

Women's Obesity Correlated With Chronic Diseases And Reproductive Dysfunction . A review

Noor Al-Huda Ali A.H. Saeed, Areej Abbas Zabbon, Ban Talib Elhaboby
Biology Department, College of Science, Mustansiriya University. Iraq.

Abstract:

Background : Worldwide, each overweight and obesity, are boosts and have pernicious impacts in lots of functions on the human body especially the reproductive validity. related to women infertility among a knob and various techniques, obese women display trouble of hypothalamic-pituitary-ovarian axis, thereafter in repeatedly undergo from menstrual dysfunction which command to anovulation as well as infertility in addition to the relation with chronic diseases.

Methods: this review is based on systematic-reviews, meta-analysis, and control trials.

Results: women obesity is correlated with unfavorabl clinical outcomes. Numerous risks were depended on the body-mass-index (BMI). The prospect of visualization decline linearly. Started from BMI ≥ 30 kg/m² . According to the World Health Organization, 70% of women were obese (≥ 30 kg/m²), 30% were overweight (≥ 35 kg/m²) and about 5% were sickly fatness (≥ 40 kg/m²). Approximately 3.3-million humans passing every section because-of validity issues associated with obesity. There are 45% correlation with diabetes, 22% correlated with heart-diseases, and 8% - 40% related to fatness-malignancies.

Keyword : women, obesity, infertility, hormone, Polycystic ovary syndrome, fatness.

Introduction

Overweight is the great risk hazard of various systemic situations, also turn out a big generic health issue because the diffusion extent epidemical rates. Obesity seems to be consistently have a strong correlation with subfertility[1,2], and in mothers, it has prime peril to the earnest pregnancy complexity [3,4].

The major function in females gonads includes the gametes production, oocytes, as well as gender hormone which monitoring the expansion of minor sexual features in female, also hold-up the gestations. Physiologically, this function is periodically spend-up among the adulthood so as menopause, it is also adjusted via endocrine or by paracrine which react to many sorts of cells that lie at the ovary [5]. If more morbid results, any altered and dysfunctional planning in this mechanism enable immediately and sinuous outcome of infertility.

In women, there are many things imitate that be through with instigating infertility, comprehensive "the ovulatory disorder, cervical/ uterine factors" the endometrium through rank 20-30% of the cases remain unexplained[6]. Some researchers found the lifestyle effects of women reproductive verdure encounter a mighty concern and body mass index (BMI), nutrients- foods, bodily activities as well as sports, stressing jobs, all of that currently is wide claimed

as a negative impact of the fertility in female [7].

The increment of a venture on precocious genetic miscarriage[8], the congenital castration [9], outcomes of poor perinatal and stillbirth as well as neonatal death [10], related to such upturn at obesity, according to greasiness correlation sub-fertile. while the way of retardant child-bearing. this leads towards growing credence of productivity remedy for enquiring the pregnancy. That intends the growing measure of obese women so as older female will discuss the fertile interference or demand supported in reproductive remedy. The commonest trouble between female during the reproductive period today is obesity. It encloses the accumulation of abnormal excessive fat which passively impacts the health condition. According to (WHO) World Health Organization, "body mass index" amounting to or above "25 kg/m²" that assumed as overweight, and if "BMI" is "30 kg/m²" or higher, it is realized as obesity [11]. Researchers in Eastern- Mediterranean-countries reports thus obesity is approached the terrifying plane and the happening of obesity diseases is elevated and appears much than "50%" of whole death reasons[12,13]. WHO records in the United States that 60% of women are overweight, while, in European-countries 30% of female inhabitation are corpulent. whereas, 5% of these females are pathologically fatty, BMI "≥ 35 kg/m²".

The negative impacts of fatty are well known in reproductive physiology, overweight female constantly "suffer from menstrual abnormality and ovulatory unrest, endometrial pathology, as well as infertility [14].

Women's Obesity epidemiology

Globally overweight is growing fast and reported as a major risk in billion adult women suffering from fatness. WHO recorded that 70% of females were obese (≥ 30 kg/m²) in USA and

European-countries, 30% were overweighted (≥ 35 kg/m²) whereas 5% of them were sickly fatness (≥ 40 kg/m²), [11,15]. Whereas, after ten years, WHO recorded that 72% of females were overweighted in the USA, 67% in Newzealand, 65% in Austrailia, 62% in the United Kingdom, and 60% in Canada. Up to 50% of them were obese (≥ 30 kg/m²), 40% were overweighted (≥ 35 kg/m²), while the rest 10% of them were sickly fatness (≥ 40 kg/m²) [16], Figure 1.

