



## Etiology of adverse prenatal Outcome in overweight women

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### ABSTRACT

To survey the etiology of adverse prenatal outcome in overweight. This comparative cohort study was conducted from 2010 to 2012. Total 440 gravid women 220 were overweight and 220 normal weight pregnant women during at the first visit of pregnancy and third trimester were assessed. The risks for preterm labor, gestational hypertension, pre-eclampsia, gestational diabetes, caesarian section and Macrosomia were higher for those who were overweight at the third trimester of pregnancy ( $P < 0.05$ ). Maternal BMI was associated with a higher risk for gestational hypertension, gestational diabetes, preterm labor, preeclampsia, caesarian section and fetal macrosomia ( $P < 0.05$ ). This research demonstrates that maternal BMI was associated with increased risks for adverse pregnancy outcomes.

**Keywords:** Etiology, Overweight Women, adverse prenatal Outcome

### INTRODUCTION

Both developed and developing countries are experiencing a rapid increase in the prevalence of obesity [1]. It has become a significant threat to health in all sectors of the population, including women of reproductive age [2]. The World Health Organization estimates that more than 1 billion people are overweight, with 300 million meeting the criteria for obesity [3]. Some research suggests that pregnancy can be one of the factors contributing to the development of obesity [4, 5]. In the United States, over one-third of women are overweight or obese at the first of pregnancy and the prevalence of pre-pregnancy overweight or obesity is increasing [6]. Studies revealed that the prevalence of overweight and obesity in most Asian countries as well [7]. Recently, the Institute of Medicine (IOM) has reported: "Women today are also heavier, and greater percentages of them are entering pregnancy overweight or obese, and many are gaining too much weight during pregnancy" [8]. In Iran, overweight and obesity prevalence among all ages and both sexes of Iranian people are seen [9]. Maternal overweight or obesity during pregnancy can lead to several adverse outcomes for mother and fetus, including preterm labor, pre-eclampsia, gestational diabetes, fetal macrosomia and caesarian section [10, 11]. Incidence of neural-tube defects, heart defects or multiple anomalies, late pregnancy stillbirths and early neonatal death, are twice in obese women in contrast to non-obese women [12, 13]. Children of obese women have a twofold increased risk of childhood obesity at 2 years of age and a 2.3-fold increased risk of childhood obesity at 4 years of age [14, 15]. In addition, several studies have linked obesity or overweight in pregnancy with low quality of life [16, 17, and 18]. Many factors have been linked with prenatal morbidity and mortality that not to be able to intervention [18]. Some pregnancy-related factors that may predict development of obesity during pregnancy are including gestational weight gain, pre-pregnancy nutritional status, age, parity and race [19, 20, and 21]. The aim of this study was to investigate etiology of adverse prenatal Outcome in overweight women.

## MATERIALS AND METHODS

At the beginning the Ethics Committee of Zahedan Medical University approved the study and all participants gave written informed consent. This study was conducted in the health centers of Zahedan University of Medical Sciences in Iran in 2010-2012. The sample was comprised of 440 pregnant women (220 overweight and 220 normal weights) who were at the first trimester of pregnancy. We were categorized pregnant women to be non-obese when their body mass index (BMI) in the first trimester was 19.8-25.9 kg/m<sup>2</sup> and to be overweight when their BMI was 26-29.9 kg/m<sup>2</sup>, according to the protocol of health of ministry in Iran. Gestational age was later confirmed through a review of the electronic medical record and was based on either the obstetrician's assessment of the LMP or both the LMP and obstetric ultrasound assessment. Sitting blood pressure was measured by using a standard mercury sphygmomanometer. Systolic and diastolic blood pressures were measured twice on the right upper arm, and the average was used for analysis. Hypertension was defined as a systolic blood pressure of  $\geq 140$  mmHg and/or a diastolic blood pressure of  $\geq 90$  mmHg, respectively. Fasting plasma glucose was determined. In obese pregnant women and the women with fasting glucose levels of  $\geq 105$  mg/dl (according to the protocol of health of ministry in Iran) we performed a screening oral glucose tolerance test with GCT test (Glucose challenge tests). Demographic variable was included maternal age, Number of pregnancies, BMI, weight gain, Gestational age at first visit, family history of diabetes and hypertension. Exclusions criteria were: history about preterm labor, previous preeclampsia and gestational diabetes, chronic disease, depression and use of special drug and take a special diet. Finally, pregnancy outcomes included the following: preterm delivery, gestational diabetes mellitus, hypertensive disorders of pregnancy, preeclampsia, caesarian section, and Macrocosmic infants were obtained.

