# Cardiometabolic Risk Factors and Pregnancy Outcomes: A Systematic Review

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#### ABSTRACT

A progressive pregnancy is associated with vast physiological and psychological alternations which are essential for a normal fetal growth. However, these alternations have association with several pregnancy complications and poor birth outcomes. The present study aims to review the association of the physiological and psychological alternations during pregnancy and birth outcomes. The literature has been done using Google Scholar, PUBMED and Research Gate. Besides, manual searching has also been done. It was observed that the development of Gestational Diabetes Mellitus (GDM), Pregnancy-induced hypertension (PIH), Preterm birth (PTB), Spontaneous cesarean section (CS), miscarriage, stillbirth, intrauterine growth restriction (IUGR), low birth weight (LBW), large-for-gestational age (LGA), small-for-gestational age (SGA), macrosomia, macrosomia and other congenital anomalies were associated with the non-modifiable and modifiable risk factors. Hence, early initiatives should be taken by modifying the daily lifestyle to reduce the detrimental effects of the harmful factors on pregnancy and birth outcomes.

Key words: Cardiometaobolic risk; Pregnancy; Birth outcomes; Nutrition; Asian Indians.

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## INTRODUCTION

With the headway of pregnancy, a rapid metabolic shift occurs to ensure the persistent supply of nutrients to the foetus from mother. During early pregnancy, increased insulin secretion increases the implementation of peripheral glucose, decreases the level fasting plasma glucose, enhances the glycogen storage in tissue and fat and deceases the lyposis. During this time increased accumulation of body fat is found which quickly breaks down in late pregnancy for fetal development<sup>1</sup>.

A pregnant woman develops physiological dyslipidemia which can be measured in laboratory by measuring serum total cholesterol (TC), triglycerides (TG), High-Density Lipoprotein Cholesterol (HDL-C), and Low-Density Lipoprotein Cholesterol (LDL-C). The gestational increase in maternal TG and Cholesterol is crucial for the production of essential fatty acids which regulates normal fetal growth and maturation<sup>2-4</sup>. Maternal cholesterol is essential for fetal brain development. Although the foetus can incorporate its required cholesterol, during early gestation, the placenta supplies a considerable amount through LDL-C, HDL-C and VLDL-C<sup>4</sup>. At late gestation period, the capacity of cholesterol production of the fetal tissues increases resulting rapid decrease in the maternal cholesterol<sup>3</sup>.

All these physiological alternations play a crucial role in the growth and development of foetus; however, studies suggest the association of these alternations with several pregnancy complications and adverse birth outcomes.

# **AIM OF THE STUDY**

The present study aims to review the association of maternal physiological and psychological responses during pregnancy with birth outcomes. Fifteen factors have been mentioned out of which three are non-modifiable factors and twelve are modifiable factors.

## **METHODOLOGY**

We did a literature search using Google Scholar, PUBMED and Research Gate to identify the relevant studies of the selected topic from the year 1980 to 2018. 49 papers were collected from PUBMED, 25 from Google Scholar and 8 from Research Gate among which 75 are full length papers and 7 are well-explained abstracts. These papers have been selected from the peer-reviewed journals with an impact factor >1. Local journal was not included in the study. The keywords used for the literature search are 'cardiometabolic risk', 'pregnancy', 'obstetric population', 'birth outcomes', 'advanced maternal age', 'teenage pregnancy', 'ethnic disparity', 'family medical history', 'dyslipidaemia', 'gestational hypertension', 'metabolic syndrome', 'obesity', 'gestational weight gain', 'high parity', 'psychological stress', 'sleep pattern', 'maternal diet', 'smoking', 'alcohol consumption', 'caffeine consumption'. Studies from all countries across the world were taken into consideration.

# **MAJOR FINDINGS**

## Non-modifiable factors

**Maternal age**: Both the early and advanced maternal age pregnancy has higher risk of complications and adverse birth outcomes. Majority of studies report maternal age >35 years to be associated with adverse obstetric outcomes; however, the onset of such incidences can be observed from the age of 30 years.

