

■ Review

## The Most Important Health Problem of the 21st Century: Investigation of Obesity in Women According to Their Life Periods

### 21. yüzyılın en önemli sağlık problemi: Yaşam dönemlerine göre obezitenin incelenmesi

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#### Abstract

Obesity is a complex disease involving an excessive amount of body fat and an important public health problem affecting all ages in both men and women. It has been shown that obesity is responsible for many genetic, environmental, neurological, physiological, biochemical, cultural and spiritual factors. World Health Organization (WHO) recommends Body Mass Index (BMI) for obesity classification due to its simplicity, cost-effectivity, and high accuracy. Apart from BMI, waist circumference measurement, weight-to-height, skinfold thickness, and circumference measurements are also used. According to the WHO, 2.8 million people die every year due to obesity. Although obesity affects all ages and social groups, women have been more overweight compared to men since and has been linked to many biological factors. However, even with the medical problems, obese women live longer than men, but not without higher healthcare costs. In this review, the effects of obesity on women's health and life will be discussed.

**Keywords:** Obesity; Women's Health; Nursing

#### Öz

Obezite, vücutta aşırı yağ birikimini içeren kompleks bir hastalıktır ve her yaşta kadın ve erkeği etkileyen önemli bir halk sağlığı sorunudur. Obeziteden genetik, çevresel, nörolojik, fizyolojik, biyokimyasal, kültürel ve ruhsal birçok faktörün sorumlu olduğu gösterilmiştir. Dünya Sağlık Örgütü (WHO) basitliği, maliyet etkinliği ve yüksek doğruluğu nedeniyle obezite sınıflandırması için Vücut Kitle İndeksi'nin (VKI) kullanılmasını önermektedir. Ancak VKI'nin dışında, bel çevresi ölçümü, kilo-boy, deri kıvrım kalınlığı ve çevre ölçümleri de kullanılmaktadır. Dünya Sağlık Örgütü'ne göre her yıl 2,8 milyon insan obezite nedeniyle ölmektedir. Obezite her yaş ve sosyal grubu etkilemekle birlikte, kadınlar birçok biyolojik faktörle ilişkili olarak erkeklerden daha kiloludurlar. Ancak, medikal problemi olan kadınlar bile erkeklerden daha uzun yaşar ancak daha yüksek sağlık bakım harcamalarına sahiptir. Bu derlemede obezitenin kadın sağlığı ve yaşamı üzerindeki etkileri tartışılacaktır.

**Anahtar Kelimeler:** Obezite; Kadın Sağlığı; Hemşirelik



### 1. Introduction

Obesity is an important public health problem affecting all ages in both men and women (1). Obesity, once considered an indicator of power, prosperity, wealth and health, is now considered a disease and the most important contributor to premature deaths in many developed countries (2, 3). According to the World Health Organization (4), 2.8 million people die every year due to obesity.

Obesity is responsible for many genetic, environmental, neurological, physiological, biochemical, cultural and spiritual factors (5, 6). Due to the multifactorial etiology, it is difficult and complex to prevent and treat. According to WHO (4), obesity is defined as “abnormal or excessive fat accumulation in the body to the extent that it impairs health”. Obesity is a chronic disease that increases the risks of other complications including cardiovascular and metabolic disease and cancer (7).

According to WHO (4), the rate of mild obesity (BMI≥25 kg/m2) in individuals 20 years and older was 34% in men, 35% in women. Severe obesity (BMI≥30 kg/m2) was 10% in men and 14% in women. The obesity rate in the world has doubled over ten years (1998-2008) (8). According to Turkey Statistical Institute (9) data, while obesity rate was 15.2% in Turkey in 2008, it increased to 31.1% by 2016 with a higher association in women (23.9%) than men (15.2%).

Although obesity affects all ages and social groups, women have been more overweight compared to men since and has been linked to many biological factors. Weight gain and obesity in women have been linked to increased pregnancies (10) and excess weight gain (11), oral contraceptive use, and lack of physical activity (12). Beginning adolescence, body fat increases faster than muscle mass in women physiologically and is associated with estrogen hormones. Menopause also contributes to increased adipose tissue. Although the effect menopause transition on body fat distribution is not clear, the formation of intra-abdominal fat tissue is known to increase (6). As stated above, obesity is a risk factor for disease. Even with these medical problems, obese women live longer than men, but no without higher healthcare costs (13, 14). In this review, the effects of obesity on women's health and life will be discussed.

### 2. Obesity

WHO recommends Body Mass Index (BMI) for obesity classification due to its simplicity, cost-effectivity, and high accuracy. BMI is calculated by dividing body weight by the square of the height [kg/height (m2)]. However, BMI is not recommended for pregnant women, athletes, and diseases

with edema (15). Obesity classification according to BMI is shown in Table 1 (16).

**Tablo 1.** Obesity Classification According to BMI

CLASSIFICATION	BMI
Underweight	<18.5
Normal	18.5-24.9
Overweight	25.0-29.9
Obese I	30.0-34.9
Obese II	35.0-39.9
Obese III (Morbid Obesity)	≥40
Reference: WHO <sup>22</sup>	

Apart from BMI, waist circumference measurement, weight-to-height, skinfold thickness, and circumference measurements are also used (17). The BMI normal values in adults are 18.5-24.9 kg/m2, and waist circumference poses a high risk for obesity in men above 102 cm and in women above 88 cm (9, 18). The increase in waist circumference increases obesity risk and disease (9).

