**MORBID OBESITY AND ITS IMPLICATIONS ON PREGNANCY**

**INTRODUCTION**

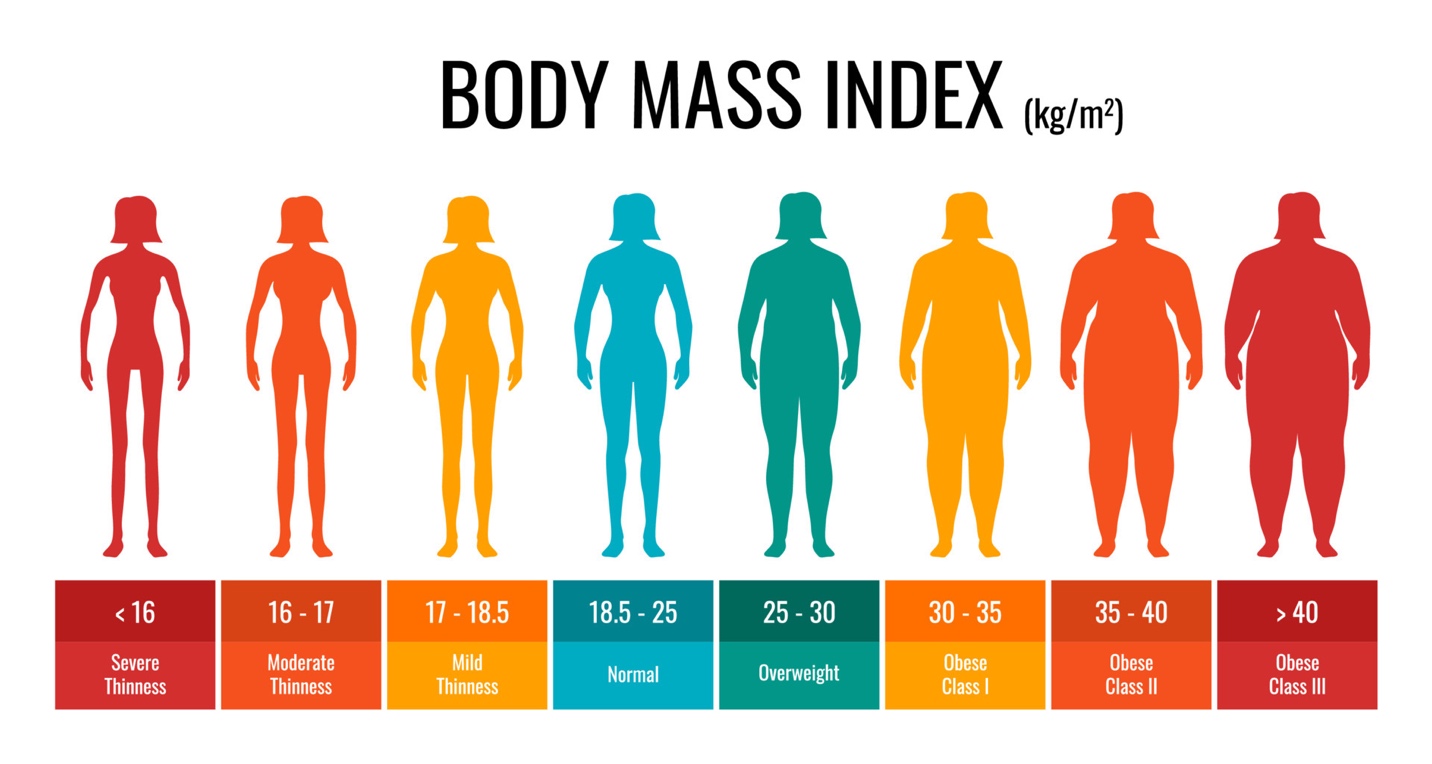
Obesity has been defined as excessive body fat that often results in impairment of health and metabolism. A body mass index (BMI) of >25 is considered overweight and >30 is obese. Obesity is now dramatically on the rise in low- and middle-income countries and was declared “a major public health problem” in 20001 The worldwide prevalence of obesity has nearly tripled between 1975 and 2016. It was estimated by WHO in 2016 that 39% of adults aged ≥18 years (39% men and 40% women) were overweight and 13% were obese which is nearly around 650 million adults worldwide2 of these 300 million being women.