A study among 29,760 China observed women of  $\geq$ 40 years to be at higher risks miscarriage, chromosomal abnormality (aOR/adjusted odds ratio 12.3), perinatal loss, intrauterine fetal death (aOR 2.3), preterm birth (PTB), low birth weight (LBW), and large-for-gestational age (LGA) infants<sup>4</sup>. Again, a birth cohort study reported highest odds for obsteric complications among the mothers of  $\geq$ 45 years age and furthermore, multiparous women were at higher risk than the primiparous women of that group i.e. diabetes (aOR 2.58 vs 2.19), chronic hypertension (CH) (aOR 4.89 vs 3.70), pregnancy-induced hypertension (PIH) (aOR 2.13 vs 1.55), and infant death<sup>5</sup>. Another study also showed >8fold risk of gestational diabetes mellitus (GDM) among mothers of >40 years age<sup>6</sup>. Another study also documented 1.7fold risk of LBW among the mothers of 35-49 years age<sup>7</sup>. A systematic review and meta-analysis again concluded that mothers with advanced age have higher risks of SGA, LBW, PTB, neonatal death, pre-eclampsia (PE), and GDM (OR/odds ratio 2.85)<sup>8</sup>.

A hospital-based cross-sectional study from Nagpur, India reported the teenage mothers to have higher risk of stillbirth (OR 2.32), preterm delivery (OR 10.24), LBW, toxaemia (OR 2.88), eclampsia (OR 8.28), fetal distress, cephalopelvic disproportion (OR 8.92) and retained placenta than the adult mothers<sup>9</sup>. A hospital-based retrospective cohort study from Nepal reported teenage mothers to have higher odds for very PTB (OR 3.02), LBW, small-for-gestational age (SGA) infants, stillbirth and neonatal death (OR 2.04)<sup>10</sup>. **Ethnicity:** 'Ethnicity' can be defined as "belonging to a social group that has a common natural cultural pattern" <sup>11</sup>. Wide ranges of disparities of obstetric outcomes are found between the women of different ethnic groups. Based on some well-explained studies the vulnerability of hazardous pregnancy outcomes in different ethnic groups are mentioned in Table 1<sup>12-17</sup>.

**Family medical history:** From few decades the family history has gained notable importance in the clinical and research practice for the risk assessment and management of diseases. The gene activities cannot be changed but the severity and occurrence of chronic diseases can be controlled by modifying the lifestyle and unhealthy behaviours. It is evident from many studies that family history of diseases like Cancer, Diabetes Mellitus, and Cardiovascular diseases etc has positive association with the occurrence of many pregnancy complications causing poor birth outcomes.

A study from Netherlands revealed doubled risk of PE among the mothers with  $\geq 1$  first degree relatives with hypercholesterolemia and/ or hypertension doubled the risk of PE<sup>18</sup>. Another study revealed higher risk of severe PE among the women with positive family history (RR/relative ratio 4.3)<sup>19</sup>. A study from South India reported >4fold risk for GDM among the mothers with a family history of diabetes<sup>20</sup>. Another study reported doubled risk for PE and transient hypertension in pregnancy among the women having >2 family members having hypertension and heart disease or stroke of >2 family members threefolded the risk of PE<sup>21</sup>. Another study from Ethiopia reported family history of hypertension as a dominant risk factor for developing PE (aOR 11.16); besides, family history of diabetes also showed strong association with the development of PE (aOR 6.17)<sup>22</sup>.

## **Modifiable factors**

**Dyslipidaemia:** A progressive pregnancy is characterized by increased level of insulin, decreased level of fasting blood glucose and dyslipidemia. All these alternations are integrated and favor normal fetal growth. But these alternations are also associated with different pregnancy complications and poor birth outcomes. On this account, a few studies with essential findings are presented in Table  $2^{23-28}$ .

**Hypertension:** According to Australian Society Consensus Statement (2), hypertension during pregnancy can be defined as a Systolic Blood Pressure/SBP  $\geq$ 140 mmHg and/or a Diastolic Blood Pressure/DBP  $\geq$ 90 mmHg respectively. This pregnancy-induced hypertension can be further divided into four categories represented in Table 3<sup>29</sup>.