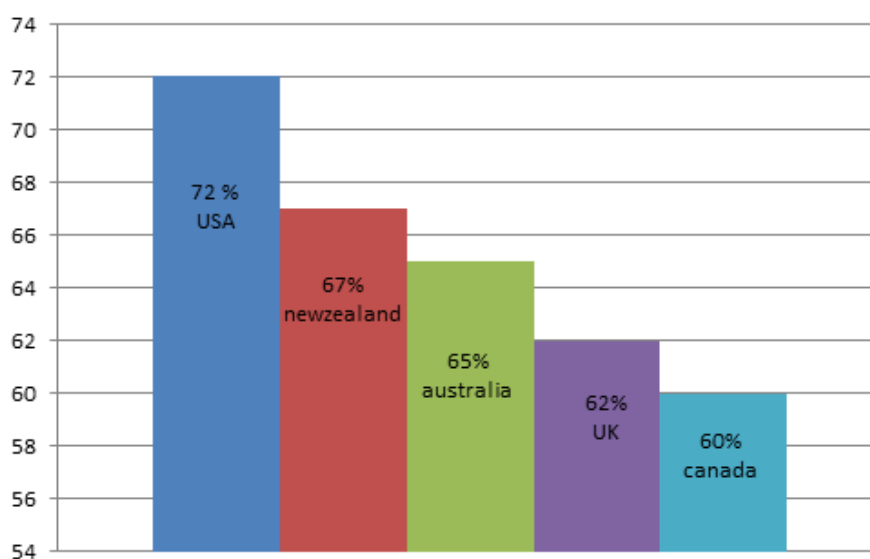


Figure 1: Epidemiology of obesity in women[16].

Body mass index and overweight

Body mass index (BMI) shows a helpful measurement of fatness, also a normal point for weight-to-height applied the rate under-weight, heaviness although fatness individual. BMI studied via divide an adults weight per kilograms via the square of the height per meters (kg/m²). As shown in ta-

ble 1, the most admitted classification was released from WHO, and National Institute for Health and Clinical Excellence (NICE). The classification is well established in a set of BMI and death-rate, then permits a correspondence in-person and group at additional risk [17,18].

Table1:**Distribution of weightiness regarding BMI**

BMI (kg/m ²)	assortment
< 19	Under-weight
25 - 19	Healthy
30 - 25.1	Over-weight
35 - 30.1	fatness I
40 - 35.1	fatness II
≥ 40	fatness III

The importance of BMI is that it is a measurement of obesity can be measured simply. It is necessary to evaluate the certain determination. The allocation of adipose tissue in a person, instead of regular value, seems of touch a danger in cross health consequence.

Particularly, abdomen-fat was correlated to increment in insulin-resistance which significantly linked to the morbidities and mortalities contrasted to collecting lipid in hips and thighs in which BMI could not calculate. Waist-surroundings were also used for the best amount on inside-body adiposis as well the danger correlation [17]. BMI incapable for differentiated among muscle to fat. persons with a similar BMI may varied body compositions. various people who presented BMI may not match the similar grade on "obesity" as well as BMI average estimated the normal differ among people. Despite this sig-

nificant definition, BMI is still determined as the most beneficial people-level measurement of obesity.

Obesity epidemiology related to chronic diseases

The propagation in fatness is growing worthy world-wide. Global fatness mission power determination the 1,2-billion human adult suffering from obesity. Furthermore, it is recorded that 312-millions of those who were overweight. About 3.3-millions humans pass on every rubric cause-of validity issue related to fatness as well, existence obesity. In this (45%) from troubles were associated with diabetes, (22%) related to heart-diseases, the rest (8% - 40%) related to fatness-malignancies [14]. Overweight propagation boosted at developing-countries in respect to the variation of life-style, comprising decreased physical-vitality, modification of diet type, in addition to the calorie reduction [15,19]. While, several factors including, "diabetes[44]; cardiovascular disease[45]; hypertension[46]; endocrine disorder[47]; hormones-dysfunction[48]; psychological-dysfunctions and dyslipidemia[49]; musculoskeletal disorders[50]; using-drug, steroids/anti-depressed" also can cause overweight- As shown in figure 2, [15]. The plane to preventing women overweight or obesity is highlighted from governments in the world health organization (WHO) to avoid death by those diseases[51,52].