### 3. Obesity and Young Adolescents

Adolescence is an important process for growth and development and encompasses cognitive and psychosocial development (19, 20). Interestingly, 15% of adult height and 50% of body weight are gained in this period (21, 22). During the growth process, changes in the amount of fat, water, and hormones occur in the body. Height and weight in adolescent girls changes in the year before menarche and continue two years following menarche (21, 22). At the beginning of adolescence, fat tissue increases in the body compared to muscle mass due to estrogen (6). The need for energy and nutrients also increases due to physiological changes and rapid body growth (21, 22). In the adolescent period, adequate and balanced nutrition is important to achieve growth and proper bone density. In addition, nutrition helps to initiate and continue menstruation in adolescent girls (23).

According to WHO (24), adolescents are considered a high-risk group for nutrition. This is due to the high prevalence of obesogenic risk factors including excessive calorie intake (25). Behaviors such as eating out the home/fast-food, skipping main meals, snacking, and eating disorders may develop (26). Today it is common for adolescents to have a more sedentary lifestyle and increased calorie consumption and consequently obesity (21). These bad habits can be permanent and negatively affect health throughout life (21).

Adolescent girls have higher obesity rates than males in primary school and puberty (20). A previous report showed that obesity prevalence increases with increasing age in girls (20). Psychological factors may be an underlying cause (20) including eating disorders (anorexia and bulimia), depression, poor body image, and/or stigma-triggered obesity (27). Young obese girls enter puberty earlier than their normal-weight peers. According to the study conducted by Kaltila-Heino et al. (28), early puberty is a risk factor for depression in young girls. Problems experienced by obese adolescent women include sexual maturation and reproductive system disorders, changes in menstruation, dysmenorrhea, risky sexual behavior and contraception, polycystic ovarian syndrome, bone density abnormalities, macromasti and increased risk of breast and endometrial cancer. In addition, many other factors may occur during the pregnancy of adolescents with obesity (29).

#### 4. Obesity and Pregnancy

In the literature, BMI is not recommended in the evaluation of pregnant women (15). However, it is recommended to measure the BMI because it provides a useful and practical assessment and is the first screening step for pregnant women in terms of obesity. The prevalence of obesity during pregnancy is observed at rates ranging from 7.56% (30) to 20% (31). One of every five women of childbearing age (2) becomes obese during pregnancy. This affects the health of pregnant women and future generations significantly (32), and causes serious health problems (33).

During pregnancy, many physiological/psychological changes occur including The excess weight gain (5). Factors such as the presence of obesity before, excess weight after (34), and late gestational age cause obesity during pregnancy (35). Obesity during pregnancy is accepted as high risk (36) and complications can develop during the antenatal, intrapartum, postpartum and neonatal periods (37).

Antenatal complications observed in pregnancy with obesity include miscarriage, congenital anomalies (32), fetal death (38), gestational hypertension (33), chronic hypertension (32), preeclampsia, gestational/chronic diabetes (33), increased hospitalization, limitations in ultrasound imaging (32), Urinary Tract Infection (UTIs) and early membrane rupture (31), and increased risk of developing metabolic syndrome (33).

Complications associated with obesity may be seen intrapartum including difficulties in monitoring fetal and uterine contractions, birth abnormalities, and anesthesia complications (32), operative vaginal delivery, prolongation of action, increase in induction use (39), bladder/perineum traumas, cesarean delivery (31, 32), difficulty in intubation,

maternal death, venous thromboembolism, birth trauma, stillbirth (40), shoulder dystocia, difficulties with epidural, and increase in postterm delivery frequency (41).

Postpartum complications include inability to lose weight (32), increased risk of infection (32, 42), breastfeeding complications (32, 43), postpartum depression (44), postpartum hemorrhage, thromboembolism (32), stress incontinence and maternal death (45). Breastfeeding complications are caused by increased prematurity and intervened birth rates as well as excessive weight in the postpartum period (13).

Neonatal complications include birth defects (46), apgar score below 4 (47), stillbirth, macrosomia (48), acidosis/respiration complications (49), hospitalization (49) and increased need for intensive care (50). In infants of obese mothers, childhood obesity, adolescent and adult metabolic diseases are more common (33, 51). This shows that children born from obese women carry risk of disease in all periods of their lives.

#### 5. Obesity and Infertility

Infertility affecting one in seven married couples (3, 52), negatively affects women's health especially by depression, anxiety, sexual dysfunction in women, and emotional well-being/quality-of-life (53). Many factors such as postponement of gestational age (53), obesity (3, 54, 55), stress (56), smoking (57) and alcohol use are considered among the causes of infertility (58). Obesity is responsible for 25-50% of infertility in women (58).