### Statistical Analysis

The SPSS version 20.0 was used to analyses the variables. Frequency and percentage were computed for variable such as maternal age, Number of pregnancies, BMI, weight gain, Gestational age at first trimester, family history of diabetes and hypertension. To compare the proportion of outcome pregnancy in both groups Chi square was used. Results will be given as mean values with 95% confidence intervals. P-values  $< 0.05$  were considered significant.

## RESULTS

400 pregnant women were eligible for inclusion in this study. The groups did not differ significantly with respect to socio demographic characteristics, age, education, parity, gestational age at initiation of prenatal care (PNC) (weeks), family history of diabetes and hypertension. In addition, Weight gain in overweight women was lower ( $8.4 \pm 3.7$ ) than the normal weight women ( $10.4 \pm 3.6$ ).

Table 1 shows the maternal characteristics between normal weight and overweight pregnant women.

The incidence of pregnancy complications of the women in the two groups is depicted in Table 2.

**Table 1: Maternal characteristics between normal weight and overweight pregnant women**

variable	Normal weight women	Overweight women	p- value
Age Education	24.4 $\pm$ 4.9	25.6 $\pm$ 5.1	0.27
Illiterate	119 (59.5%)	117 (58.5%)	0.9
Primary school	48 (24%)	50 (25%)	
High school	38 (19%)	36 (18%)	
College and graduate	15 (7.5%)	17 (8.5%)	
Parity	2	2	0.12
BMI	22.2 $\pm$ 2.1	28.5 $\pm$ 3.9	$< 0.0001$
Weight gain (kg)	10.4 $\pm$ 3.6	8.4 $\pm$ 3.7	0.002
Gestational age at initiation of PNC	13.2 $\pm$ 3.1	13 $\pm$ 3.0	0.82
family history of diabetes	116 (52.7%)	104 (47.27%)	NS
family history of hypertension	102 (46.36)	118 (53.63)	NS

Only One hundred forty two (35%) number of women experienced a normal pregnancy, free from any complication. In contrast 64.5% of both groups had a variety of complication. Furthermore, the independent risk of each complication or intervention in the overweight group was compared with the normal weight group, which indicated that the incidence of emergency C-section (n=101) and preterm delivery (n=30) was higher in the overweight

women compared to another group. There was a significant high rate macrosomia (n=37), gestational diabetes (n=10), hypertension (n=19) and preeclampsia (n=10) in overweight group.

**Table 2: Pregnancy complications between normal weight and overweight pregnant women**

Variable	Normal weight women (n=214)	Overweight women (n=210)	p-value
Preterm delivery	10 (4.67%)	30 (14.28%)	0.00
Gestational diabetes mellitus	4 (1.86%)	10 (4.76%)	0.01
Hypertensive disorders of pregnancy	4 (1.86%)	18 (8.57%)	0.01
Preeclampsia	2 (2.8%)	10 (4.76%)	0.04
Emergency Caesarian section	60 (28.03%)	101 (48.09%)	0.00
Macrosomic infants	12 (5.6%)	37 (17.6%)	0.00