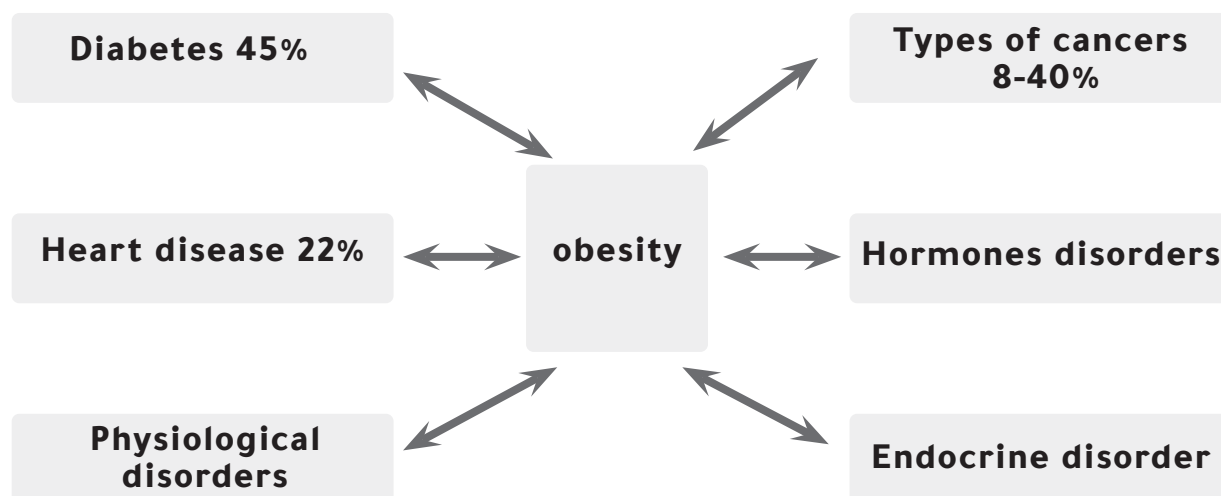


Figure 2:
Women obesity epidemiology related to chronic diseases[14].

Women

Hormones involved on reproduction were passively affected in addition to weight. Individually, through fat cells (white-adipocytes), leptin hormone output, the adipokine works in the hypothalamic, wherever, reproductively hormones "Gonadotrophin/releasing-hormone (GnRH)" was created [20]. Leptin is furthermore produce of obesity-gene [21]. Leptin interacting to hypothalamus reduction appetite, otherwise, the transformation at that genes resulted in augmentation appetite, driving to unavoidable obesity [22]. Leptins are related-HPG-axis which stimulate emission of GnRH via hypothalamus, thereafter follicle-stimulating-hormone, while luteinizing-hormone through the frontal pituitary. Pre-adulthood persons with leptin insufficiency miss conducting puberty age.

whether administratively presented leptin, transformation reflector so as pubertal age take back. Leptin is extra passed on grown follicles products via ovaries, which shows the position of oocyte grown, and embryo expansion [20,21].

person weight increment as well suggested that correlated with the expansion of (Polycystic ovary syndrome), [22]. Some specified aspects linked with Polycystic-ovary-syndrome permitting a hint in diagnosing-syndrome involving "hyper-androgenism, unequal-periods, ovulation, fertility[23]. The fatness of PCOS causes an enlarge hormonal and metabolic descent, while, in female, fertile destroys and oocyte-modality. PCOS also effective out of assistance-reproductive-technology at overweight women, driving on an increase the termination average[24].

Reproductive functions in Obesity

The association of fatness with reproductively mission are familiar from numerous ages [25, 26] and yet it is being searched [27]. The passive influence of fatness in reproduction effects is now recognized. whereas, hard to describe a technique of obese impact systematic reproduction, because of a multifactorial complicated and many techniques correlation with infertile and overweight. Insulin-resistance, leptins grade were increased and, hyper-androgenemias execute of overweight females. likewise, ovulation and modification at adipokines grade as well as, HPG-axis of females-overweight inspire systematically reproduction [28, 29].