The cause of decreased obesity-related fertility/infertility is changes in the secretion and metabolism of sex hormones, estrogens and androgens, and disruption of the balance between the hypothalamus, pituitary and ovarian axes (3, 59). The relationship between adipose tissue and gonads is bidirectional. Adipose tissue affects gonadal functions via adipokine secretions such as resistin, ghrelin, adiponectin and leptin (60). The effect of leptin on reproductive functions regulates early embryo cleavage and development (61). While it has a stimulating effect on the hypothalamic-pituitary axis, it is inhibitory on newly developing follicles (62). Obesity is associated with an increase in serum leptin and follicular fluid. Leptin acts on specific follicular cell receptors, and causes a decrease in insulin-induced steroidogenesis in both granulosa and theca cells (63). Leptin stimulates estrogen in granulosa cells and inhibits LH (62). Insulin changes in obese women is also important for infertility and anovulation (64). Insulin is important for ovarian function and causes increased androgen production in obese women. Increased aromatization of androgens to estrogens causes reduced sex hormone-binding globulin (SHBG) levels resulting in increased estradiol and free



testosterone (3, 52). This condition worsens hyperinsulinemia, resulting in increased androgen/estradiol ratio and LH hypersecretion, which affects the ovarian microenvironment and folliculogenesis (65, 66). As a result, obesity affects assisted reproductive technology and fertility at every stage (67, 68), fertilization, embryo development and implantation (69). It has been shown that there are important differences in various hormones and metabolites of the patients with obesity in the IVF cycle compared to non-the patients with non-obesity (70). Increased insulin resistance (IR) (71), lower oocyte utilization rates, higher need for gonadotropin use, and low number of cryopreserved embryos has been identified in IVF treatment in obese women (68, 72). Since female obesity and infertility are interrelated, healthcare professionals are recommended to educate women in ways to control obesity. When increased BMI and advanced age align, a significant effect on fertility success occurs (3).

## 6. Obesity and PCOS

PCOS is a hormonal disorder that generally affects women during the peripubertal period. Genetic and environmental factors are thought to play a role in its etiology (73). Although PCOS is not common among women with normal weight, clinical features are associated with IR in obese women (74). Basal metabolic rate decreases with hyperandrogenism and IR in women with PCOS (75). This causes weight gain in women with PCOS (13). Obesity is more common in women with PCOS (76) and emerging obesity worsens PCOS symptoms (13).

With the addition of obesity to PCOS, production of estrogen increases as a result of the peripheral concentration of androgens. One of the most important endocrine changes in obesity is the increase in basal blood insulin. The increase in body fat mass causes increased insulin secretion and IR (77). Following IR and hyperinsulinemia, changes occur in the secretion of gonadotropins secreted from the hypothalamus. Especially LH increases and FSH decreases (78). Hepatic production of SHBG is prevented in obese women following hyperandrogenism. The decrease in SHBG and the increase of peripheral aromatization of androgens to estrogens result in increased circulating free estrogen in obese women (78). This results in increased negative feedback of the hypothalamic-pituitary axis. This negatively affects gonadotropin secretion and ovulation and adequate ovarian follicle development (79). As a result, fertilization ability decreases and abortion rates are quite high in obese women (78, 80). Interestingly, the follicular phase lasts longer and the luteal phase is shorter in women with BMI $\geq$ 25. In obese women and PCOS, losing weight increases

fertility chance (81, 82). Obesity as well as undernutrition have been considered indicators of reproductive system dysfunction and menstrual irregularity.

### Obesity and Female Cancers

Obesity is expected to cause at least 12 types of cancer and recently replaced smoking as the highest risk factor for cancer (83). Obesity is directly related to cancer development, recurrence, and death in women (84). In this respect, the WCRF recommends a BMI between 21 and 23 (85). Obesity is a risk factor for cervix (86), ovarian (87), endometrium (88), and breast cancer (89) and is responsible for 88% of cancer-related deaths (90, 91).

**Endometrium Cancer:** The risk of endometrial cancer has been determined to be 1.52 times higher in obese women (92). Similarly, endometrial cancer-related mortality rates have increased due to obesity (93, 94). Adipose tissue contributes to stimulation of hormone production, inflammatory response, and cellular proliferation pathways (95) and causes endometrial cancer (96). Dysfunctional adipose tissue has been shown to release of pro-inflammatory cytokines, and cause changes in crucial signalling pathways (97). These inflammatory processes cause IR, abnormal responses in natural/adaptive immunity, and lead to a tumorigenic environment (98). One of the important adipokines in these pathological processes is leptin (99). Recently, pathological and molecular differences between type-I and type-II endometrial cancer have been revealed. For example, type I tumors are caused by endometrial hyperplasia, while type II tumors are typically associated with pathognomic features. Both types of tumors are frequently seen in obesity (100).

**Cervical Cancer:** The relationship between cervical cancer and obesity (101) is controversial (102). Conflicting reports have debated obesity as a risk factor for cervical cancer (103, 104). In cervical cancer, IGF-1 has been found to play a role in disease development/progression (105, 106). Insulin and IGF-1 concentrations are associated with obesity. A relationship between obesity, cervical cancer (107), and cancer-related death is higher in obese women (108).

