blood to the placenta. The infant may obtain insufficient blood and oxygen, as well as fewer nutrients, if the placenta does not receive enough blood. This can result in foetal development limitations, or sluggish growth. Seizures and stroke can occur if preeclampsia is not untreated.



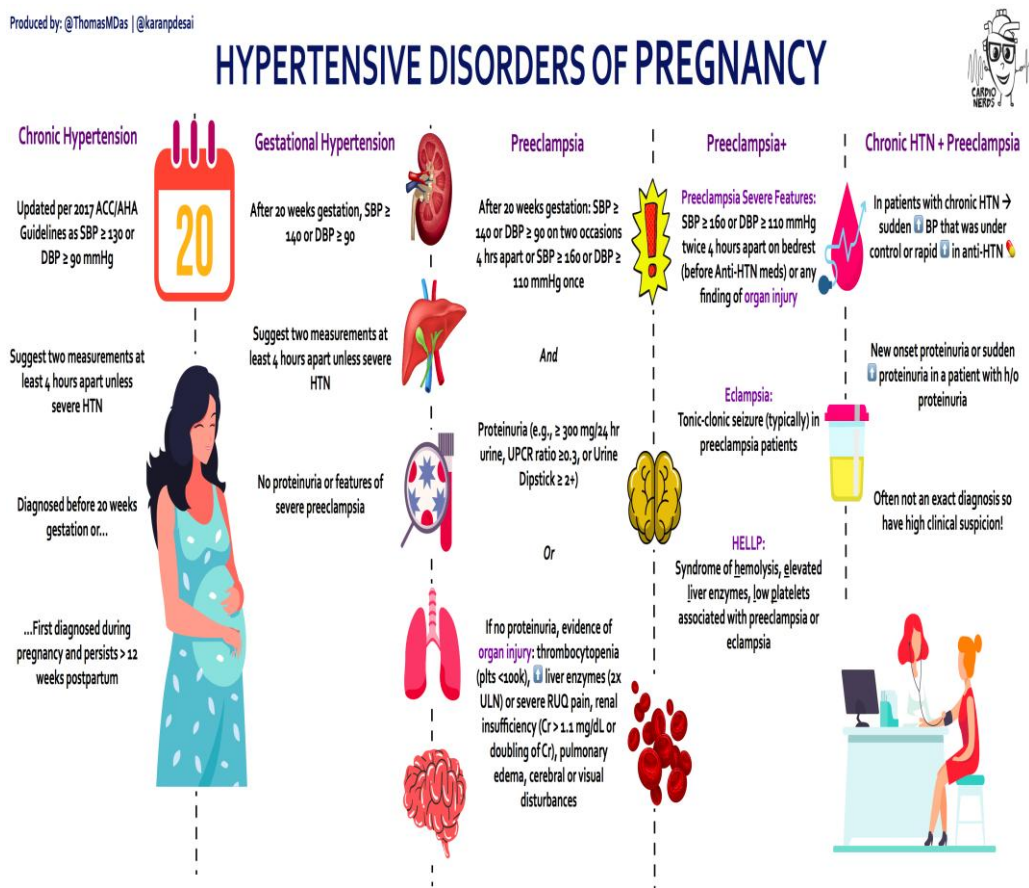
Fig :- pre-eclampsia during pregnancy



## HYPERTENSION

Gestational hypertension is a type of hypertension that occurs when a woman primarily has high blood pressure during pregnancy and no additional heart or renal concerns. It is usually discovered after 20 weeks of pregnancy or when the baby is close to being born. Hypertension during pregnancy carries a number of dangers, including decreased blood flow to the placenta, which can result in less oxygen and nutrients being delivered to the baby. This can result in a premature baby's sluggish growth, low birth weight, tragic mortality, neonatal death, and deadly growth limits. If a patient is at high risk for hypertension, he or she is given low-dose aspirin to prevent it. Primary hypertension is the most prevalent cause of chronic hypertension in 90 percent of young women. . women's with past records of hypertensive disorder have higher risk of cardiovascular diseases as compare to those who have not any past record , Some explanations suggest that inflammation performs a role in the progression of cardiovascular diseases, which can be confirmed by measuring the levels of c-reactive protein (CRP) and interleukin 6 (IL6), which are elevated over 17 years postpartum in patients with hypertension, and thus these biomarkers can be used to predict future cardiovascular disease in those patients.