In the United States, over 30% of reproductive age group women are obese3,4

As per the national family health survey-5NFHS-5 data (2019-21), 23% of women and 22.15 of men are overweight in India. While 40% of women and 12% of men are abdominally obese in the country5. Rising rate of obesity in women of reproductive age group has negatively impacted both the mother and fetus and pose a challenge for maternal care. 0ne in five women of reproductive age in the UK is obese while about 4 in 10 women in India have a waist circumference higher than the prescribed cut-off mark for abdominal obesity5.

Obesity has a negative impact on fertility and is associated with increased incidences of congenital malformations and early abortions.

|  |  |
| --- | --- |
| Obesity | BMI (kg/m2) |
| Class I | ≥30 to <35 |
| Class II | ≥35 to <40 |
| Class III (morbid obesity) | ≥40 |
| Class IV (super obesity) | ≥50 |



**PATHOPHYSIOLOGY**

Excessive adipose tissue in obesity functions as an endocrine tissue. Excess adipose tissue is also associated with inflammation and linked to insulin resistance and cardiovascular diseases. Obese females have high levels of C-reactive protein (CRP) and interleukin -6 (IL-6)6. High CRP levels have shown to cause endothelial dysfunction and impaired insulin sensitivity in non-pregnant population. Hence, inflammation caused by obesity may be a cause of increased risk of pre-eclampsia, gestational diabetes and thromboembolism in pregnancy7. Maternal serum leptin which is released by adipose tissue is elevated in obese women. Elevated leptin levels are associated with placental ischemia and endothelial dysfunction.

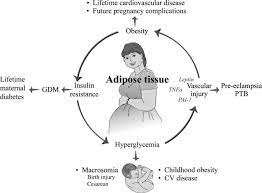


image 18: effects of obesity

**MATERNAL EFFECTS**

*ANTEPARTUM-*

PRE-ECLAMPSIA

There is a 2-3-fold increased risk of pregnancy induced hypertension (PIH) in women with obesity. Insulin resistance, endothelial cell activation, dyslipidemia and raised cytokines have been implicated as link between obesity and high blood pressure9.

A study stated that risk of pre-eclampsia doubles with each 5kg/m2 increase in BMI10.

GDM

Maternal obesity is directly related to an increased risk of developing GDM with an odds ratio (OR) of 2.1 in overweight, 3.6 in obese and 8.6 in severely obese women11

Interpregnancy weight change is important in subsequent development of GDM> an increase in BMI of 1-2 units between two pregnancies has been shown to increase the risk of GDM by 20-40%12

Obese females with GDM are more likely to require insulin for adequate glycemic control.

THROMBOEMBOLISM

Maternal obesity has four times greater risk of developing venous thromboembolism compared to non-obese counterparts with maximum risk being in the post-partum period. RCOG recommends that all women with class 3 obesity (BMI ≥ 40) should be considered for prophylactic LMWH for 10 days after delivery13.

CARDIOVASCULAR

Maternal obesity increases the risk of peripartum cardiomyopathy. Leptin has a role in vascular dysfunction leading to cardiovascular compromise and leads to transition to a chronic nonischemic cardiomyopathy14.

METABOLIC SYNDROME OF PREGNANCY

Obese females have a higher proportion of saturated subcutaneous fat and have a tendency to accumulate more fat centrally than lean women. Central obesity is linked with adverse metabolic outcomes including gestational hypertension, pre-eclampsia and GDM. In normal pregnancy, initially insulin secretion increases without much change in insulin sensitivity. Later on, insulin mediated glucose utilization is decreased thus increasing insulin secretion by several times.