**Ovarian Cancer:** In ovarian cancer, high BMI before cancer diagnosis increases the risk (109). Community-based studies have shown that every five-kg increase in women's weight is associated with the risk of ovarian cancer (110, 111).

**Breast Cancer:** Understanding the relationship between obesity and breast cancer is important due to its prevalence in women (112). This relationship has been revealed in many studies (113,

114). Adipose tissue of obese individuals produce inflammatory cytokines/mediators, creating a favorable environment for cancer (115-117). In obesity, high levels of leptin cause more preadipocytes that reduce adipocyte maturation (117). In obesity, as the adipose tissue expands causing an imbalance in oxygen levels, which induces gene expression changes. Hypoxia-inducing Factor-1 (HIF-1), a molecular oxygen sensor, can directly regulate the expression of leptin VEGF, and adipopectin (118). In obese adipose tissue, adipopectin/leptin ratio decreases (119). High serum and intratumor leptin levels may cause worsening of breast cancer prognosis (120).

## 7. Conclusion

Obesity negatively affects the physical, psychological and sociological health of women and is associated with higher mortality and morbidity rates. It is among the primary roles and responsibilities of caregivers to determine the risk factors related to age, to identify the early phase risks, to provide advice for regular and balanced nutrition and to regularly control weight. It is believed that with proper education will help women understand the complications associated with development of obesity. It is important to integrate obesity practices into care protocols and clinical practice. Healthcare workers should ensure multidisciplinary cooperation in order to prevent obesity in women and offer joint programs with other institutions/organizations to prevent obesity.

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## Author contribution

Study conception and design: RAI, and FT; data collection: RAI, and FT; analysis and interpretation of results:RAI, and FT; draft manuscript preparation: RAI, and FT. All authors reviewed the results and approved the final version of the manuscript.

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## Kaynaklar

1. Waters E, de Silva-Sanigorski A, Hall BJ, Brown T, Campbell KJ, Gao Y, et al. Interventions for preventing obesity in children. *Cochrane Database Syst Rev* 2011: CD001871.
2. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; 384: 766-81.
3. Talmor A, Dunphy B. Female obesity and infertility. *Best Pract Res Clin Obstet Gynaecol* 2015; 29: 498-506.
4. Prevention and management of the global epidemic of obesity. Report of the WHO Consultation on Obesity Geneva: WHO; 1997 [Available from: file:///C:/Users/tr/Documents/Downloads/WHO\_NUT\_NCD\_98.1\_(p1-158).pdf]
5. Ergin AB. Obezitenin kadın sağlığı ve toplumsal cinsiyet açısından değerlendirilmesi. *KASHED* 2014; 1: 41-54.
6. Kanter R, Caballero B. Global gender disparities in obesity: a review. *Adv Nutr* 2012; 3: 491-8.
7. Kozakowski J, Gietka-Czernel M, Leszczynska D, Majos A. Obesity in menopause - our negligence or an unfortunate inevitability? *Prz Menopauzalny* 2017; 16: 61-5.
8. Stevens GA, Singh GM, Lu Y, Danaei G, Lin JK, Finucane MM, et al. National, regional, and global trends in adult overweight and obesity prevalences. *Popul Health Metr* 2012; 10: 22.
9. Türkiye'de Obezite Oranı: Türkiye İstatistik Kurumu; 2016 [Available from: [http://tuik.gov.tr/PreTablo.do?alt\\_id=1068](http://tuik.gov.tr/PreTablo.do?alt_id=1068)]
10. Nazlıcan E, Demirhindi H, Akbaba M. Adana İli Solaklı ve Karataş Merkez Sağlık Ocağı Bölgesinde yaşayan 20-64 yaş arası kadınlarda obezite ve ilişkili risk faktörlerinin incelenmesi. *Düzce Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi* 2011; 1: 5-12.
11. Rong K, Yu K, Han X, Szeto IM, Qin X, Wang J, et al. Pre-pregnancy BMI, gestational weight gain and postpartum weight retention: a meta-analysis of observational studies. *Public Health Nutr* 2015; 18: 2172-82.
12. Pegington M, French DP, Harvie MN. Why young women gain weight: A narrative review of influencing factors and possible solutions. *Obes Rev* 2020; 21: e13002.
13. Meldrum DR. Introduction: Obesity and reproduction. *Fertil Steril* 2017; 107: 831-2.
14. Waters H, DeVol R. Weighing down America: the health and economic impact of obesity 2016 [Available from: <http://www.milkeninstitute.org/publications/view/833>].
15. Yavuz R, Tontuş HÖ. Erişkin, adolesan ve çocukluk yaş grubunda obeziteye klinik yaklaşım. *Journal of Experimental and Clinical Medicine* 2013; 30: 1.



16. WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *The Lancet* 2004; 157-63.
17. Yücel BB, Toprak D. 6-16 Yaş Arası Obez Çocuklarda Antropometrik Ölçümlerin Ve Biyokimyasal Parametrelerin Değerlendirilmesi. *Ankara Med J* 2016; 16: 27-40.
18. Lau DC, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. *CMAJ* 2007; 176: S1-13.
19. Ersoy R, Çakır B. Obezite. *Turkish Medical Journal* 2007; 1: 109-11.
20. Güler Y, Gönener HD, Altay B, Gönener A. Adölesanlarda obezite ve hemsirelik bakımı. *Fırat Sağlık Hizmetleri Dergisi* 2009; 4: 165.
21. Aksoydan E, Cakir N. Adölesanların Beslenme Alışkanlıkları, Fiziksel Aktivite Düzeyleri ve Vücut Kitle İndekslerinin Değerlendirilmesi. *Gülhane Tıp Dergi* 2011: 264-70.
22. Cordeiro LS, Lamstein S, Mahmud Z, Levinson FJ. Adolescent malnutrition in developing countries: a close look at the problem and at two national experience. *Standing Committee on Nutrition (SCN News)* 2005; 31: 6-13.
23. Karacaören A. Adölesanlarda duygu değişiklikleri ile yeme eğilimi ilişkisinin değerlendirilmesi *Ankara: Başkent Üniversitesi*; 2019.
24. World Health Organization. Nutrition in adolescence: issues and challenges for the health sector: Issues in adolescent health and development: World Health Organization; 2005.
25. Erkekoğlu P, Giray B, Şahin G. Çocukluk ve adölesan dönemde kullanılan antiobezitik ilaçların toksikolojik açıdan değerlendirilmesi. *Hacettepe Tıp Dergisi* 2007; 38: 199-211.
26. Chandra-Mouli V, Haider R, Moreira A. Adolescent nutrition. Lessons learnt and challenges ahead. Editorial. *Standing Committee on Nutrition. SCN News* 2006; 31: 40-2.
27. Zhu H, Luo X, Cai T, Li Z, Liu W. Self-control and parental control mediate the relationship between negative emotions and emotional eating among adolescents. *Appetite* 2014; 82: 202-7.
28. Kaltiala-Heino R, Kosunen E, Rimpela M. Pubertal timing, sexual behaviour and self-reported depression in middle adolescence. *J Adolesc* 2003; 26: 531-45.
29. Elizondo-Montemayor L, Hernandez-Escobar C, Lara-Torre E, Nieblas B, Gomez-Carmona M. Gynecologic and Obstetric Consequences of Obesity in Adolescent Girls. *J Pediatr Adolesc Gynecol* 2017; 30: 156-68.
30. Panaitescu AM, Rotaru D, Ban I, Peltecu G, Zagrean AM. The Prevalence of Underweight, Overweight and Obesity in a Romanian Population in the First Trimester of Pregnancy - Clinical Implications. *Acta Endocrinol (Buchar)* 2019; 15: 323-32.
31. Yu CK, Teoh TG, Robinson S. Obesity in pregnancy. *BJOG* 2006; 113: 1117-25.
32. Kominiarek MA, Chauhan SP. Obesity Before, During, and After Pregnancy: A Review and Comparison of Five National Guidelines. *Am J Perinatol* 2016; 33: 433-41.
33. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *BMJ* 2017; 356: j1.
34. Akyol MA. Çocukluk Çağında Metabolik Sendrom: Maternal Obezite, Gestasyonel Diyabet, Doğum Ağırlığı İlişkisi. 1 ed. Tayfur M, Yabancı AN, editors. Ankara: Hatipoğlu Yayınevi; 2015.