A population-based study from Canadian province of Nova Scotia reported women with GH, PE and CH were 1.5, 2.5 and 3.3 times more prone to SGA and >3fold risk of stillbirth was found among the women with CH<sup>30</sup>. A prospective study from UK noticed >2fold risk of LBW and >3fold risk of PTB among the mothers with superimposed PE<sup>31</sup>. Another study from Indonesia again reported doubled risk of SGA and LGA infants, and very LBW (aOR 8.68) and LBW infants (aOR 5.71) were observed among the severe preeclamptic mothers<sup>32</sup>. Again, a study reported nearly doubled risk of PTB among the preeclamptic mothers<sup>33</sup>. A prospective observational study also observed >2fold risk of PTB among the hypertensive women and >8fold risk among the women with CH<sup>34</sup>.

**Metabolic syndrome:** Gerald Reaven introduced the concept of Metabolic syndrome (MS) as an aggregation of independent, coronary heart disease risk factors in an individual including insulin resistance, hypertension, hypertriglyceridemia and low HDL cholesterol. In addition, Kalpan suggested that the visceral obesity as another factor of the syndrome. The association of these factors with several pregnancy complications and poor birth outcomes is evident from many studies.

A prospective cohort study from Greece reported significant association of PTB (RR 2.24), and IUGR (RR 3.67) among the MS mothers<sup>35</sup>. Higher

prevalence of macrosomia, stillbirth and any poor perinatal outcome was observed among the MS mothers than the non-MS mothers, in a cross-sectional study from South-central Africa<sup>36</sup>. Another multicentre prospective cohort study revealed higher risk of GDM (RR 3.71), SGA and LGA, spontaneous PTB and PE among the MS mothers<sup>37</sup>. A retrospective cohort study from Netherlands documented 3.77fold risk of recurrent PE among MS mothers<sup>38</sup>. A retrospective cohort study from Ontario reported 3.1, 5.5 and 7.7fold risk of placental dysfunction with one, two, and ≥three factors of MS<sup>39</sup>.

Overweight and obesity: Overweight or obesity in women, is more susceptible for infertility. Even if they conceive, most of the pregnancies are associated with many complications and the risk of such complications increases with the overt obesity. A populationbased cohort study from Sweden showed higher odds for PE (aOR 5.74), stillbirth (aOR 4.02), CS (aOR 2.90), shoulder dystocia (aOR 5.31), meconium aspiration (aOR 5.07), fetal distress (aOR 2.99), early neonatal death (aOR 5.63) and LGA (aOR 4.16) among the morbid obese women<sup>40</sup>. Again a population-based cohort study from Canada reported increasing odds for GDM (aOR 2.80 vs 5.43), PIH (aOR 2.38 vs 3.00), antepartum venous thrombolism (aOR 2.17 vs 4.13), induced labour (aOR 1.94 vs 2.77), CS (aOR 1.60 vs 2.46) and wound infection (aOR 1.67 vs 4.79) from moderate to severe obesity<sup>41</sup>. Another population-based cohort study reported increasing odds for GDM (aOR 3.5, 7.7 and 11.0, respectively), PE (aOR 1.9, 3.0 and 4.4, respectively), macrosomia (aOR 1.6, 2.2 and 2.7, respectively), and stillbirth (aOR 1.4, 1.6 and 1.9, respectively) from overweight to obese and severe obese women<sup>42</sup>. Similar magnitude of risk for GDM, CS, macrosomia and LGA among overweight and obese women were found in a study from China43. Another study revealed ~2fold risk of PTB among the obese women and risk of fetal death increased from lean to overweight and obese44.

**Gestational weight gain:** In 2009, the Institute of Medicine (IOM) published a revised guideline of gestational weight gain (GWG) based on the pre-pregnancy BMI, using WHO BMI cutoff points<sup>45</sup> (Table 4). Although the recommendations were based on the American population; many studies reported its potentiality to fit in other populations also.