In pregnant females with obesity, there is loss of reduction of fasting glucose in early pregnancy and a significant increase in peripheral and hepatic insulin resistance. Also, in obesity there is a chronic low-grade inflammation state which causes increase in insulin resistance and hence a lower threshold to develop metabolic syndrome than their lean counterparts15.

RESPIRATORY

Obesity accentuates the effect of elevated intra-abdominal pressure and reduction in lung volumes associated with pregnancy.

The incidence of obstructive sleep apnea (OSA) is greater in obese females. It is recommended that all women with class III or more obesity should be screened for OSA prior to pregnancy.

Pregnant women with OSA regardless of BMI are more likely to develop pre-eclampsia, cardiomyopathy and pulmonary embolism16.

ENDOCRINOLOGY

Maternal obesity is a significant risk factor for development of gestational diabetes. Vitamin D deficiency is more common in obese females and pre-pregnancy obesity is linked with both maternal and neonatal vitamin D deficiency17. It is reported that about 60% of women with obesity have vitamin D deficiency as compared to 35% of normal weight women18.

Hypovitaminosis D is associated with increased risk of developing pre-eclampsia, worsening glucose tolerance, low birth weight and increased cesarean section rates19.

GESTATIONAL WEIGHT GAIN

Around 40-50% of women with obesity gain greater than the recommended weight during pregnancy which is a risk factor for postpartum weight retention and metabolic dysfunction. The Institute of medicine (IOM) recommends a weight gain of 11-20lbs for all patients with obesity throughout the course of their pregnancy20.

Limited weight gain may be beneficial in reducing risk of cesarean section and postpartum weight retention but there is also known risk of SGA infants. Hence it is better to determine BMI at patients first prenatal visit with targeted counseling regarding recommendations for weight gain.

ANTENATAL ULTRASOUND AND FETAL WELL BEING ASSESSMENT

Ultrasound detection of congenital anomalies has a lower sensitivity in obese women. Also due to increased volume of distribution measurement of serum analytes can be altered, and cell free fetal DNA screening is more likely to be indeterminate.

A detailed second trimester ultrasound for all obese patients with additional techniques like transvaginal ultrasound or placing the probe over maternal umbilicus is recommended21.

MRI can be employed for patients with obesity but due to limited availability and high cost it is routinely not offered22.

Leopold maneuvers and vaginal examination may not be accurate when assessing fetal presentation in pregnant women with obesity making ultrasound necessary in such situations.

Localization and tracing of fetal heart rate with external fetal monitor may be inadequate in obesity. Recently GE Monica Novii Wireless Patch system has shown to improve fetal heart tracings in women with obesity23.



*INTRAPARTUM-*

PROLONGED LABOUR

Obesity is a risk factor for increased chances of need for induction of labor, prolonged labor, increased chances for need of ARM, shoulder dystocia, post-partum hemorrhage and increased cesarean section rate. Rate of successful VBAC is also much lower in obese women24

ANAESTHETIC CONSIDERATIONS

Obesity is associated with increased risk with induction of general anesthesia due to edema of epiglottis and also there is difficulty in gaining venous access.

Difficult epidural anesthesia with increased chances of epidural failure. Incidence of failed regional anesthesia in super obese population is around 12-17%25

Intraoperative BP monitoring, patient positioning and post operative analgesia is also a matter of concern in obese women.

CESAREAN SECTION

Up to 50% of women with super obesity undergo cesarean section while the rate in women with BMI 40-49.9 kg/m2 is 43% and in those with BMI 30-39.9kg/m2 is 33%.26

Prophylactic antibiotics are generally recommended in higher doses for obese women as it has been shown that the BMI of patient is inversely proportional to concentration of cefazolin in adipose tissue at the time of skin incision27.

Abdominal skin preparation is recommended with ≥2 chlorhexidine-alcohol swabs.

NICE recommends that all women having a cesarean section with over 2 cm of subcutaneous fat should have suturing of fat to minimize risk of wound infection and separation 28.