## DISCUSSION

Obesity and overweight is as a chronic disease that is cause of disability in life activities and effected on outcome of pregnancy. The recent National Health and Nutrition Examination Survey found that in the United States, more than one third of women are obese, more than one half of pregnant women are overweight or obese, and 8% of reproductive-aged women are extremely obese[21]. This study compares outcome pregnancy between normal weight and overweight pregnant women. Results of study demonstrated that no significant different between Maternal characteristics in both group. Our study suggests that overweight, measured by BMI, predisposes women to complicated pregnancies and increased obstetric interventions such as preterm labor, preeclampsia, GDM, emergency caesarean section, Hypertensive disorders of pregnancy (HDP) and macrosomia. Our data support prior studies, Baeten et al., report that maternal obesity is regarded a high-risk obstetric condition and is associated with pregnancy complications and adverse outcomes [22]. In contrast, some pregnancy complications were lower in normal weight group. Robinson et al and Leonie et al show in two separate studies that obese women are at high risk for pre-Eclampsia which is in line with the results of this study [23, 24].According to the literature, there is a strong association between obese maternal environment pregnancy and oxidative stress compared with normal pregnancy. Recent researches have been shown that maternal obesity induced mitochondrial dysfunction with an increase in mitochondrial reactive oxygen species and oxidative stress in oocytes, zygotes and embryonic life [25, 26]. Moreover, embryonic development may is affected by oxidative stress [27].Similarly, Obesity oroverweight has linked with preeclampsia [28, 29] as well as circulating inflammation markers [30].C-reactive protein, cytokines, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), and interleukin-8 (IL-8) which are significant marker of inflammation, are elevated in obese pregnant women [31]. The findings of our study confirm the association between increasing BMI and the risk of hypertension disorder of pregnancy (HDP). These findings are consistent with those of previous studies in showing an association between increasing maternal BMI and an increased risk of hypertensive disorders of pregnancy [32, 33].Margaret reported that when BMI is rising, the incidence of HDP is rising too. Hypertensive disorders of pregnancy are associated with various metabolic abnormalities that are known risk factors for cardiovascular disease and maternal mortality .So; she is suggested that all of women with HDP should be followed after pregnancy for increasing their survival [34]. In addition, Tabatabaei reported that the risks of gestational hypertension and pre-eclampsia had been higher for Iranian women who are overweight or obese [35]. In 2011, Sea claimed that the risk of preterm birth is higher in women with below-average BMI, significantly [36].According to our study BMI is also considered a risk factor for preterm labor. The biological mechanisms for the positive association between obesity and the risk of preterm labor are unknown. But sedentary lifestyle can lead to preterm labor[37]. However some studies are against our finding, for instance, in 2015, Pakniat reported that the difference between preterm labor in women with Underweight, Normal weight, Overweight were not significant (P=0.75) [38]. In addition, a systematic review in 2010 indicated that in developed country ,underweight women are more to have preterm labors overall adjusted RR 1.29, 95% CI 1.15–1.46 [39]. Recent studies have been shown a novel mechanism for relationship between maternal cortisol and length of pregnancy. In 2015, Laura and colleagues claimed that low maternal cortisol in obese women can lead to decrease activation of hypothalamic- pituitary-adrenal- axis (HPAA) and the length of gestational age is desponds on. Laura suggested that the adverse complications in obese pregnant women may lead to, increasing fetal size and prolonged pregnancy by deregulation of the HPAA [40]. Previous studies investigating the relationship between maternal obesity and GDM. Our results were consistent with the findings of these studies. Obesity or overweight before or during pregnancy is a known risk factor for developing gestational diabetes (GDM) and hypertension [41]. GDM, defined as diabetes first diagnosed during pregnancy, and is particularly prevalent and increasing in the Asian countries, rapidly [42]. Therefore, this condition and elevated fasting plasma glucose levels during pregnancy have all been reported to be significant risk factors for macrosomia [43, 44].Ethnic differences can play a main role in the risk for fetal macrosomia [45]. Also,

evidence from observational studies and clinical trials indicates that dietary energy intake and the source of energy influences glucose metabolism and insulin responses [46]. Moreover, for preventing of GDM and macrosomia, Romon and their colleague have recommended that nutrition counseling should be directed at an adequate carbohydrate intake of 250 g/day, while maintaining a low fat diet to limit the total energy intake [47]. In our study, Overweight women consistently have been shown to be at increased risk for emergency cesarean compared with normal weight pregnant women. This finding is consistent with the studies by Jenson and Hung [48, 49]. We recommend overweight women should be counseled preconception and during antenatal care for avoiding adverse pregnancy outcome.

