

## Chapter 45

### Obesity and the Preconception Period

Aysel ÖZDEMİR, Z. Burcu YURTSAL and Büşra CESUR

#### INTRODUCTION

Obesity affects health of all age and gender groups. Its presence even among parents before conception has potential to ruin the life of the new coming sibling. It is like telling a story from the very beginning but not a fiction, a true story with scientific proofs. That's why; I believe a paper dedicated to obesity should start from the preconception, involving both the mother and the father; and probably being a provocative idea, from the early ancestors.

Prenatal obesity increases risk of maternal gestational diabetes mellitus, excessive weight gain during gestation, preeclampsia, pre and post-natal complications, failure of losing weight in the postpartum period. Prepregnancy is a period that we can intervene to promote a healthy pregnancy and delivery. Measures taken at these stages probably will positively affect the health status of the mother and the baby.

Obesity being a part of metabolic syndrome is proven to be the cause of many diseases. Obese individuals are at risk of hypertension, diabetes, pulmonary embolism etc. Obese woman at their fertile ages may have menstrual problems, polycystic ovarian syndrome, poor cardiometabolic health, insulin resistance, lipid disorders and so on (Diamanti-Kandarakis, 2007; Dietl, 2005). Woman who are obese are also at risk of pulmonary diseases like obstructive sleep apnoea. Obese woman may have reproductive problems like difficulty in conceiving, poor health during pregnancy.

Preconception health is health of women and men during the period of reproduction, a period that they can have a child. The things that can be done for a baby's health should start from the period of preconception. The health of a baby that will be born in the future will be affected by the current health status of the parents. So preconception health will deal with all the people in their reproductive age. In a way we can say the health of future generations will depend on the general health status of the population.

Preconception health care is given by the doctor or other health care providers. It is unique for each person, since the health status of everyone differs together with genetic characteristics. A nutritional status beyond normal will also have negative effects on the child's health. So we have to individualize the interventions according to the needs of the father or mother candidates. Preconception health is important not only for the ones planning to have babies but; for all women and men at their reproductive age, since unplanned pregnancies account for half of the pregnancies. In this paper we will focus on the effects of preconception parental obesity, preconception factors that will cause obesity of the child in the future. Preconception health has the ultimate importance for the baby. Prepregnancy body mass index causes many important obstetrical problems. These include; preeclampsia, gestational

diabetes, preterm delivery, caesarean delivery. In a study by Schummers *et al.* 10% difference in prepregnancy body mass index was associated with at least a 10% lower risk of preeclampsia, gestational diabetes, indicated preterm delivery, macrosomia, and stillbirth. The results highlight importance prepregnancy weight loss and provide an achievable target for the mothers (Schummers *et al.*, 2015).

### **MATERNAL FACTORS**

Maternal obesity during gestational period causes many adverse cardiac and metabolic risks in the child. Proposed mechanisms involve increased amount of nutrients passing placenta causing possible permanent adaptations in appetite, energy metabolism and neuroendocrine functions. These in turn ease the becoming of the child a risky individual for cardiovascular and metabolic diseases which are in fact associated with each other with complex connections. Maternal obesity also increases risk of large for gestational age fetus, fetal complications and childhood obesity.

Prenatal obesity increases risk of maternal gestational diabetes mellitus, excessive weight gain during gestation, preeclampsia, pre and post-natal complications, failure of losing weight in the postpartum period. Prepregnancy is a period that we can intervene to promote a healthy pregnancy and delivery. Measures taken at these stages probably will positively affect the health status of the mother and the baby. The condition of the mother's body during prepregnancy period will affect the quality of ovum and the fertilization. In theory an obese woman is under risk of metabolic syndrome and hence metabolic diseases. The inflammatory condition, infections, endocrine functions all have potential to affect the health of the ovum and hence fetus. Oxidative stress is also a potential factor that may play a role in the fertilization process. Oocyte dysfunction may be caused by oxidative dysfunction (Sobinoff *et al.*, 2013). Oxidative stress is also associated with obesity (Loffredo *et al.*, 2012). A malfunctioning body may produce dysfunctional ovum and before fertilization certain risks for the baby and the mother may arise. A maternal factor; that may cause obesity of the fetus, child or adult deserves attention. Maternal obesity and overweight is an important problem. So we can expect maternal obesity to encounter many problems during the pre-gestational period. We can say maternal obesity is certainly associated with various common diseases in the child.

The offspring's cardiometabolic health is impaired with maternal prepregnancy obesity. A study examined the association of both the mother and father's prepregnancy body mass indexes and its association with childhood body fat distribution, cardiometabolic outcomes. Higher maternal and paternal prepregnancy body mass indexes had detrimental effects on childhood body mass index, total body and abdominal fat measures, systolic blood pressures, insulin levels and high-density lipoprotein levels (Gaillard *et al.*, 2014). In this paper the authors concluded that the prepregnancy body mass index might influence the cardiometabolic health of the child through mechanisms directly related to uterus.