A systematic review and meta-analysis documented >3 units increasing gestational BMI to double the risk of LGA, GDM, macrosomia and CS. Women with normal pre-pregnancy BMI with notable increase in gestational BMI at first pregnancy had higher risks of LGA infants (aOR 2.10) and GDM (aOR 3.10)<sup>46</sup>. A study from Chennai again reported higher odds for PTB, CS, macrosomia and PE (OR 2.1, 1.9, 1.6 and 2.8, respectively) among the women with GWG above the IOM recommendation. Overweight women excess GWG had higher risk of CS, macrosomia (OR 2.3) and PE (OR 2.8) also<sup>47</sup>. Higher risk of PE, CS, HBW and long birth length (RR 4.84, 3.94, 2.12 and 2.33, respectively) among the women with high GWG was obtained from another study from Thailand<sup>48</sup>. A cohort study from Australia reported excess GWG, overweight and obese pre-pregnancy BMI to develop pregnancy complications (aOR 2.15, 2.16 and 3.33, respectively)<sup>49</sup>. Another study suggested high risks of hypertension, CS, induced labour, macrosomia and LGA (OR 4.8, 3.6, 3.7, 4.0 and 4.7, respectively) for GWG ≥15.0 kg50.

**Parity:** The link of maternal high parity and various obstetric complications is well-documented in several studies and it is one of the most commonly mentioned factors related to pregnancy related complications in obstetric researches.

A study from USA observed association of higher parity with greater odds for LBW, PTB, SGA and LGA infants<sup>51</sup>. Another study reported 3fold risk of developing GDM among the multiparous women<sup>6</sup>. Another study from UK revealed doubled risk of late stillbirth among

Table 1: Racial disparities in high risk pregnancy and birth outcomes.								
Authors	Year	Place	Pregnancy complications and outcomes	Racial disparity				
Singh GK et al <sup>12</sup>	1994	New York, US	LBW	OR 2.48 for Black, 1.09 for American Indian, 1.15 for Philipino, 0.79 for Japanese and 0.78 for Chinese.				
Gould JB et al <sup>13</sup>	2003	California, US	PIH	OR 2.63 for US-born White, 2.77 for foreign born Indian, 3.65 foreign born Mexican and 1.86 for US-born Black.				
			PE/ eclampsia	OR 4.90 for US-born White, 7.55 for foreign born Indian, 6.28 foreign born Mexican and 3.80 for US-born Black.				
			Placenta previa/ abrupt	OR 9.66 for US-born White, 4.30 for foreign born Indian, 9.63 foreign born Mexican and 7.75 for US-born Black.				
Rosenberg TJ et al <sup>14</sup>	2005	US	Chronic diabetes	aOR 2.46 for non-hispanic Blacks, 5.31 for non-hispanic Whites, 1.22 for non-hispanic Asians, and 2.58 for Hispanics.				
			GDM	aOR 1.40 for non-hispanic Blacks, 1.15 for non-hispanic Whites, 1.00 for non-hispanic Asians, and 1.67 for Hispanics.				
			СН	aOR 8.11 for non-hispanic Blacks, 8.82 for non-hispanic Whites, 17.58 for non-hispanic Asians, and 8.57 for Hispanics.				
			РІН	aOR 11.70 for non-hispanic Blacks, 11.51 for non-hispanic Whites, 18.11 for non-hispanic Asians, and 6.66 for Hispanics.				
Tsai PS et al <sup>15</sup>	2013	Hawaii, US	GDM	OR 1.71 for Hawaiian/Pacific islanders, 1.88 for Filipino, and 1.53 for other Asians.				
			Macrosomia	OR 1.19 for White, 1.52 for Hawaiian/Pacific islanders, 3.18 for Filipino, and 1.78 for other Asians.				
James-Todd T et al <sup>16</sup>	2014	New York, USA	PE	aOR 1.50 for non-hispanic Black, 1.46 for Hispanic, 0.59 for East Asian, and 0.75 for South Asian.				
			Spontaneous preterm delivery	aOR 1.28 for non-hispanic Black, 0.99 for Hispanic, 0.61 for East Asian, and 0.90 for South Asian.				
			Medically indicated preterm delivery	aOR 1.65 for non-hispanic Black, 1.72 for Hispanic, 0.92 for East Asian, and 0.68 for South Asian.				
			SGA	aOR 1.94 for non-hispanic Black, 1.48 for Hispanic, 0.69 for East Asian, and 2.29 for South Asian.				
			LGA	aOR 0.62 for non-hispanic Black, 0.82 for Hispanic, 0.61 for East Asian, and 0.53 for South Asian.				
Ghosh G et al <sup>17</sup>	2014	US	Gestational hypertension (GH)	aOR 0.80 for non-hispanic Black, 0.66 for Hispanic, 0.61 for Asian/Pacific islanders and 0.71 for multiracial/others.				
			Mild PE	aOR 1.26 for non-hispanic Black, 1.10 for Hispanic, 0.62 for Asian/Pacific islanders and 0.92 for multiracial/others.				
			Severe PE	aOR 1.31 for non-hispanic Black, 0.83 for Hispanic, 0.96 for Asian/Pacific islanders and 0.92 for multiracial/others.				
			Eclampsia	aOR 0.81 for non-hispanic Black, 0.73 for Hispanic, 0.96 for Asian/Pacific islanders and 0.89 for multiracial/others.				
			СН	aOR 1.43 for non-hispanic Black, 0.66 for Hispanic, 0.49 for Asian/Pacific islanders and 0.89 for multiracial/others.				
			Superimposed PE	aOR 1.96 for non-hispanic Black, 1.08 for Hispanic, 0.53 for Asian/Pacific islanders and 1.32 for multiracial/others.				