35. Lee CY, Koren G. Maternal obesity: effects on pregnancy and the role of pre-conception counselling. *J Obstet Gynaecol* 2010; 30: 101-6.
36. Al Wattar BH, Pidgeon C, Learner H, Zamora J, Thangaratinam S. Online health information on obesity in pregnancy: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2016; 206: 147-52.
37. Yanikkerem E, Mutlu S. Maternal obezitenin sonuçları ve önleme stratejileri. *TAF Preventive Medicine Bulletin* 2012; 11: 353-64.
38. Aune D, Saugstad OD, Henriksen T, Tonstad S. Maternal body mass index and the risk of fetal death, stillbirth, and infant death: a systematic review and meta-analysis. *JAMA* 2014; 311: 1536-46.
39. Hajagos-Toth J, Ducza E, Samavati R, Vari SG, Gaspar R. Obesity in pregnancy: a novel concept on the roles of adipokines in uterine contractility. *Croat Med J* 2017; 58: 96-104.
40. Knight-Agarwal CR, Williams LT, Davis D, Davey R, Cochrane T, Zhang H, et al. Association of BMI nad interpregnancy BMI change with birth outcomes in an Australian obstetric population: a retrospective cohort study. *BMJ* 2016; 6: 1-9.
41. Simic M, Wahlin IA, Marsal K, Kallen K. Maternal obesity is a potential source of error in mid-trimester ultrasound estimation of gestational age. *Ultrasound Obstet Gynecol* 2010; 35: 48-53.
42. Taşdemir D, Karaman E, Yıldız A, Han A, Karaman Y, Talay H. Obezitenin term gebelerde maternal ve fetal sonuçlara etkisi: Bir olgu kontrol çalışması. *Istanbul Kanuni Sultan Süleyman Tıp Dergisi (IKSST)* 2015; 7: 73-8.
43. Kürklü N, Kamarlı H. Maternal Obezitenin Emzirmeye Etkisi. *Journal of Anatolia Nursing and Health Sciences* 2016; 19: 53-6.
44. Lacoursiere DY, Baksh L, Bloebaum L, Varner MW. Maternal body mass index and self-reported postpartum depressive symptoms. *Matern Child Health J* 2006; 10: 385-90.
45. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Obesity in Pregnancy, Management of (C-Obs49) (March 2013, revised September 2013) [Available from: <https://www.ranzcog.edu.au/college-statements-guidelines.html>].
46. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA* 2009; 301: 636-50.
47. An X, Zhao Y, Zhang Y, Yang Q, Wang Y, Cheng W, et al. Risk assessment of morbidly obese parturient in cesarean section delivery: A prospective, cohort, single-center study. *Medicine (Baltimore)* 2017; 96: e8265.
48. Chen CN, Chen HS, Hsu HC. Maternal Prepregnancy Body Mass Index, Gestational Weight Gain, and Risk of Adverse Perinatal Outcomes in Taiwan: A Population-Based Birth Cohort Study. *Int J Environ Res Public Health* 2020; 17.
49. Sullivan EA, Dickinson JE, Vaughan GA, Peek MJ, Ellwood D, Homer CS, et al. Maternal super-obesity and perinatal outcomes in Australia: a national population-based cohort study. *BMC Pregnancy Childbirth* 2015; 15: 322.
50. Vinturache AE, McDonald S, Slater D, Tough S. Perinatal outcomes of maternal overweight and obesity in term infants: a population-based cohort study in Canada. *Sci Rep* 2015; 5: 9334.

51. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* 2005; 115: e290-6.
52. Yılmaz FÇ, Yardımcı H. eden Kütle İndeksinin İnfertilite Üzerine Etkisi. *Hacettepe University Faculty of Health Sciences Journal* 2015; 1: s1.
53. Amanak K, Karaöz B, Sevil Ü. Modern Yaşamın İnfertilite Üzerine Etkisi. *TAF Preventive Medicine Bulletin* 2014; 13.
54. Bhattacharya S, Porter M, Amalraj E, Templeton A, Hamilton M, Lee AJ, et al. The epidemiology of infertility in the North East of Scotland. *Hum Reprod* 2009; 24: 3096-107.
55. Bosdou JK, Kolibianakis EM, Tarlatzis BC, Fatemi HM. Sociocultural influences on fertility in the Middle East: the role of parental consanguinity, obesity and vitamin D deficiency. *Fertil Steril* 2016; 106: 259-60.
56. Agarwal A, Aponte-Mellado A, Premkumar BJ, Shaman A, Gupta S. The effects of oxidative stress on female reproduction: a review. *Reprod Biol Endocrinol* 2012; 10: 49.
57. Cinar O, Dilbaz S, Terzioğlu F, Karahalil B, Yucel C, Turk R, et al. Does cigarette smoking really have detrimental effects on outcomes of IVF? *Eur J Obstet Gynecol Reprod Biol* 2014; 174: 106-10.
58. Weiss RV, Clapauch R. Female infertility of endocrine origin. *Arq Bras Endocrinol Metabol* 2014; 58: 144-52.
59. van der Steeg JW, Steures P, Eijkemans MJ, Habbema JD, Hompes PG, Michgelsen HW, et al. Predictive value of pregnancy history in subfertile couples: results from a nationwide cohort study in the Netherlands. *Fertil Steril* 2008; 90: 521-7.
60. Metwally M, Li TC, Ledger WL. The impact of obesity on female reproductive function. *Obes Rev* 2007; 8: 515-23.
61. Brannian JD, Hansen KA. Leptin and ovarian folliculogenesis: implications for ovulation induction and ART outcomes. *Semin Reprod Med* 2002; 20: 103-12.
62. Moschos S, Chan JL, Mantzoros CS. Leptin and reproduction: a review. *Fertil Steril* 2002; 77: 433-44.
63. Spicer LJ. Leptin: a possible metabolic signal affecting reproduction. *Domest Anim Endocrinol* 2001; 21: 251-70.
64. Pantasri T, Norman RJ. The effects of being overweight and obese on female reproduction: a review. *Gynecol Endocrinol* 2014; 30: 90-4.
65. Levens ED, Skarulis MC. Assessing the role of endometrial alteration among obese patients undergoing assisted reproduction. *Fertil Steril* 2008; 89: 1606-8.
66. Schwartz MW, Seeley RJ. Seminars in medicine of the Beth Israel Deaconess Medical Center. Neuroendocrine responses to starvation and weight loss. *N Engl J Med* 1997; 336: 1802-11.
67. Luke B, Brown MB, Stern JE, Missmer SA, Fujimoto VY, Leach R, et al. Female obesity adversely affects assisted reproductive technology (ART) pregnancy and live birth rates. *Hum Reprod* 2011; 26: 245-52.
68. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. *Reprod Biomed Online* 2011; 23: 421-39.
69. Karaca N, Batmaz G, Aydın S. Effect of obesity on fertility. *Bezmialem Science* 2015; 3: 78-82.
70. Robker RL, Akison LK, Bennett BD, Thrupp PN, Chura LR, Russell DL, et al. Obese women exhibit differences in ovarian metabolites, hormones, and gene expression compared with moderate-weight women. *J Clin Endocrinol Metab* 2009; 94: 1533-40.
71. Gosman GG, Katcher HI, Legro RS. Obesity and the role of gut and adipose hormones in female reproduction. *Hum Reprod Update* 2006; 12: 585-601.
72. Jungheim ES, Moley KH. Current knowledge of obesity's effects in the pre- and periconceptional periods and avenues for future research. *Am J Obstet Gynecol* 2010; 203: 525-30.
73. Kadioğlu M, Beji KN. Polikistik Over Sendromu ve Hemşirelik Yaklaşımı. *FN Hem Derg* 2013; 21: 187-97.
74. Yildiz BO, Azziz R, Androgen E, Society P. Ovarian and adipose tissue dysfunction in polycystic ovary syndrome: report of the 4th special scientific meeting of the Androgen Excess and PCOS Society. *Fertil Steril* 2010; 94: 690-3.
75. Georgopoulos NA, Saltamavros AD, Vervita V, Karkoulias K, Adonakis G, Decavalas G, et al. Basal metabolic rate is decreased in women with polycystic ovary syndrome and biochemical hyperandrogenemia and is associated with insulin resistance. *Fertil Steril* 2009; 92: 250-5.
76. Yildirim B, Sabir N, Kaleli B. Relation of intra-abdominal fat distribution to metabolic disorders in nonobese patients with polycystic ovary syndrome. *Fertil Steril* 2003; 79: 1358-64.
77. Gimble JM. Adipose tissue-derived therapeutics. *Expert Opin Biol Ther* 2003; 3: 705-13.
78. McKinney A. A lifestyle perspective on infertility and pregnancy outcome. *Am J Lifestyle Med* 2015; 9: 368-77.
79. Nestler JE. Obesity, insulin, sex steroids and ovulation. *Int J Obes Relat Metab Disord* 2000; 24 Suppl 2: S71-3.
80. Nho JH. Lifestyle Intervention for Obese Women. *J Lifestyle Med* 2017; 7: 51-4.
81. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. *Lancet* 2007; 370: 685-97.
82. Teitelman M, Grotegut CA, Williams NN, Lewis JD. The impact of bariatric surgery on menstrual patterns. *Obes Surg* 2006; 16: 1457-63.
83. Furer A, Afek A, Sommer A, Keinan-Boker L, Derazne E, Levi Z, et al. Adolescent obesity and midlife cancer risk: a population-based cohort study of 2.3 million adolescents in Israel. *Lancet Diabetes Endocrinol* 2020; 8: 216-25.
84. Arnold M, Pandeya N, Byrnes G, Renehan PAG, Stevens GA, Ezzati PM, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. *Lancet Oncol* 2015; 16: 36-46.
85. World Cancer Research Fund. 2nd ed. Washington, DC, USA: American Institute for Cancer Research; 2007.
86. Gu W, Chen C, Zhao KN. Obesity-associated endometrial and cervical cancers. *Front Biosci* 2013; 5: 109-18.