Maternal obesity during gestation elicits problems affecting the fetus and the mother. However not only pregnancy obesity, but pre-pregnancy obesity causes problems in the fetus or the newborn. In a recent study; prepregnancy obesity prevalence is considerably high and had increased from 17.6% in 2003 to 20.5% in 2009 highlighting "the need to address obesity as a key component of preconception

care, particularly among high-risk groups” as stated by the authors of a study conducted in USA (Fisher *et al.*, 2013).

It is clear that in obese woman rate of having obese children is higher. The combined effect of excess maternal gestational weight gain and prepregnancy obesity resulted in higher infant birth weight, rapid weight gain in the first 3 months of life, with a sustained weight elevation throughout the first year of life. These findings highlight the importance of the preconception and prenatal periods for paediatric obesity prevention (Heerman *et al.*, 2014). Prepregnancy weight gain and nutritional characteristics will probably affect the fetus or the newborn, but how. An interesting study gives clues about the mechanisms. A recent study of Graus-Nunes *et al.* in mice evaluated the effects of maternal obesity on pancreas structure and carbohydrate metabolism in early adult life (Graus-Nunes *et al.*, 2015). In his study mice fed standard chow and high fat diet was compared. In their study; maternal high fat diet consumed during the preconception period and throughout the gestation and lactation periods in mice promoted metabolism and pancreatic programming in first and second generation male offspring. The results of the study showed that obesity and high fat diet has intergenerational effects.

Maternal obesity during gestational period brings up many problems that have potential to effect mothers and the child’s future health. Maternal obesity during gestation increase the risks of pregnancy related complications for mother and the newborn (Metwally *et al.*, 2007). Also there is considerable data addressing the impact of factors like parental life style on more than one generation’s health. Maternal and paternal obesity prior to conception alters the molecular composition of both oocytes and sperm and ultimately increases the incidence of obesity and metabolic disorders in offspring according to Lane *et al.* (Lane *et al.*, 2014). This in turn makes us to think that a healthy nutrition before conception also helps to have healthy ovum as reported by Hammiche *et al.* who said that embryos from women who consumed diets rich in omega-3 fats had visibly different cellular morphology and improved quality compared to embryos from other women (Hammiche *et al.*, 2011). In mouse models of obesity; females on a high fat diet had dramatically increased oocyte lipid content. Oocyte lipid content in turn was associated with cellular lipotoxicity and oxidative stress, and poor embryo and fetal development (Luzzo *et al.*, 2012; Wu *et al.*, 2010). Also there is evidence that maternal obesity effects the pancreatic development of the offspring in animal models. This in turn may be the causal factor for future diabetes and obesity (Brighenti *et al.*, 2013).

It is obvious that to have a healthy period of pregnancy and birth, perinatal and postnatal period for mother and the offspring; measures should be taken early. Women at child-bearing age must be in good nutritional status prior to conception. That brings out the need for change or development of new objectives targeting preconception nutrition and healthy life style. As stated by Gardiner *et al.* “women of reproductive age should be counselled to consume a well-balanced diet including fruits and vegetables, iron and calcium-rich foods, and protein-containing foods as well as 400 micrograms of folic acid daily” (Gardiner *et al.*, 2008).

Body weight before, during and postpartum period need to be taken into consideration and interventions should be carried out to prevent women of childbearing age from weight retention and being overweight and obese (Gunderson,

2009). Mehta *et al.* in a study held in African-American population aimed to determine the possible association of diabetes during pregnancy and childhood obesity. Data collected from mothers of children at ages of 2-5 years revealed that children of diabetic woman were more likely to be obese. Interestingly logistic regression analysis showed that diabetes and maternal prepregnancy body mass index determined childhood obesity (Mehta *et al.*, 2012).

In a retrospective analysis on 366,886 singletons; birth abdominal circumference and weight significantly increased with increasing pregestational body mass index, and decreased with smoking (Tanvig *et al.*, 2013). In a study that included 103 women who were not pregnant at baseline and gave birth to full-term singletons during the follow-up period it was found that rate of excessive pregnancy weight gain was increased by being overweight preconception, and decreased with adequate preconception physical activity levels (Weisman *et al.*, 2010). In a study included 599 term babies born Australia; the variable strongly associated with increased body fat percentage were neonatal female sex, maternal Caucasian ethnicity and increased gestational (Au *et al.*, 2013).