lable 2: Maternal dyslipidaemia and birth outcomes.						
Authors	Year	Area of study	Nature of study	Major findings		
Enquobahrie DA et al <sup>23</sup>	2004	Seattle, Tacome, and Washington	Prospective cohort	Higher level of TG (13.6%), TC (3.9%), LDL-C (10.4%) and LDL/HDL (15.5%) among the pre-eclampsic mothers. High concentration of TC, LDL, LDL/HDL and TG increased the risk of PE by 3.60, 2.91, 3.98 and 4.15 times, respectively.		
Nederlof M, et al <sup>24</sup>	2015	Amsterdam	Prospective community- based cohort	Maternal abnormal TG level increased the risk of major nonsyndromic congenital anomalies (including cardiovascular anomalies) of offsprings (estimated probability= 3.6 for 5th percentile and 2.9 for 95th percentile).		
Li G et al <sup>25</sup>	2015	Beijing, China	Prospective cohort	Significant increased level of TG, TC, LDL-C, LDL/HDL ratio among the GDM mothers than the control mothers. aOR for GDM was 1.8fold and 2.7 among the lean and obese mothers, respectively.		
Jin W et al <sup>26</sup>	2016	China	Population- based	Late pregnancy high TG level increased risk of GDM (aOR 1.37), PE (aOR 1.50), intrahepatic cholestasis of pregnancy (aOR 1.28), PTB (aOR 1.04), LGA (aOR 1.13), macrosomic (aOR 1.19) infants.		
Hashemipour S et al <sup>27</sup>	2017	Iran	Cohort	Along with GDM 1SD increase of maternal TG level increases the risk of macrosomia 4.2 and 1.9 times in normal and overweight women, respectively.		
Ji Y et al <sup>28</sup>	2018	Boston	Prospective birth cohort	Maternal low HDL-C was found to be responsible for CS, LGA, prematurely born, LBW of offspring along with higher risk of ADHD.		

#### Table 2: Maternal dyslipidaemia and birth outcomes

Table 3: Australian Society Consensus Statement Classification of PIH.