Cesarean section can be associated with hemodynamic instability and massive hemorrhage.

There is an increased risk of hypoventilation in obese females

*POSTPARTUM-*

GENERAL

It includes safe transfer, repositioning, hygiene maintenance etc.

Patients must be encouraged to mobilize early and frequent ambulation to minimize risk of thromboembolism.

Impaired wound healing with higher rates of wound infection has been seen more commonly in women with obesity. There is a 30-50% risk of wound complications in women with BMI>50kg/m2.

BLEEDING RISK

Obesity is a risk factor for postpartum hemorrhage irrespective of the mode of delivery. Prophylactic use of uterotonics in such patients can be considered29,30.

VTE

Pregnancy itself is a risk factor for development of venous thromboembolism and with obesity in pregnancy the risk further accentuates with an OR 5.3 in women with BMI> 30kg/m2.31

ACOG recommends mechanical compression devices and pharmacological thromboprophylaxis with additional risk factors like known thrombophilia or prior VTE events32.

The ACCP recommendations are based on Caprini score which is a risk assessment tool that includes swollen legs, smoking, diabetes, BMI> 25kg/m2, blood transfusion and duration of surgery >45 minutes, patient confinement to bed >72 hours, etc33.A score of ≥ 5 warrants use of mechanical compression devices and pharmacological thromboprophylaxis in combination.

RCOG recommends all women with class 3 obesity should be considered for prophylactic LMWH in appropriate doses for their weight for 10 days after delivery.

BREASTFEEDING

Breastfeeding helps in decreasing the risk of obesity and diabetes in the offspring and also helps in post-partum weight loss. The overall risk of diabetes, hypertension, cardiovascular diseases, ovarian and breast cancer also decreases in mother34.

Obesity is associated with reduced rates of breastfeeding and particularly delayed stage II lactogenesis. The likely cause being elevated baseline progesterone levels in obese women, difficult positioning and impaired prolactin response to neonatal suckling35.

CONTRACEPTION

Contraceptive counselling is an important component of antenatal care in obese women with emphasis on long-acting reversible contraception (LARC)

Estrogen containing contraceptives have an added risk of VTE in obese women and hence are not recommended. Women with obesity have a 24 times higher risk of VTE when using combined hormonal contraceptives36.

The US CDC and MEC for contraceptive use designates combined hormonal contraception as category 2 after 6 weeks postpartum in obese women without any risk factors for VTE and cardiovascular disease36,37

Non hormonal or progestin only methods are safe in obesity (MEC 1)

LARC methods (IUD, Nexplanon) are recommended as first line contraception by ACOG36,37

**FETAL EFFECTS**

PREGNANCY LOSS

Women with obesity have an elevated risk of spontaneous abortion and recurrent miscarriages38.

Risk of abortion increases by 30% with a BMI of >3039.

FETAL ANOMALIES

Maternal obesity increases the risk of neural tube defects (NTD), orofacial defects, cardiac and limb reduction defects in neonates39,40. A study conducted by Watkins et al showed that each excess BMI of 1kg/m2 resulted in a 7% increased risk of NTD41. This may be related to decreased folic acid levels reaching the fetus due to decreased maternal absorption. Obese females have an increased chances of having babies with congenital heart defects (CHD) like TOF, septal defects, TGA etc. There is also an increased risk of diaphragmatic hernia42

GROWTH ABNORMALITIES

Pre-pregnancy obesity is a risk factor for large for gestational age infants as well as fetal macrosomia43. There is also evidence that severe FGR is common in women with obesity and umbilical artery doppler abnormalities are more frequent with increasing obesity44.

MACROSOMIA

Fetuses of obese females are 2-4 times more likely to be large for gestational age with higher percentage of body fat45.Macrosomia is an independent risk factor for shoulder dystocia during labor, risk of injuries due to difficult delivery and low Apgar score and arterial pH at birth.