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## MYOCARDIAL INFRACTION

Even if the patient has pre-eclampsia, the ESC guidelines for the management of cardiovascular disease during pregnancy recommend a (class 1) electrocardiogram and serum troponin measurement in pregnant women with chest pain. Elevation of serum troponin during pregnancy should suggest myocardial ischemia. Although underlying atherosclerotic illnesses appear to be the most common cause of myocardial infraction during pregnancy, thrombosis, coronary artery dissection, and collagen vascular disorders are other possibilities. In contrast to the rest of the world, where maternal mortality is declining, rates in the United States are continuing to grow. Pregnancy-related myocardial infraction is responsible for more than 20% of maternal cardiac mortality. MI (myocardial infraction) occurs in 2.8 to 8.1 per 1000,000 deliveries, four times the rate of MI in non-pregnant, reproductive-aged women. Age >35 years is one of the most consistent risk factors for myocardial infraction. Smoking, hypertension, and diabetes mellitus are some of the additional risk factors.

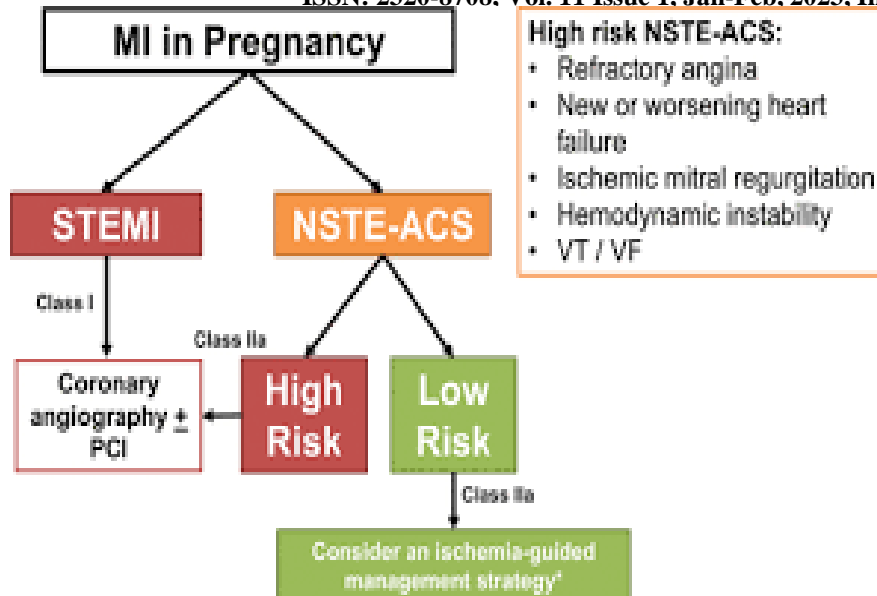


Fig :- myocardial infraction during pregnancy

### MYOCARDITIS:

Myocarditis during pregnancy is quite uncommon. Asymptomatic, mild nonspecific symptoms to cardiogenic shock and/or life-threatening arrhythmias are all possible clinical manifestations. CRP, BNP, pentraxin3, gal-3, and GDF-15 are some of the biomarkers that rise routinely in myocarditis at a different level than high sensitivity troponin. In myocarditis, unlike acute myocardial infraction, CRP levels rise faster than high-sensitivity troponin levels. Some of the most common causes of myocarditis are infections (most commonly caused by the common cold, influenza, or covid-19), bacteria, fungus, or parasites, which can induce cardiac inflammation. Fetal myocarditis is depicted visually as a thickened, hyperechogenic, and weakly contractile myocardium with a low ejection fraction, with or without tricuspid dysfunction.