### CONCLUSION

The authors believe that this study is important for general health care. We found that maternal BMI increased risks adverse pregnancy outcomes. More knowledge should be acquired in this issue.

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### REFERENCES

- [1] Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, Bahalim AN, Farzadfar F, Riley LM, Ezzati M. Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Body Mass Index) National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011; 377:557–567. [PMC free article][PubMed]
- [2] World Health Organization (WHO). Obesity and overweight. Fact sheet No.311. 2006. [<http://www.who.int/mediacentre/factsheets/fs311/en/index.html>]. Last accessed 21 April 2010.
- [3] World Health Organization (2010) global strategy on diet, physical activity and health. Obesity and overweight.
- [4] Linné Y, Rössner S. Interrelationships between weight development and weight retention in subsequent pregnancies: the SPAWN study. *Acta Obstetrica et Gynecologica Scandinavica*, 2003: Volume 82, Issue 4, pages 318–325.
- [5] Linné Y1, Barkeling B, Rössner S. Long-term weight development after pregnancy. *Obes Rev*. 2002 May; 3(2):75-83.
- [6] Kim SY, Dietz PM, England L, Morrow B, Callaghan WM. Trends in pre-pregnancy obesity in nine states, 1993-2003. *Obes*. 2007; 15:986–993. [PubMed]
- [7] Lal A, Moodie M, Ashton T, Siahpush M, Swinburn B. Health care and lost productivity costs of overweight and obesity in New Zealand. *Aust N Z J Public Health*. 2012; 36(6):550–556. [PubMed]
- [8] Institute of Medicine [accessed March 2012]; Weight gain during pregnancy: reexamining the guidelines. [PubMed]
- [9] Jafari-Adli SH, Jouyandeh Z, Qorbani M, Soroush A, Larijani B, and et al. Prevalence of obesity and overweight in adults and children in Iran; a systematic review. *J Diabetes MetabDisord*. 2014; 13: 121.
- [10] Scott-Pillai R, Spence D, Cardwell C, Hunter A, Holmes V. The impact of body mass index on maternal and neonatal outcomes: A retrospective study in a UK obstetric population, 2004–2011. *BJOG*. 2013; 120(8):932–939. doi: 10.1111/1471-0528.12193. [PubMed] [Cross Ref]
- [11] Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. Extreme obesity in pregnancy in the United Kingdom. *Obstet Gynecol*. 2010; 115:989–97.
- [12] Cunningham FG, Gant NF, Leveno KJ, Gilstrap III LC, Hauth JC, Wenstrom HT. *Williams Obstetrics*. McGraw-Hill: New York, 2014.
- [13] Wong S, Ordean A, Kahan M; Society of Obstetricians and Gynecologists of Canada. SOGC clinical practice guidelines: Substance use in pregnancy: no. 256, April 2011. *Int J Gynaecol Obstet*. 2011 Aug; 114(2):190-202.
- [14] Davies GA, Maxwell C, McLeod L, Gagnon R, Basso M, Bos H, and et al. Obesity in pregnancy. *J ObstetGynaecol Can*. 2010 Feb; 32(2):165-73.
- [15] Mette Tanvig, Christina A. Vinter, Jan S. Jørgensen, Sonja Wehberg, Per G. Ovesen and et al. Effects of Lifestyle Intervention in Pregnancy and Anthropometrics at Birth on Offspring Metabolic Profile at 2.8 Years: Results from the Lifestyle in Pregnancy and Offspring (LiPO) Study. *J ClinEndocrinolMetab*. 2015 Jan; 100(1):175-83.