PRETERM DELIVERY

Obesity is associated with increased risk of preterm delivery43

STILLBIRTH AND NICU ADMISSION

Late and unexplained fetal demise is more common in fetuses of obese mothers. Women with a BMI ≥50 have 5.7 times greater risk of stillbirth compared to normal BMI women at 39 weeks gestation and 13.6 times risk at 41 weeks46.

Rate of NICU admissions are also 3.5 times higher in babies born to obese mothers35.

**MANAGEMENT**

First line intervention – education and advice on diet and exercise. It is done at individual level including an MDT approach that involves a dietician and at population level via the role of public health education. Creating awareness about general principles regarding healthy eating and physical exercise as well as diet and activities in pregnancy and post-partum period.

Role of government and initiatives like healthy food vouchers and taxes on sugar containing food items.

Second line intervention- anti-obesity drugs or surgery

Three main category of anti-obesity drugs used in non-pregnant females

1. Orlistat: inhibits intestinal fat absorption
2. Sibutramine: reduces oral intake
3. Ephedrine: increases thermogenesis and metabolic rate

Metformin helps in weight reduction by increasing insulin sensitivity in peripheral tissues. Metformin and orlistat are US FDA category B drugs for use in pregnancy47.

Bariatric surgery is an option for women with severe obesity not responding to non-surgical methods48,49. Recommendations are to wait for period of 12-18 months after bariatric surgery before conceiving. Post bariatric surgery women will require nutritionist care in pregnancy as bypass surgery results in deficiencies of both micro-nutrients like iron, folic acid, vitamin B12, vitamin K etc.

Pregnancy also increases the risk of intestinal obstruction in these patients.

**KEY POINTS**

* Obesity is a global health problem and has significant effects on women of reproductive age group
* It is important to have a careful antenatal planning as obesity is associated with increased maternal and fetal risks.
* Pre-conception education and counselling along with proper care during pregnancy and post-partum period is key to successful maternal and fetal outcomes

Reference:

1. World Health Organization, Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. Geneva: World Health Organization: 2000.
2. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>.
3. Ogden C, Carroll M, Curtin L, McDowell M, Tabak C, Flegal K. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA*. (2006) 295:1549–55. doi: 10.1001/jama.295.13.1549
4. American College of Obstetricians and Gynecologists. Obesity in pregnancy: ACOG practice bulletin, number 230. *Obstet Gynecol.* (2021) 137:e128– 44. doi: 10.1097/AOG.0000000000004395
5. Abdominal obesity in India: analysis of the National Family Health Survey-5 (2019–2021) data Chaudhary, Monika et al.The Lancet Regional Health - Southeast Asia, Volume 14, 100208
6. Ryan EA, Enns L. Role of gestational hormones in the induction of insulin resistance. / ClinEndocrinol Metab. 1988;67:341-347
7. Freinkel N. Banting Lecture 1980. Of pregnancy and progeny, Diabetes 1980;29:10231035
8. <https://doi.org/10.1111/j.1552-6909.2008.00222.x>
9. Chu SY, Callaghan WM, Kim SY, et al. Maternal obesity and risk of gestational diabetes mellitus. Diabetes Care 2007:30:2070-2076.
10. O’Brien TE, Ray JG, Chan WS. Maternal body mass index and the risk of preeclampsia: a systematic overview. *Epidemiology*. (2003) 14:368– 74. doi: 10.1097/01.EDE.0000059921.71494.D1
11. Langer 0, Yogev Y. Xenakis EM, et al. Overweight and obese in gestational diabetes: the inspact on pregnancy outcome. Am J Obster Gynecol. 2005;192:1768-1776
12. Edwards LE, Hellerstedt WL, Alton IR, et al. Pregnancy complications and birth outcomes In obese and normal weight women: effects of gestational weight change. Obster Gynecol. 1996,87:4231-4237.
13. American College of Obstetricians and Gynaecologists'guidance. Obesity in Pregnancy Practice Bulletin Number 156, December 2015.
14. Taylor BD, Ness RB, Olsen J, Hougaard DM, Skogstrand K, Roberts JM, et al. Serum leptin measured in early pregnancy is higher in women with preeclampsia compared with normotensive pregnant women. *Hypertension*. (2015) 65:594–9. doi:10.1161/HYPERTENSIONAHA.114.03979
15. Erez-Weiss I, Erez O, Shoham-Vardi I, et al. The association between maternal obesity. glucose tolerance and hypertensive disorders of pregnaney in non-diabetic pregnant women. Hypertens Pregnancy 2005:24125 136.
16. Louis JM, Mogos MF, Salemi JL, Redline S, Salihu HM. Obstructive sleep apnea and severe maternal-infant morbidity/mortality in the United States, 1998–2009. *Sleep*. (2014) 37:843–9. doi: 10.5665/sleep.3644
17. imon R. Catherine R-P, Nicholas C. H, Selby P, and John W. *Vitamin D in Pregnancy*. Oxford, UK: Royal College of Obstetricians and Gynaecologists (2014).
18. Bodnar LM, Catov JM, Roberts JM, Simhan HN. Prepregnancy obesity predicts poor vitamin D status in mothers and their neonates. *J Nutr.* (2007) 137:2437–42. doi: 10.1093/jn/137.11.2437
19. Simon R. Catherine R-P, Nicholas C. H, Selby P, and John W. *Vitamin D in Pregnancy*. Oxford, UK: Royal College of Obstetricians and Gynaecologists (2014)
20. Guidelines IoMUaNRCUCtRIPW. *Weight Gain During Pregnancy: Reexamining the Guidelines* (2009). Washington, DC: National Academies Press.
21. American Institute of Ultrasound in Medicine. AIUM practice parameter for the performance of detailed second- and third-trimester diagnostic obstetric ultrasound examinations. *J Ultrasound Med.* (2019) 38:3093– 100. doi: 10.1002/jum.15163
22. Maxwell C, Glanc P. Imaging and obesity: a perspective during pregnancy. *Am J Roentgenol.* (2011) 196:311–9. doi: 10.2214/AJR.10.5849
23. Monson M, Heuser C, Einerson BD, Esplin I, Snow G, Varner M, et al. Evaluation of an external fetal electrocardiogram monitoring system: a randomized controlled trial. *Am J Obstet Gynecol.* (2020) 223:244.e1– .e12. doi: 10.1016/j.ajog.2020.02.012
24. Hood DD, Dewan DM. Anaesthetic and obstetric outcome in morbidly obese patients.Anesthesiology 1993:79:1210-1218.
25. Vallejo MC. Anesthetic management of the morbidly obese parturient. *Curr Opin Anaesthesiol.* (2007) 20:175–80. doi:10.1097/ACO.0b013e328014646b