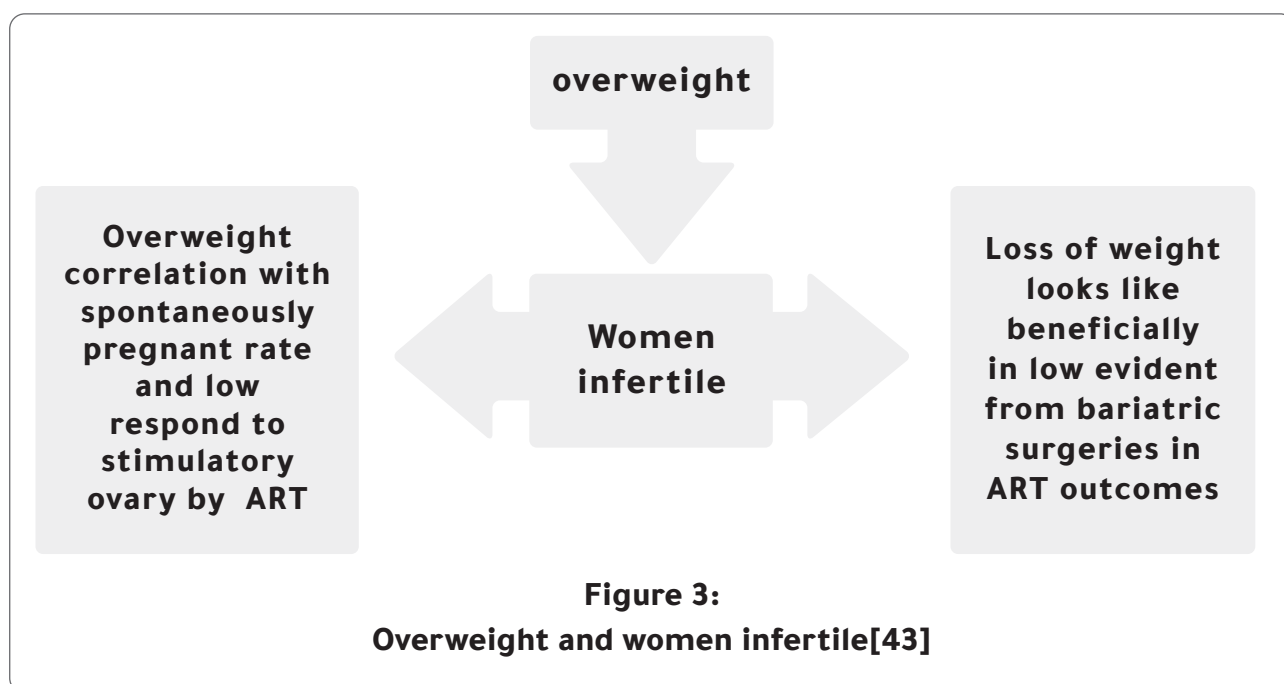
Respectively, after the decreased average of pregnancies, increment of the termination ratio, also increment gestational complexity, as well as alive child-birth ratio reduced on fatness-females on each of normal as well as helped discernment. Fat-ness can reduce the position of reproduction via manipulating two ovaries [29]. HPG-axis suffered on account of hormonal variation, as well, most of the substratum grades. LH levels, estrogens, insulins, triglycerides, much low-density endometrium lipoprotein, are boosted, the high-density-lipoprotein grades lowering on fatness females. All those modifications including an HPG-axis crumble as well as several gynecologic impacts happen [30].

Overweight correlated infertile

Infertile means a deficiency in pregnancies or curative granter fertilization in females below 35 years old, even after 6 months, the female 36 years old and above [31]. It is the most recurrent trouble on systematic reproduction in developed-countries. numerous fatness women eligible to earn pregnancy besides the overweight, an increment currency in obese women on infertility. Some studies reported that many females taking medicine to support them getting pregnant was fatness[32]. Researches pretended a period in demand can be realized an unprompted pregnancy average is boosted and pregnancy average is reduced in obese, comprising even ovulatory obese females [33,34]. Various studies have shown an infertile-hazard is triple high-level for obese than non-obese [35], the fertilities appeared to be destroyed at each naturally although the assistance ideation cycle [36, 37]. The possibility for pregnancies is decreased to 6% / unit for BMI overriding 30 kg/m², [38]. Several previous studies showed the correlation between obesity and lower fertility average, and reported that obesity in early puberty can vary the reproductive functions[39]. Obesity why infertility in different ways, through impaired ovarian follicular growth, oocyte development, fertilization, embryo growth, and implantation [40]. Obesity constrains