Classification	Definition
Preeclampsia	Hypertension after 20th gestational week with one or more of the following- Proteinuria, renal insufficiency, liver disease, neurological problems, hematological disturbance and fetal growth restriction.
Gestational Hypertension	Hypertension alone appearing after 20th gestational week.
Chronic Hypertension	Presence or history of hypertension preconception or in the first half of pregnancy.
Preeclampsia superimposed on Chronic	Onset of preeclampsia in a woman with Chronic Hypertension.
Hypertension	

Table 4: IOM Recommendations of gestational weight gain based on pre-pregnancy BMI.

Pre-pregnancy BMI	BMI Range (kg/m2)	Total Weight Gain (kg)
Underweight	<18.5	12.5 - 18.0
Normal Weight	18.5- 24.9	11.5 - 16.0
Overweight	25.0- 29.9	7.0 - 11.5
Obese	≥30.0	5.0 - 9.0

multiparous women<sup>52</sup>. A prospective study from Turkey observed higher frequency of GDM among the multiparous mothers than the primiparous<sup>53</sup>. Again a cohort study documented higher frequency of GDM, GH, and spontaneous PTB, and induced labour, among the grandmultiparous mothers; neonatal ICU admission, congenital anomalies, LBW and low Apgar score at 5 minutes of infants was also frequent in this group<sup>54</sup>.

#### Modifiable lifestyle factors

**Psychological Stress:** Maternal psychological stress during pregnancy is a well-known modifiable risk factor which has adverse effect on pregnancy and poor maternal and fetal health conditions. A prospective cohort study documented higher risk of PTB among the women with higher pregnancy-related anxiety (RR 2.1), anxiety for life events (RR 1.8) and racial discrimination (RR 1.4)<sup>55</sup>. Another cohort study documented external stressors like food insecurity, child illness, crowded home, unemployment and poor coping skill to ~3fold the odds of LBW<sup>56</sup>. A study from Brazil reported maternal distress to double the risk of LBW and prematurity<sup>57</sup>. Another case-control study reported ~3fold risk of spontaneous birth among the women with high life event stress<sup>58</sup>. A study revealed ~3fold odds for pregnancy losses among the women with ≥1 negative life events stress<sup>59</sup>.

**Sleep pattern:** Sleep disturbances is a common phenomenon of progressing pregnancy affecting both maternal and fetal poor birth

outcomes as suggested by the researches since decades. A prospective cohort study from New Zealand reported >3fold risk of LGA for pregnancy-onset breathing pauses, 2-3fold risk of SGA for sleep disturbance for nasal congestion and breathing pauses and >3fold risk of fetal distress due to sleep disturbances for leg twitching<sup>60</sup>. Another study revealed 3.5fold risk of PE for snoring, 5fold risk of LBW and 8fold risk of stillbirth for supine sleep of mothers<sup>61</sup>. A cross-sectional study from USA also reported women with frequent snoring to double the risk of hypertension and/or PE , GDM and unplanned CS. Besides, frequent gasping doubled the risk of hypertension and/or PE. Sleeping disordered breathing had a 2fold risk of GDM, and unplanned CS<sup>62</sup>. Again, a study reported >2fold odds for GDM among the mothers with sleep-disordered breathing, and >3fold odds with frequent snoring<sup>63</sup>.

**Diet:** Maternal dietary pattern is a matter of great concern as malnutrition of mothers during pregnancy may lead to poor fetal health along with several morbid conditions and mortality. A cross-sectional survey from Ghana reported increased risk of LBW with eating outside home, pica practice and avoidance of fish consumption<sup>64</sup>. A prospective study from Europe stated higher dioxin-diet of mother to be associated with 121 gram reduction in infants' birth weight<sup>65</sup>. A Norwegian mother-child cohort study suggested increasing risk of PE with lower score on vegetables, plant foods and vegetable oil consumption and higher score on processed meat, salty snacks and sweet drinks consumption<sup>66</sup>. Another multi-ethnic Asian cohort study

reported higher score on the vegetable-fruit-rice-based diet and low score on seafood-noodle-based diet and pasta-cheese-processed-meat diet to increase the risk of GDM<sup>67</sup>. Another study also reported higher risk of developing PE among the women with high sugar content food consumption<sup>68</sup>. Higher prevalence of PIH among the mothers with high adherence to traditional diet and low adherence to Mediterranean diet were found in another study<sup>69</sup>.