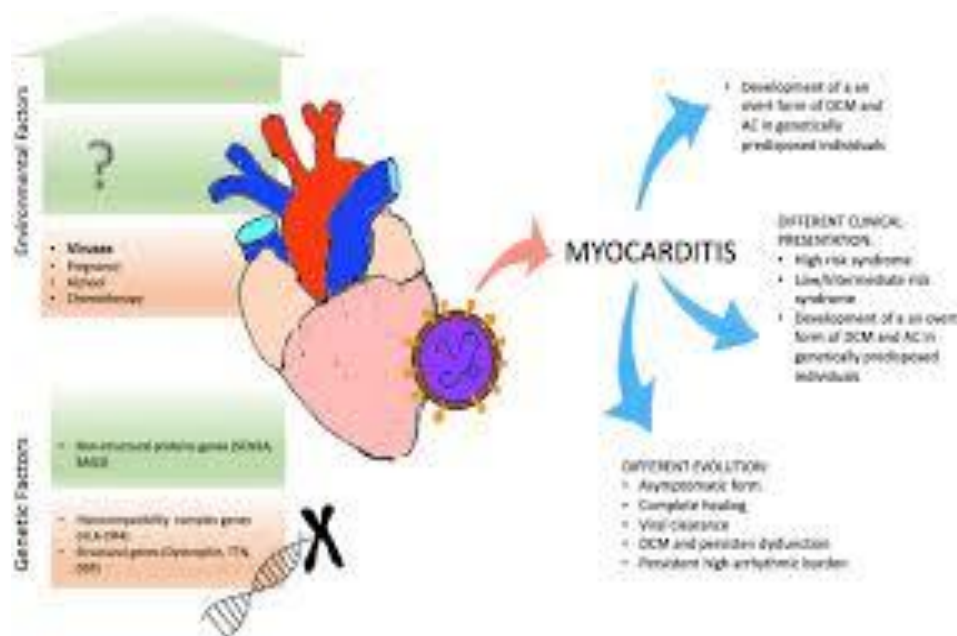


fig :- Myocarditis during pregnancy

### RISK FACTORS:

- 1) Maternal cardiovascular disease is a risk factor.
- 2) During pregnancy risk factor for acute coronary syndrome.
- 3) Cardiovascular risk screening postpartum.

### **1. MATERNAL CARDIOVASCULAR DISEASE IS A RISK FACTOR:**

- The race of non-Hispanic black people.
- Getting older ( more than 40 years).
- Adiposity.
- Pre-eclampsia, Edamsia, haemolysis, increased liver enzymes, and low platelet count syndrom are all hypertension problems that occur during pregnancy.
- Long-term illness (chronic hypertension or pre-gestational diabetes mellitus ).
- Sleep apnoea (obstructive sleep apnoea) ( moderate to severe).
- A history of premature births.
- There is a history of heart disease in your family.
- Cardiotoxic medication exposure.

### **2. PREGNANCY RISK FACTORS FOR ACUTE CORONARY SYNDROME:**

- Race of non-Hispanic black people.
- A high BMI (body mass index).
- Diabetes mellitus is a type of diabetes.
- Hyperlipidaemia.
- There is a strong family history of heart disease.
- Pregnancy-related hypertensive diseases
- Previous dissection of a coronary artery.
- Transfusion of blood.
- Infection during the postpartum period.
- Maternal age is over 30 years old.

### **3. CARDIOVASCULAR RISK SCREENING POSTPARTUM: -**

#### **1) MEDICAL BACKGROUND:**

- Tobacco use (number cigarettes per day, number of years smoked).
- Engage in physical activities (time per week, duration).
- Breast feeding is an option (how long).
- Hypertension, diabetes, or cardiovascular illness in the past.
- A first-degree relative with a history of heart disease, hypertension, or diabetes.

#### **2) PHYSICAL EXAMINATION:**

- Blood pressure at rest and heart rate, as well as BMI and waist circumference.

#### **3) BIOCHEMICAL TESTING:**

- Glucose levels after a fast (or oral glucose tolerance testing if patient had gestational diabetes).
- screening for protein in the urine ( protein:creatinine ratio).



#### 4) NUTRITION ASSESSMENT:

- Diet counselling.