the Hypothalamic- Pituitary- Gonadal (HPG) axis via boosted free estrogen level through increment revulsion of androgens to estrogens at adipose tissue. By Increasing the estrogen, the Gonadotropin-releasing hormone (GnRH) decreasing, by negative returns. Whereas, the HPG axis affects motive the irregular and ovulation cycles. Overweight women exposing to highly risk of the menstrual disorder as well as anovulation, the menstrual dysfunction in obese women is fourfold more common than in

normal women[25]. Many kinds of researches have shown the correlation between ovulation infertility and obesity [41,42]. The anovulation is a usual consequence for (hyper-insulinemia, insulin-resistance, hyper-androgenism) of steroid-genesis while ovary. The anovulation and obesity are well correlated to PCOS, it is about "35% - 60%" of PCOS patients are obese with "menstrual disorder, and infertility" which is most frequent with PCOS in obese than a non-obese person [43]. Figure 3.



Woman infertility pathophysiology

Many different conditions can affect female productivity. most are directly associated with reproductive organs pathophysiology, while the rest fundamentally depends on professional sides which include a factorize of lifestyle like the hyper-caloric

supply which generally increased the body weight and promotes obesity.

Reproductive organs dysfunction

As shown in figure4: The clinical problems caused by obesity and affecting women reproductive organs