- [16] Rooney BL, Schauburger CW, Mathiason MA. Impact of perinatal weight change on long-term obesity and obesity-related illnesses. *ObstetGynecol* 2005; 106: 1349–1356.
- [17] Jodie M. Dodd, Angela Newman, Lisa J. Moran, Andrea R. Deussen, Rosalie M, and etal. The effect of antenatal dietary and lifestyle advice for women who are overweight or obese on emotional well-being: the LIMIT randomized trial. *ActaObstetriciaETGynecologica Scandinavica* 2015.
- [18] Amador-Licona N1, Guízar-Mendoza JM. Daytime sleepiness and quality of life: are they associated in obese pregnant women? *Arch Gynecol Obstet*. 2012 Jan; 285(1):105-9.
- [19] M Baeten, E A Bukusi, and M Lambe. Pregnancy complications and outcomes among overweight and obese nulliparous women. *Am J Public Health*. 2001 March; 91(3): 436–440.
- [20] Bahadoran P, Mohamadirizi S. Relationship between physical activity and quality of life in pregnant women. *Iran J Nurs Midwifery Res*. 2015 Mar-Apr; 20(2): 282–286.
- [21] Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA* 2012; 307:491–7.
- [22] Baeten JM, Bukusi EA, Lambe M (2001) Pregnancy complications and outcomes among overweight and obese nulliparous women. *Am J Public Health* 91: 436-440?
- [23] Robinson HE, Dconnell CM, Joseph KS, Mcleod NL (2005) maternal outcomes in Pregnancies complicated by obesity. *ObstetGynecol* 160: 1357-1364.
- [24] Leonie KC, Johannes BP, Allan MC, McIntyre D (2006) the prevalence and impact of overweight and obesity in an Australian obstetric population. *Med J Aust* 184: 56-59.
- [25] Heerwagen, M.J.R., Miller, M.R., Barbour, L.A., and Friedman, J.E. Maternal obesity and fetal metabolic programming: a fertile epigenetic soil. *Am J PhysiolRegulIntegr Comp Physiol*. 2010; 299:711–722
- [26] Malti, N. Merzouk H. Merzouk S.A. Loukidi, B. Karaouzene, N. Malti, A. Narce M. Oxidative stress and maternal obesity: Feto-placental unit interaction. *Placenta* 35 2014; 411-416.
- [27] Dennery, P.A. Effects of oxidative stress on embryonic development. *Birth Defects Res C Embryo Today*. 2007; 81: 155–162.
- [28] Liu X, Du J, Wang G, Chen Z, Wang W, Xi Q. Effect of pre-pregnancy body mass index on adverse pregnancy outcome in north of China. *Archives of Gynecology and Obstetrics*. 2011; 283: 65-70.
- [29] Sheiner E, Levy a, Menes TS, Silverberg D, Katz M, Mazor M. Maternal obesity as an independent risk factor for caesarean delivery. *Paediatric and Perinatal Epidemiology*. 2004; 18(3): 196-204.
- [30] C.W.G. Redman, I.L. Sargent. Placental Stress and Pre-eclampsia: A Revised View. *Placenta*, 2009 Volume 30, Supplement, Pages 38–42.
- [31] Ribatti, D., Conconi, M.T., and Nussdorfer, G.G. Nonclassic endogenous novel regulators of angiogenesis. *Pharmacol Rev*. 2007; 59: 185–205
- [32] Bodnar LM, Catov JM, Klebanoff MA, Ness RB, Roberts Epidemiology. Prepregnancy body mass index and the occurrence of severe hypertensive disorders of pregnancy. 2007 Mar; 18(2):234-9.
- [33] Cameron AJ, Welborn TA, Zimmer PZ. Overweight and obesity in Australia: the 1999-2000 Australian Diabetes, Obesity and Lifestyle study. *MJA*. 2003; 178(9):427–432. [PubMed]
- [34] Margaret E. Samuels-Kalow, Edmund F. Funai, Catalin Buhimschi, Errol Norwitz and etal. Prepregnancy body mass index, hypertensive disorders of pregnancy, and long-term maternal mortality. *Am J Obstet Gynecol*. 2007 Nov; 197(5): 490.e1–490.e6.
- [35] Tabatabaei M. Gestational weight gain, pre pregnancy body mass index related to pregnancy outcomes in Kazerun, Fars, Iran. *J Prenatal Med*, 2011; 5: 35-40.
- [36] Sea Kyung CH, In Yang P, Jong Chul SH. The effects of pre-pregnancy body mass index and gestational weight gain on perinatal outcomes in Korean women. *Reproductive Biology and Endocrinology*. 2011; 9: 6.
- [37] Misra DP, Strobino DM, Stashinko EE, Nagey DA, Nanda J. Effects of physical activity on preterm birth. *Am J Epidemiol*. 1998; 147:628–635.
- [38] Pakniat H; Mohammadi F; Ranjkesh F. The impact of Body Mass Index on pregnancy Outcome. *Journal of Midwifery & Reproductive Health*. 2015; Volume 3, Issue 2, Page 361-367.
- [39] Zhen Han, Sohail Mulla, Joseph Beyene, Grace Liao and Sarah D McDonald. Maternal underweight and the risk of preterm birth and low birth weight: a systematic review and meta-analysis. *International Journal of Epidemiology*. 2010; volume 40, issue 1, page: 65-101.
- [40] Laura I. Stirrat, James R. O'Reilly, Sarah M. Barr, Ruth Andrew, Simon C. Riley, and etal. Decreased maternal hypothalamic-pituitary-adrenal axis activity in very severely obese pregnancy: Associations with birthweight and gestation at delivery. *Psychoneuroendocrinology*. 2016; 63:135-143.