#### BIOMARKERS OF COVID-19 DISEASE AND THERE SEVERITY IN PREGNANCY :-

A case series study on inflammatory biomarkers in pregnant women was recently published in the Natural journal Scientific Reports, allowing for an accurate COVID-19 prediction in pregnant women. C reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, and D-dimer have all been identified as prognostic tools to monitor the progress of SARS-CoV-2 infection, and alongside leukocyte count and neutrophil to lymphocytes ratio (NLR), several such inflammatory biomarkers have been identified as prognostic tools to monitor the progress of SARS-CoV-2 infection. During the COVID-19, a meta analysis of 20 trials was conducted, resulting in 4843 COVID-19 participants, the effect of elevated CRP ( $>10\text{mg/L}$ ) on outcomes shows that COVID-19 patients with elevated CRP have an almost fourfold higher risk of poor outcomes (pooled-OR:3.97;95 percent ci: 2.89-5.45;p0.000001).

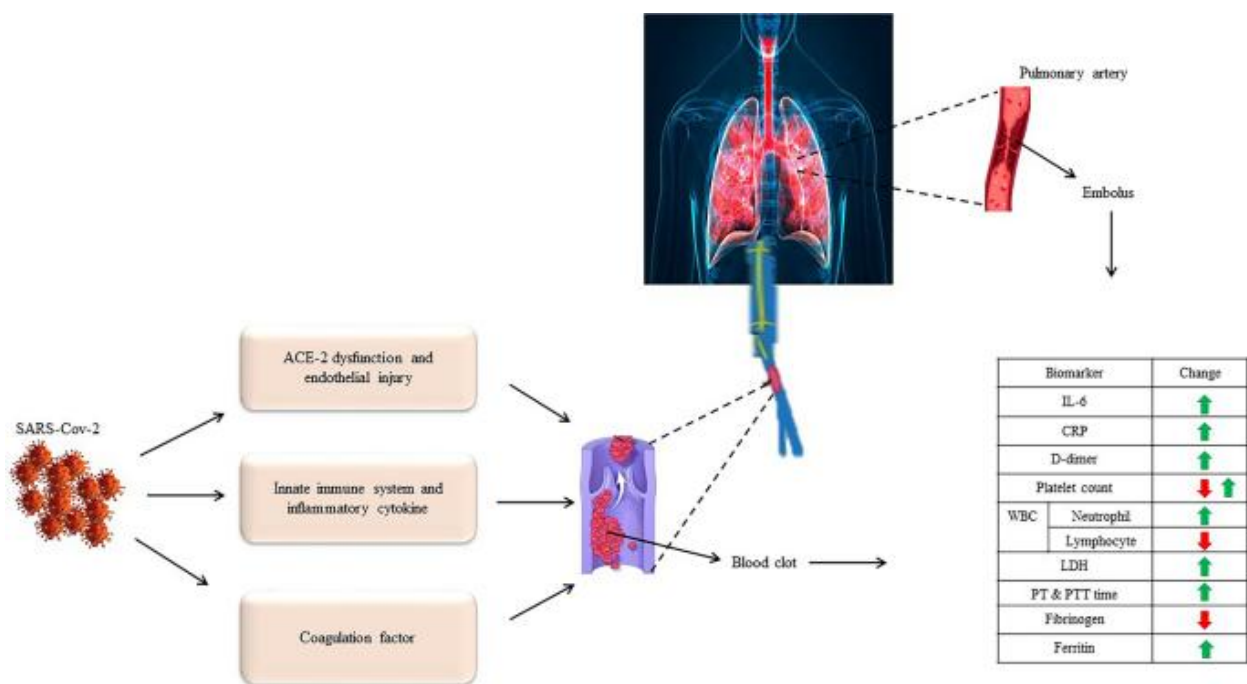


Fig :- Inflammatory biomarkers during COVID-19 and there risk in pregnancy

#### CONCLUSION

Various CVDs are described in the above description, as well as several types of biomarkers, such as diagnostic, prognostic, predictive, or safety biomarkers. Currently, during COVID-19, researchers are looking into inflammatory biomarkers and their intensity throughout pregnancy, and the research is still underway. Pre-eclampsia, hypertension, congenital heart disease, myocarditis, and myocardial infarction are the most common and serious complications during pregnancy, and these are the leading causes of mother and foetal morbidity. Various countries have different maternal mortality ratios, which I discuss in detail in my review article.

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