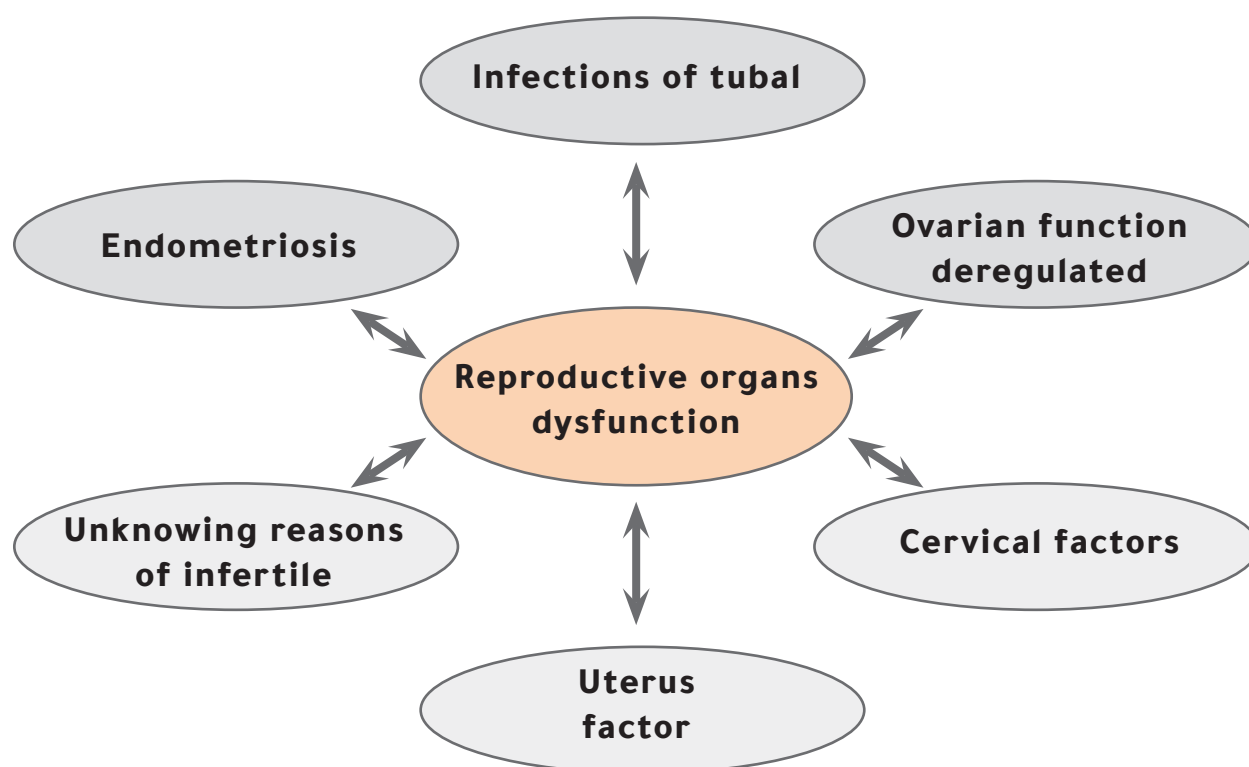


Figure 4:
women reproductive organs dysfunction caused by obesity[10]

• **Ovarian function deregulated:** It is a result of interaction hormones and complex balance during the ovulation, any alteration in these mechanisms can influence the physiology. Polycystic ovary syndrome (PCOS) is the most common cause of ovulation failure [6]. Such situation is correlated-to detention of follicle ripeness which results at small follicles modeling, defective, and dysmenorrhea of ovulation. Other causes involved hypothalamus dysfunction and pituitary-gland which driving to immature eggs output, and resulting in invasive surgery to a repeated ovarian cyst and disorders ovulatory dependents

on extra-ovarian pathology which including hypothyroidism or hyperthyroidism.

• **Infections of tubal:** The patients with tubal sickness are different, and concluded after infecting detriment, obstructing, pelvic adherence and close to surgical, while perhaps indeterminate other. At this competition, pelvic inflammation sickness, the main etiologies incident at anatomical, also functional defects in a tube as well as victorious correlated with infectious via "*Chlamydia-Trachomatis*", "*Neisseria-Gonorrhoea*" that only drives on tubal concerning infertile [7].

• **Endometriosis:** the inveterate situation described via development on endometrial-tissue of regions, another reason for uterine-cavity, much popularly on a pelvic-cavity, involving the ovary. Tubule defect may place finally on chronic inflammatory correlated with the development of endometrial-tissues, around 25-35% of females suffer from endometrial sustain sub-fertile [8].

• **Cervical factors:** cervixes play a great job on reproduction. supplies traffic pathway to semen, permits the semen for arrival through uterine-bowl then finally through the fallopian-tube. semen faculty for profit the arrival of upmost-tract which affected via mucus-cervix during the canal of cervixes. Thereafter, whole situations convert a mucosal-film of cervixes can agree with a block of ascertainment in semen across the tube [10].

• **Uterus factor:** uterus disorder like "damage at adherence-molecule, polyp, sub mucosal fibroid, asymptomatic-neoplasm, frequent-miscarriage", can be theatrically inspired by blastocysts-engrafted. Reconnoitering the uterine-sinus via hysteroscopy, this compulsory is existence on unexplainable bleedings[9].

• **Unknown reasons for infertile:** beside thus characterized of main pathological reproductively, another condition such as "hormones-modification, constituent-disorder of inflammation dissolvable-agents or

chronic-modifications at metabolic ways in a genital organ", which is associated with infertile while subsist for valued at clinical researches [9].

Conclusion

Overweight women must have information about the importance about reducing weight before pregnancy, also promote them to lose-weight to reduction the poor-obstetric outcome according to obesity. The best treatment for women with high BMI is weight loss especially with pre-pregnancy and should not be delayed because of increasing age. Today, the correlation between high BMI and opposite fertility outcomes is well known. Many mechanisms are suggested explaining how infertility can be caused by overweight, whereas, the exactly pathophysiologic way is not understanding clearly.

References

1. Glaw DC, Maclehose RF, Longnecker MP(2007). Obesity and time to pregnancy. Hum Reprod;22:414-20.
2. Awartani KA, Nahas S. Al Hassan SH, Al Deery MA, Coskun S(2009). Infertility outcome in sub groups of obese population. Reprod Biol Endocrinol;52:52.
3. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, et al(2001). Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. Int J Obes Relat Metab Disord;25:1175-82.