Among woman with preconception BMI  $>50 \text{ kg/m}^2$ ; had a higher rate of 21% emergency caesarean section compared to rate of in women with BMI  $\leq 50 \text{ kg/m}^2$  (21% versus 12%; respectively). Woman with BMI higher than  $50 \text{ kg/m}^2$  had more macrosomic neonates and more pregnancy complications in a study by Bonnesen (Bonnesen *et al.*, 2013). It is clear that prenatal and preconception body weight of the mother deserves attention. A study by Heerman *et al.* (2014) highlighted the importance of excess maternal gestational weight gain and prepregnancy obesity. They resulted in higher infant birth weight, rapid weight gain in the first 3 months of life accompanying a sustained weight elevation throughout the first year of life (Heerman *et al.*, 2014). In a study conducted in Thai woman prepregnancy obesity did not increase risk for gestational diabetes mellitus, preeclampsia and fetal macrosomia but, risk for developing gestational hypertension increased significantly (Kongubol & Phupong, 2011). Regardless of gestational weight gain, women with obese prepregnancy BMI ( $\geq 30 \text{ kg/m}^2$ ) had increased rate of gestational hypertension, gestational diabetes and large for gestational age babies. But the authors report also that; preterm labour and small for gestational age increases with underweight prepregnancy BMI ( $<18.5 \text{ kg/m}^2$ ) (Shin & Song, 2014). Walfisch and Koren stated that preconception counselling might provide a unique "time window" for an intervention, prior to the pregnancy, that in turn might reduce maternal and fetal risks (Walfisch & Koren, 2011). Preconception cigarette smoking, overweight/obesity, adequate physical activity, heavy alcohol consumption, and fair/poor self-rated health were measured in adolescence and early adulthood in a study. Birth weight as an outcome, was classified as low ( $<2,500 \text{ g}$ ), normal ( $2,500\text{-}4,000 \text{ g}$ ), and macrosomic ( $>4,000 \text{ g}$ ). In that study adult-onset overweight significantly increased risk of delivering a macrosomic baby (Strutz *et al.*, 2012). Maternal prepregnancy obesity was one of the factors that were significantly associated with developmental delay in early childhood after moderately preterm birth in the study of Kerstjens *et al.* (Kerstjens *et al.*, 2013). Providing preconception nutritional and exercise care, and guidance during pregnancy and post pregnancy for appropriate weight loss is recommended for the health of the mother and baby (Liat *et al.*, 2015).

## PATERNAL EFFECTS

Maternal body mass index possibly is related to direct intrauterine mechanisms and paternal body mass index has a role for shared family-based, lifestyle-related characteristics or genetic factors. In an experimental study; a high-fat diet was used to induce obesity but not diabetes in male C57Bl6 mice, which were subsequently mated to normal-weight females. They demonstrated that a high-fat diet induced paternal initiation of subfertility in both male and female offspring of two generations of mice (Fullston *et al.*, 2012). Preconception paternal obesity was associated with DNA methylation profiles in the offspring. This study in turn “provides evidence for transgenerational effects of paternal obesity that may influence the offspring's future health status” as stated by the authors (Soubry *et al.*, 2013). This study was also received comments from different colleagues. They concluded that paternal obesity affects the normal IGF2 methylation in the sperm and this in turn alters the expression of IGF2 in the baby (Moore & Stanier, 2013). In a study that evaluated both paternal and maternal effects on pregnancy; paternal lifestyle factors did not exert an independent effect on the investigated outcomes. However; maternal prepregnancy BMI and maternal smoking during pregnancy influenced the risk of hypertensive pregnancy complications, gestational diabetes mellitus and small for gestational age fetus. In that study; paternal and maternal lifestyles being positively correlated, made the authors to conclude that both partners should be involved in preconception counselling regarding the investigated outcome measures (Mutsaerts *et al.*, 2014).

Both maternal and paternal prepregnancy body mass index is related to increased adiposity levels and a worse cardiometabolic risk profile in their offspring (Gaillard *et al.*, 2014). Paternal prepregnancy BMI has also been associated with blood pressure of the offspring at five years (Lawlor *et al.*, 2004). Childhood hypertension affects the adulthood health. These data address the need for early preventive measures to achieve the target of having a healthy child. What can we recommend a man before he can have a child would be prevention of obesity, having a normal and healthy nutrition, if present giving up smoking, avoiding toxic substances or addictions. Similar results can be seen in the data provided by Chen *et al.* in their study both maternal and paternal body mass indexes were associated with cardiovascular risk factors in the child.

In conclusion; to bear a healthy child measures have to be taken from the very beginning. Preconception is period with ultimate importance which will affect all the process. Both maternal and paternal factors contribute to obesity of the offspring. Also preconception body mass index is has great impact on health of the child. Certainly more data is needed to come into a conclusion about the topic.

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