**Smoking:** The International Agency for Research on Cancer has detected more than 10 Cancer causing chemical from tobacco/cigarette smoke<sup>70</sup>. The harmful effect of maternal smoking before and during pregnancy on both mother and foetus is reported by many studies. An epidemiological study from Canada reported increasing risk of LBW and PTB with increasing number of cigarettes per day<sup>71</sup>. A population-based cohort study from Netherlands showed >3fold risk for LBW and the increasing risk of PTB with the number of cigarettes during late pregnancy<sup>72</sup>. A historical cohort study reported reduced birth weight and ~2fold odds for LBW and IUGR for maternal inter-pregnancy smoking<sup>73</sup>. Besides, higher concentration of LDL and Malondialdehyde and lower concentration of total antioxidant capacity of amniotic fluid was observed among the smoking mothers<sup>74</sup>.

Alcohol consumption: Inter-pregnancy alcohol consumption is unsafe as it passes through the mother's blood to the foetus causing several complications and several lifelong physical, behavioral, and intellectual disabilities including Fetal Alcohol Syndrome. A prospective investigation from US reported increasing risk of PTB with mild to moderate intake (OR 2.88 to 2.96)<sup>75</sup>. A case-control study from Italy reported  $\geq$ 3 die unit maternal inter-pregnancy alcohol intake to double the risk of SGA<sup>76</sup>. In another study from New Zealand,  $\geq$ 1 alcoholic drinks/day during pregnancy increased the risks of LBW (aOR 4.81) and PTB (aOR 2.51)<sup>77</sup>. A study from New York revealed >2fold risk of spontaneous abortion among the mothers with inter-pregnancy alcohol consumption<sup>786</sup>.

**Caffeine consumption:** Caffeine (1,3,7-trimethylxanthine), commonly known as "Ancient wonder drug" is declared as a harmful food in addition with alcoholic beverages by Food and Drug Administration (2010)<sup>79</sup>. Heavy caffeine intake reduces the capacity of reproduction and delay the conception by hormone alternation. A case-control study from California reported maternal inter-pregnancy heavy caffeine consumption to threefold the risks LBW, IUGR and PTB<sup>80</sup>. A study from US reported >2fold risk of LBW and IUGR for ≥300 mg/day early pregnancy maternal caffeine consumption<sup>81</sup>. Another study from USA reported maternal early pregnancy caffeine consumption >300 mg/day along with nausea is associated with 5.4fold risk of spontaneous abortion<sup>82</sup>.

# DISCUSSION

With the growing industrialization, pregnancy at the later stage of reproductive period has become more common among the women. To attain better education and career, the women prefer to get married or conceive at a later age. On the other hand, pregnancy during adolescence or, teenage pregnancy is also a very common event in the low literate and poor socio-economic societies. To become pregnant at early or advanced age is a matter of personal choice; however, it is evident from the research studies that with both the early and advanced maternal age, pregnancy becomes more susceptible to several complications including GDM, PIH, pregnancy loss, PTB, premature, LBW babies with other birth defects.

GDM is an eventual sequel of IR and a serious pregnancy burden which is accounted to affect 14.0% of pregnancies across the world. On the account of the risk factors of GDM, epidemiological studies are exasperated by diverse confounding factors which obscurate to find out any particular underlying mechanism for the attribution of this health burden. However, the common risk factors include overweight, obesity, advance maternal age, family history etc. All these factors also trigger dyslipidaemia which is another principle risk factor for cardiovascular dysfunction causing morbidity all over the world. A progressive pregnancy is characterized by dyslipidemia which favors normal fetal growth. But these alternations are also associated with different pregnancy complications and poor birth outcomes (Table 2).