4. Jacobsen AF, Skjeldestad FE, Sandset PM(2008). Ante-and post natal risk factors of venous thrombosis: a hospital-based case control study. *J Thromb Haemost*;6:905-12.
5. McGee EA, Hsueh AJ(2000). Initial and cyclic recruitment of ovarian follicles. *Endocr Rev*.;21:200-214.
6. Templeton A(2000). Infertility and the establishment of pregnancy-overview. *Br Med Bull*.;56:577-587.
7. Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC(2007). Diet and lifestyle in the prevention of ovulatory disorder infertility. *Obstet Gynecol*.;110:1050-1058.
8. Lashen H, Fear K, Sturdee DW(2004). Obesity is associated with increased risk of first trimester and recurrent miscarriage: matched case-control study. *Hum Reprod*;19:1644-6.
9. Rasmussen SA, Chu SY, Kim SY, Schmid CH, Lau J(2008). Maternal obesity and risk of neural tube defects: a meta-analysis. *Am J Obstet Gynecol*;198:611-19.
10. Kristensen J, Vestergaard M, Wisborg K, Kesmodel U, Secher NJ(2005). Prepregnancy weight and the risk of stillbirth and neonatal death. *BJOG*;112:403-08.
11. World Health Organization(1997). Preventing and managing the global epidemic. In: Report of the World Health Organization on obesity. Geneva: World Health Organization;.
12. Musaiger A, O(2004). Overweight and obesity in the Eastern Mediterranean Region: can we control it. *Eastern Mediterranean Health Journal*.;10: 6;789-793,.
13. Sibai A. M, L. Nasreddine, A. H. Mokdad, N. Adra, M. Tabet, and N. Hwalla,(2010). Nutrition transition and cardiovascular disease risk factors in Middle East and North Africa countries: reviewing the evidence, *Annals of Nutrition and Metabolism*, ; 57:3-4. 193-203,.
14. Haslam DW, James WP(2005). Obesity. *Lancet*.;366:1197-1209.
15. Norman RJ, Noakes M, Wu R, Davies MJ, Moran L, Wang JX(2004). Improving reproductive performance in overweight/obese women with effective weight management. *Hum Reprod Update*.;10:267-80.
16. World Health Organization(2007). Preventing and managing the global epidemic Report of the World Health Organization on obesity. Geneva: World Health Organization;.
17. National Institute for Health and Clinical Excellence(2006). Obesity. Guidance on the Prevention, Identification, Assessment and Management of Overweight and Obesity in Adults and Children. London: National Institute for Health and Clinical Excellence (NICE),.
18. Sattar N, Clark P, Holmes ANN, Lean MEJ, Walker I, Greer IA(2001). Antenatal waist circumference and hypertension risk. *Obstet Gynecol*;97:268-71.
19. Zaboon Areej, Saeed Noor Al-Huda, Sattar Dalal and A. Rahman Sabah(2020). Obesity and overweight:

- A review. The journal of research on the Lepidoptera; 51(2) : 879-889.
20. Mitchell, M.; Armstrong, D. T.; Robker, R. L.; Norman, R. J. (2005) . "Adipokines: implications for female fertility and obesity". *Reproduction*; 130 (5): 583-597.
 21. Johnson, Martin H. (2012). *Essential Reproduction*. John Wiley & Sons.
 22. Pandey, Shilpi; Pandey, Suruchi; Maheshwari, Abha; Bhattacharya, Siladitya (2010). "The impact of female obesity on the outcome of fertility treatment". *Journal of Human Reproductive Sciences*. 3 (2): 62-67.
 23. Gabor T., Kovacs (2007). Polycystic ovary syndrome.
 24. Wang, Jim X.; Davies, Michael J.; Norman, Robert J. (2001) "Polycystic ovarian syndrome and the risk of spontaneous abortion following assisted reproductive technology treatment". *Human Reproduction*; 16 (12): 2606-2609.
 25. Rogers J, Mitchell GW (1952). The relation of obesity to menstrual disturbances. *N Engl J Med*; 247:53-6.
 26. Jungheim ES, Travieso JL, Carson KR, Moley KH (2012). Obesity and reproductive functions. *Obstet Gynecol Clin North Am*; 39:479-93.
 27. Pasquali R, Pelusi C, Genghini S, Cacciari M, Gambineri A. Obesity and reproductive disorders in women. *Hum Reprod Update*. 2003;4:359-72.
 28. Bellver J, Melo MA, Bosch E, Serra V, Remohi J, Pellicer A. Obesity and poor reproductive outcome: the potential role of the endometrium. *Fertil Steril*. 2007;88:446-51.
 29. Parihar M. Obesity and infertility. *Reviews in Gynecological Practice*. 2003;3:120-6.
 30. World Health Organization. *Obesity: Preventing and managing the global epidemic*. Geneva: World Health Organization, 2000.
 31. Practice Committee of American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. *Fertil Steril*. 2013;99:63.
 32. Vahratian A, Smith YR. Should access to fertility-related services be conditional on body mass index? *Hum Reprod*. 2009;24:1532-37.
 33. Gesink Law DC, Maclellan RF, Longnecker MP. Obesity and time to pregnancy. *Hum Reprod*. 2007;22:414-20.
 34. Wise LA, Rothman KJ, Mikkelsen EM, Sørensen HT, Riis A, Hatch EE. An internet-based prospective study of body size and time-to-pregnancy. *Hum Reprod*. 2010;25:253-64.
 35. Rich-Edwards JW, Goldman MB, Willet WC, Hunter DJ, Stamfer MJ, Colditz GA, et al. Adolescent body mass index and infertility caused by ovulation disorders. *Am J Obstet Gynecol*. 1994;171:171-7.
 36. Zaadstra BM, Seidell JC, Van Noord PA, te Velde ER, Habbema JA, Vrieswijk B, Karbaat J. Fat and female fecundity: Prospective study of effect of body fat distribution on conception rates. *BMJ*. 1993;306:484-7.