26. Subramaniam A, Jauk VC, Goss AR, Alvarez MD, Reese C, Edwards RK. Mode of delivery in women with class III obesity: planned cesarean compared with induction of labor*. Am J Obstet Gynecol.* (2014) 211:e1– 9. doi: 10.1016/j.ajog.2014.06.045
27. Pevzner L, Swank M, Krepel C, Wing DA, Chan K, Edmiston CE. Effects of maternal obesity on tissue concentrations of prophylactic cefazolin during cesarean delivery. *Obstet Gynecol.* (2011) 117:877– 82. doi: 10.1097/AOG.0b013e31820b95e4
28. Rasmussen KM, Yaktine AL. Weight gain during pregnancy: reexamining the guidelines. National Academies Press. 2009
29. Blomberg M. Maternal obesity and risk of postpartum hemorrhage. *Obstet. Gynecol*. (2011) 118. doi: 10.1097/AOG.0b013e31822a6c59.
30. Butwick AJ, Abreo A, Bateman BT, Lee HC, El-Sayed YY, Stephansson O, et al. Effect of maternal body mass index on postpartum hemorrhage. *Anesthesiology.* (2018) 128:774–83. doi:10.1097/ALN.0000000000002082
31. Bates SM, Middeldorp S, Rodger M, James AH, Greer I. Guidance for the treatment and prevention of obstetric-associated venous thromboembolism. *J Thromb Thrombolysis.* (2016) 41:92–128. doi: 10.1007/s11239-015- 1309-0
32. American College of Obstetricians and Gynecologists’ Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No 196: Thromboembolism in Pregnancy. *Obstet Gynecol.* (2018) 132:e1–e17. doi: 10.1097/AOG.0000000000002706
33. D’Alton ME, Friedman AM, Smiley RM, Montgomery DM, Paidas MJ, D’Oria R, et al. National partnership for maternal safety: consensus bundle on venous thromboembolism. *Anesthesia Analgesia*. (2016) 123. doi: 10.1213/ANE.0000000000001569
34. Westerfield KL, Koenig K, Oh R. Breastfeeding: common questions and answers. *Am Fam Physician.* (2018) 98:368–73.
35. Crane IMG, White J, Murphy P, et al. The effect of gestational weight gain by body mass Index on maternal and neonatal outcomes. J Obstet Gynaecol Can. 2009:31:28-35.
36. Martin A, Krishna I, Ellis J, Paccione R, Badell M. Super obesity in pregnancy: difficulties in clinical management. *J Perinatol*. (2014) 34:495– 502. doi: 10.1038/jp.2014.4
37. Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, et al. U.S. medical eligibility criteria for contraceptive use, 2016. *MMWR Recomm Rep*. (2016) 65:1–103. doi: 10.15585/mmwr.rr6 503a1
38. Cedergren ML. Maternal morbid obesity and the risk of adverse pregnancy outcome. Obstetrics and Gynecology 2004;103:219-224.
39. Poston L, Caleyachetty R, Cnattingius S, Corvalán C, Uauy R, Herring S, et al. Preconceptional and maternal obesity: epidemiology and health consequences. *Lancet Diabetes Endocrinol.* (2016) 4:1025–36. doi: 10.1016/S2213-8587(16)30217-0
40. American College of Obstetricians and Gynecologists. Obesity in pregnancy: ACOG practice bulletin, number 230. *Obstet Gynecol.* (2021) 137:e128– 44. doi: 10.1097/AOG.0000000000004395
41. Lim CC, Mahmood T. Obesity In pregnancy, Best Practice and Research Clinical Obstetrics and Gynecology 2015:29:309-319.
42. Fowden AL, Ward /W, Wooding FP, et al. Programming placental nutrient transport capacity. J Physiol. 2006,572:5-15.
43. Marchi J, Berg M, Dencker A, Olander EK, Begley C. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. *Obes Rev.* (2015) 16:621–38. doi: 10.1111/obr.12288
44. Tanner LD, Brock And C, Chauhan SP. Severity of fetal growth restriction stratified according to maternal obesity. *J Matern Fetal Neonatal Med.* (2020):1–5. doi: 10.1080/14767058.2020.1773427
45. Kupfermine MJ, Peaceman AM, Wigton TR, et al. Pre-pregnancy weight and the risk of stillbirth and neonatal death. BJOG, 2005;112:403-408,
46. Yao R, Ananth CV, Park BY, Pereira L, Plante LA, Consortium PR. Obesity and the risk of stillbirth: a population-based cohort study. *Am J Obstet Gynecol.* (2014) 210:457.e1–9. doi: 10.1016/j.ajog.2014.01.044
47. Maggard MA, Yermilov I, Li Z, et al. Pregnancy and fertility following bariatric surgery: a systematic review. JAMA. 2008,300:2286-2296.
48. International Diabetes Federation ID Diabetes Atlas 7th Edition. www.diabetesatlas.org.Jan 2017.
49. Hod M, Kapur A, Sacks DA, et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on gestational diabetes mellitus: a pragmatic guide for diagnosis, management and care. International Journal of Gynecology and Obstetrics 2015:131:5173-5211.