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- [41] Junhong Leng,1,2 Ping Shao,2 Cuiping Zhang,2 Huiguang Tian,2 Fuxia Zhang and etal. Prevalence of Gestational Diabetes Mellitus and Its Risk Factors in Chinese Pregnant Women: A Prospective Population-Based Study in Tianjin, China. *PLoS One*. 2015; 10(3): e0121029.
- [42] Racial/ethnic disparities in gestational diabetes mellitus: findings from a population-based survey. Hunsberger M, Rosenberg KD, Donatelle RJ *Womens Health Issues*. 2010 Sep; 20(5):323-8.
- [43] Liu Y, Dai W, Dai X, Li Z. Pre pregnancy body mass index and gestational weight gain with the outcome of pregnancy: a 13-year study of 292,568 cases in China. *ArchGynecol Obstet*. 2012 Oct; 286(4):905-11.
- [44] Shi P, Yang W, Yu Q, Zhao Q, Li C, Ma X, Jin L, Han X, Zhang Y, Yan W . Overweight, gestational weight gain and elevated fasting plasma glucose and their association with macrosomia in chinese pregnant women. *Matern Child Health J*. 2014 Jan; 18(1):10-5.
- [45] Gestational diabetes screening after HAPO: has anything changed? Mulla WR, Henry TQ, Homko CJ *CurrDiab Rep*. 2010 Jun; 10(3):224-8.
- [46] Galgani JE, Uauy RD, Aguirre CA, Díaz EO. Effect of the dietary fat quality on insulin sensitivity. *Br J Nutr*. 2008 Sep; 100(3):471-9.
- [47] Romon M, Nuttens MC, Vambergue A, Vérier-Mine O, Biauxque S, Lemaire C, Fontaine P, Salomez JL, Beuscart R. Higher carbohydrate intake is associated with decreased incidence of newborn macrosomia in women with gestational diabetes. *J Am Diet Assoc*. 2001 Aug; 101(8):897-902.
- [48] Jensen DM, Damm P, Sørensen B, Mølsted-Pedersen L, Westergaard JG, Ovesen P, Beck-Nielsen H Pregnancy outcome and prepregnancy body mass index in 2459 glucose-tolerant Danish women. *Am J Obstet Gynecol*. 2003 Jul; 189(1):239-44.
- [49] Hung S, Morrison DR, Whittington LA, Fein SB Prepartum work, job characteristics, and risk of cesarean delivery. *Birth*. 2002 Mar; 29(1):10-7.