37. Crosignani PG, Ragni G, Parazzini F, Wyssling H, Lombrosso G, Perrotti L. Anthropometric indicators and response to gonadotrophin for ovulation induction. *Hum Reprod.* 1994;9:420-3.
38. Van der Steeg JW, Steures P, Eijkemans MJ, Habbema JD, Hompes PG, Burggraaff JM, et al. Obesity affects spontaneous pregnancy chances in subfertile ovulatory women. *Hum Reprod.* 2008;23:324-8.
39. Lake JK, Power C, Cole TJ. Women's reproductive health: the role of body mass index in early and adult life. *Int J Obes Relat Metab Disord.* 1997;21:432-38.
40. Jungheim ES, Travieso JL, Hopeman MM. Weighing the impact of obesity on female reproductive function and fertility. *Nutr Rev.* 2013;71:3-8.
41. Bolumar F, Olsen J, Rebagliato M, Saez-Lloret I, Bisanti L. Body mass index and delayed conception: a European Multicenter Study on Infertility and Subfecundity. *Am J Epidemiol.* 2000;151:1072-9.
42. Clark AM, Thornley B, Tomlinson L, Galletley C, Norman RJ. Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Hum Reprod.* 1998;13:1502-5.
43. Al-Azemi M, Omu FE, Omu AE. The effect of obesity on the outcome of infertility management in women with polycystic ovary syndrome. *Arch Gynecol Obstet.* 2004;270:205-10.
44. Maskarinec G, Jacobs S, Park SY, et al (2017). Type II diabetes, obesity, and breast cancer risk: the multiethnic cohort. *Cancer Epidemiol Biomarkers Prev.*;26(6):854-861.
45. Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE (2016). Cardiovascular disease in women: clinical perspectives. *Circ Res.*;118(8):1273-1293.
46. Seravalle G, Grassi G (2017). Obesity and hypertension. *Pharmacol Res.*;122:1-7.
47. Joham AE, Palomba S, Hart R (2016). Polycystic ovary syndrome, obesity, and pregnancy. *Semin Reprod Med.*;34(2):93-101.
48. Silvestris E, de Pergola G, Rosania R, Loverro G (2018). Obesity as disruptor of the female fertility. *Reprod Biol Endocrinol.*;16(1):22.
49. Palmer MK, Toth PP (2019). Trends in lipids, obesity, metabolic syndrome, and diabetes mellitus in the United States: an NHANES analysis (2003-2004 to 2013-2014). *Obesity.*;27(2):309-314.
50. Anandacoomarasamy A, Caterson I, Sambrook P, Fransen M, March L (2008). The impact of obesity on the musculoskeletal system. *Int J Obes.*;32(2):211-222.
51. World Health Organization (2020). Global action plan for the prevention and control of NCDs 2013 - 2020. 2013.
52. World Health Organization (2021). Noncommunicable diseases country profiles 2018.