87. Nagle CM, Dixon SC, Jensen A, Kjaer SK, Modugno F, deFazio A, et al. Obesity and survival among women with ovarian cancer: results from the Ovarian Cancer Association Consortium. *Br J Cancer* 2015; 113: 817-26.
88. Arem H, Irwin ML. Obesity and endometrial cancer survival: a systematic review. *Int J Obes (Lond)* 2013; 37: 634-9.
89. Nindrea RD, Aryandono T, Lazuardi L, Dwiprahasto I. Association of Overweight and Obesity with Breast Cancer During Premenopausal Period in Asia: A Meta-Analysis. *Int J Prev Med* 2019; 10: 192.
90. Gelsomino L, Naimo GD, Catalano S, Mauro L, Ando S. The Emerging Role of Adiponectin in Female Malignancies. *Int J Mol Sci* 2019; 20.
91. Park J, Morley TS, Kim M, Clegg DJ, Scherer PE. Obesity and cancer-mechanisms underlying tumour progression and recurrence. *Nat Rev Endocrinol* 2014; 10: 455-65.
92. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 2003; 348: 1625-38.
93. Secord AA, Hasselblad V, Von Gruenigen VE, Gehrig PA, Modesitt SC, Bae-Jump V, et al. Body mass index and mortality in endometrial cancer: A systematic review and meta-analysis. *Gynecol Oncol* 2016; 140: 184-90.
94. Shaw E, Farris M, McNeil J, Friedenreich C. Obesity and Endometrial Cancer. *Recent Results Cancer Res* 2016; 208: 107-36.
95. McDonald ME, Bender DP. Endometrial Cancer: Obesity, Genetics, and Targeted Agents. *Obstet Gynecol Clin North Am* 2019; 46: 89-105.
96. Iskander K, Farhour R, Ficek M, Ray A. Obesity-related complications: few biochemical phenomena with reference to tumorigenesis. *Malays J Pathol* 2013; 35: 1-15.
97. Divella R, De Luca R, Abbate I, Naglieri E, Daniele A. Obesity and cancer: the role of adipose tissue and adipo-cytokines-induced chronic inflammation. *J Cancer* 2016; 7: 2346-59.
98. Conroy MJ, Dunne MR, Donohoe CL, Reynolds JV. Obesity-associated cancer: an immunological perspective. *Proc Nutr Soc* 2016; 75: 125-38.
99. Uchikova E, Uchikov P, Parahuleva P. [Obesity and Endometrial Carcinogenesis]. *Akush Ginekol (Sofia)* 2015; 54: 34-7.
100. Daley-Brown D, Oprea-Ilies GM, Lee R, Pattillo R, Gonzalez-Perez RR. Molecular cues on obesity signals, tumor markers and endometrial cancer. *Horm Mol Biol Clin Invest* 2015; 21: 89-106.
101. Aquila I, Ricci P, Oliverio A, Gratteri S. Role of the body mass index in the genesis of ascites in ovarian cancer: a forensic case and review of the literature. *BMJ Case Rep* 2018; 11.
102. Olsen CM, Green AC, Whiteman DC, Sadeghi S, Kolahdooz F, Webb PM. Obesity and the risk of epithelial ovarian cancer: a systematic review and meta-analysis. *Eur J Cancer* 2007; 43: 690-709.
103. Charkhchi P, Schabath MB, Carlos RC. Breast, Cervical, and Colorectal Cancer Screening Adherence: Effect of Low Body Mass Index in Women. *J Womens Health (Larchmt)* 2020.
104. Donkers H, Smits A, Eleuteri A, Bekkers R, Massuger L, Galaal K. Body mass index and sexual function in women with gynaecological cancer. *Psychooncology* 2019; 28: 48-53.
105. Benedetto C, Salvagno F, Canuto EM, Gennarelli G. Obesity and female malignancies. *Best Pract Res Clin Obstet Gynaecol* 2015; 29: 528-40.
106. Huang YF, Shen MR, Hsu KF, Cheng YM, Chou CY. Clinical implications of insulin-like growth factor 1 system in early-stage cervical cancer. *Br J Cancer* 2008; 99: 1096-102.
107. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. *Eur J Cancer Prev* 2016; 25: 232-8.
108. Frumovitz M, Jhingran A, Soliman PT, Klopp AH, Schmeler KM, Eifel PJ. Morbid obesity as an independent risk factor for disease-specific mortality in women with cervical cancer. *Obstet Gynecol* 2014; 124: 1098-104.
109. Jung SY, Kim YA, Jo M, Park SM, Won YJ, Ghang H, et al. Prediagnosis obesity and secondary primary cancer risk in female cancer survivors: A national cohort study. *Cancer Med* 2019; 8: 824-38.
110. Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet* 2014; 384: 755-65.
111. Olsen CM, Nagle CM, Whiteman DC, Ness R, Pearce CL, Pike MC, et al. Obesity and risk of ovarian cancer subtypes: evidence from the Ovarian Cancer Association Consortium. *Endocr Relat Cancer* 2013; 20: 251-62.
112. Picon-Ruiz M, Morata-Tarifa C, Valle-Goffin JJ, Friedman ER, Slingerland JM. Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention. *CA Cancer J Clin* 2017; 67: 378-97.
113. Alsolami FJ, Azzeh FS, Ghafouri KJ, Ghaith MM, Almaimani RA, Almasmoum HA, et al. Determinants of breast cancer in Saudi women from Makkah region: a case-control study (breast cancer risk factors among Saudi women). *BMC Public Health* 2019; 19: 1554.
114. Engin A. Obesity-associated Breast Cancer: Analysis of risk factors. *Adv Exp Med Biol* 2017; 960: 571-606.
115. Picon-Ruiz M, Pan C, Drews-Elger K, Jang K, Besser AH, Zhao D, et al. Interactions between Adipocytes and Breast Cancer Cells Stimulate Cytokine Production and Drive Src/Sox2/miR-302b-Mediated Malignant Progression. *Cancer Res* 2016; 76: 491-504.
116. Gilbert CA, Slingerland JM. Cytokines, obesity, and cancer: new insights on mechanisms linking obesity to cancer risk and progression. *Annu Rev Med* 2013; 64: 45-57.
117. McArdle MA, Finucane OM, Connaughton RM, McMorrow AM, Roche HM. Mechanisms of obesity-induced inflammation and insulin resistance: insights into the emerging role of nutritional strategies. *Front Endocrinol (Lausanne)* 2013; 4: 52.
118. Trayhurn P. Hypoxia and adipose tissue function and dysfunction in obesity. *Physiol Rev* 2013; 93: 1-21.
119. Ollberding NJ, Kim Y, Shvetsov YB, Wilkens LR, Franke AA, Cooney RV, et al. Prediagnostic leptin, adiponectin, C-reactive protein, and the risk of postmenopausal breast cancer. *Cancer Prev Res (Phila)* 2013; 6: 188-95.
120. Niu J, Jiang L, Guo W, Shao L, Liu Y, Wang L. The Association between Leptin Level and Breast Cancer: A Meta-Analysis. *PLoS One* 2013; 8: e67349.