Hypertensive disorders during pregnancy include chronic and gestational hypertension, pre-eclampsia and eclampsia which convolute ~10% pregnancies worldwide leading to morbidity and mortality. Hypertension is a component of MS along with dyslipidaemia and obesity and it degenerates blood flow to heart and brain causing heart attack, stroke, heart failure, Angina and peripheral artery disease. The identified risk factors include obesity, a family history of hypertension, alcohol intake, sleep deficiency, unhealthy diet pattern, psychological stress and smoking. So, beyond a doubt, lifestyle play crucial role in the development of PIH. Hence, self-initiative is the key solution to reduce the magnitude of such risks.

Overweight and obesity are the conventional risk factors inducing dyslipidaemia, MS, hypertension, IR and other cardiovascular dysfunctions. Gestational weight should be a matter of concern and gained as per pre-pregnancy BMI. Weight gain may be predisposed by the genetic factors but diverse environmental factors like socioeconomic condition, diet pattern, physical inactivity, stress, sleep disorder etc. Several adverse pregnancy outcomes have been documented in epidemiological studies; hence, recommended GWG is of special concern to eliminate the detrimental effects.

Maternal diet with high saturated and trans-fat and cholesterol is another evident risk factor for all these pregnancy complicating conditions. Excess cholesterol in blood causes atherosclerosis leading to heart attack. Excess TG and LDLC are the main artery blocking plaques which are eliminated by HDLC. Smoking, heavy alcohol and caffeine consumptions upsurge such risks. Choosing own diet is a matter of personal choice hence, self-initiative is essential to eliminate the diet associated fatal effects on pregnancy outcomes. Besides, quitting smoking and alcohol is the best solution as prevention is always better than intervention.

Maternal psychological stress during pregnancy is a well-known modifiable risk factor which has adverse effect on pregnancy and poor maternal and foetal health condition as well. During the gestational period maternal endocrine, nervous and immune systems are calibrated to support a successful pregnancy, but these processes are interrupted by the psychological distress. In long-term consequences psychological stress increases the risk of atherosclerosis eventuating cardiac instability and myocardial ischemia. Psychological stress increases the secretion of stress hormones which increases the heart rate and BP contributing to endothelial dysfunction.

Psychological stress often leads to sleep deficiency. It is caused by the physical, hormonal and physiological alternations associated with pregnancy and about 66-94% of women face the sleeping disorders which increase with the progress of pregnancy. However, this may produce substantial threat to the cardiovascular health of both mother and foetus. Deficient sleep obstructs the optimum regulation of the stress hormones which leads to hypertensive disorders, coronary heart disease, dyslipidaemia etc. Therefore, 6-10 hours' sleep is recommended for a healthy pregnancy survival.

The present review attempts to elucidate the contribution of cardiometabolic risk factors to pregnancy and birth outcomes. Cardiac dysfunction accounts for 10% of obstetric death worldwide and its long-term consequences includes resurrection of the morbid conditions in both mothers and child in future life. Hence, special care should be given on the raised issues for a healthy pregnancy survival.

## LIMITATIONS

The limitations of this review are the non-availability of sufficient information from all countries of the world and it covers mostly the developed countries. Scarcity of data mainly from developing countries is denoted in the review. It may be due to lack of inquisitiveness of researchers or the information is yet not published. Hence, a comprehensive review is required covering both developed and developing country' scenario of pregnancy complications, birth outcomes and the underlying mechanism of modifiable and nonmodifiable factors.

## **SCOPE OF FUTURE STUDIES**

Database is very limited from developing countries (example- India); hence in future some comprehensive studies must be concentrated on the obstetric population of these countries to find out the effect of maternal anthropometry, metabolic profile, hemodynamic factors/ blood pressure, dietary intake, and psychological stress on birth outcomes. The outcome information of such studies will also help to find out the probable early prevention of many non-communicable diseases among the pregnant mothers, neonates and young adults.

# **CONFLICTS OF INTERESTS**

There is no conflict of interest so far as authorship and funding is concerned.

# **AUTHORSHIP**

MM was responsible for preparation of the draft manuscript. AG was responsible for the study design, final version of the manuscript.

# ETHICAL STATEMENTS

The study was approved by the University Research Board.

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