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Review of literature: Etiology of obesity, risk factors, and the role of genetics

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Abstract

Obesity is considered one of the global most significant public problem as it has been associated with different diseases and even death. It is an excess accumulation of fat in the body as a result of increase calorie intake compared to energy expenditure. It is considered as multifactorial condition as many factors play role in its occurrence including genetic susceptibility, external environmental factors, individual attitude.

The exact etiology of obesity is intermingled with different factors and nowadays because of development of different aspects of life, sedentary life style dominates the social communities, reduced physical activities, all these factors can enhance the risk of obesity. Furthermore, disturbances of the endocrine system like Cushing's syndrome, hypothyroidism, diabetes type II. The genetic obesity it will be divided into two groups: 1) The monogenic type, the Poly genic type, syndrome associated obesity. Many individuals are suffering from obesity because of different genes that they already have which encourage them to high calorie diet with more food consumption, unlimited and uncontrolled food intake together with reduced physical activity.

In conclusion the etiology, risk factors, as well as genetic susceptibility all are combined and correlated to each other as they may act separately or together to induce onset of obesity. The physical exercise and energy expenditure are having the key role., in addition to endocrine hormonal disturbances.

Keywords: Obesity; Etiology; Risk Factors; Genetics

1. Introduction

Obesity is considered one of the global most significant public problem as it has been associated with different diseases and even death (1). According to WHO reports about one third of the population are suffering from obesity all over the world which means that scientists are facing a serious health problem as it is considered as an epidemic problem in USA (2). It is an excess aggregation of fat in the body due to increase calorie intake compared to energy expenditure and it is diagnosed when the body mass index 30 and higher (3).

It might enhance the possibility of developing different diseases and health injuries including cardiac disease, stroke, hypertension (4), 2nd type of diabetes mellitus (5) osteoarthritis (6), sleep apnea (7), nonalcoholic steatohepatitis, gallstones, even some kinds of cancers are more likely to accrue in obese people like breast cancer, female reproductive system different cancers, renal with associated prostatic cancers, and colorectal cancers.

It is considered as multifactorial condition as many factors play role in its occurrence including genetic susceptibility, external environmental factors, individual attitude (9).

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Different types of cancers are associated with weight gain like colorectal, breast cancers, ovarian and uterine tube carcinoma, gastrointestinal and accessory gland cancers. Excess weight gain especially around menopause can enhance the possibility of breast cancer in women (10).

2. Etiology and risk factors of obesity

The exact etiology of obesity is intermingled with different factors and nowadays because of development of different aspects of life, sedentary life style dominates the social communities, reduced physical activities, prolong sitting time at home even at work all these factors may increase the risk of obesity (11). High calories food intake especially high fat and carbohydrate diet (12). Glucocorticoid are responsible for metabolism of protein, carbohydrate and lipids by reducing the release of insulin hormone and stimulating blood glucose level which initiates the action of lipoprotein lipase to activate excess lipid deposition (13).

In China, Health and Nutrition Survey was done in the period of 1990-2015 they stated that there was an increase in the fat consumption about 12.5% among people which in turn enhances the prevalence of obesity to about 38% (14). In addition, the food rich in fat stimulate more food consumption. Bad eating habits like eating while watching television and video gaming, increase consumption of junk food are correlated with central obesity and higher possibility of developing cardiovascular diseases (16).

Obesity is intercorrelated with diabetes type II in the way that obesity is considered as a risk factor for diabetes and the latter is directly affected by obesity and both are influenced directly by limited physical exercise (17). Obese people suffer from peripheral insulin resistant and in diabetes type II there is inadequate release of insulin to meet this resistance and sometimes insulin level is high in those patients but still in adequate to maintain normal blood glucose level (18).

Other causes of obesity may include hormonal disturbances like Cushing's syndrome which resulted from chronic exposure to glucocorticoid which led to central obesity and wasting of upper and lower limbs (19).

In hypothyroidism there is an insufficient release of thyroid hormones which directly inhibit the metabolic rate and reduces the energy expenditure leading to weight gain (20).

Polycystic ovaries syndrome is highly associated with insulin resistance more than half of affected patients are suffering from overweight. In addition, obesity can enhance the androgenic hormone release by ovaries (21).

In Growth hormone deficiency there is high risk of developing obesity as this hormone maintain energy consumption, stimulate muscle and bony building, osteoblast accumulation and lipolysis (22, 23).

Gonadal hormones deficiency may related to obesity as these hormones are associated to lipid metabolism enhancing fatty mobilization from internal viscera this is why elderly males suffer from obesity (24, 25).

2.1. The role of genetics in obesity

The role of genetics in susceptibility to obesity has been widely studied since 1907 (26). The Up-to-date genetic knowledge and accurate description of the nucleotide variations has helped us to advance our thoughts about molecular techniques of weight management (27).

Adopted twins seems to have body weight and body mass index similar to their biological parents rather than their adopted parents (28). Other studies showed that overfilling of food among identical twins revealed noticeable association of weight gain than among others. further studies reported that people with genetic susceptibility to obesity are already have emotional and unmanageable desire to eat (29).

To understand causes of genetic obesity it will be divided into two groups:

• The monogenic type which is infrequent but serious associated with only one gene mutation or abnormality situated in leptin- melanocortin pathway in fact about thirty varient mutations concerning this pathway involved melanocortin gene were detected (30). They cause interruption in the controlling process of appetite and weight as it is correlated with irregular food consumption manner, further more different endocrinological problem and many hormones may be affected by receptors in arcuate nucleus of hypothalamus (31). The main cause is the autosomal recessive genetic mutations in the leptin and melanocortin route that regulate the

process of dietary intake by nuclei of hypothalamus, in addition to proopiomelanocortin and proconvertase 1 genes are also reported (32, 33).

- The Poly genic type in which many genes and many fragments of gene families are included together with environmental factors associated with obesity (34). In spite of being two different types (monogenic and polygenic obesity) it is found that they may have the same biological causes. Furthermore, the central nervous system is regulating food consumption and has the main role in affecting body weight in the two types of obesity (35).
- Syndrome associated obesity which inherited in monogenic form and characterized by phenotype variation and it is correlated with mental retardation, dysmorphic characters, different organ malformations (36).

Many researchers reported that about 9 of the exome sequencing trios associated genes are known to cause mental retardation and development abnormality were detected in the examined patient and there are 2 specific genes that have a direct correlation with obesity (37).

Many individuals are suffering from obesity because of different genes that they already have which encourage them to high calorie diet with more food consumption, unlimited and uncontrolled food intake together with reduced physical activity (38).

Leptin hormone is released by fatty cell to the satiety centers in hypothalamus to stop eating. In addition, high levels of leptin hormones are detected in overweight people which indicate resistance or sometimes leptin receptors in the brain are deficient which will subsequently encourage more food consumption (39).

One of the rare causes of obesity is Prader–Willi syndrome which is a congenital neurodevelopmental disorder patients presented with short stature, uncontrolled high food intake, early onset obesity and small hands and foot. It occurs due to deficiency in the gene's expression on the long arm of chromosome 15(q11-13) (40).

3. Conclusion

The etiology and risk factors of obesity are combined and correlated to each other as they may act separately or together to induce onset of obesity. The physical exercise and energy expenditure are having the key role., in addition to endocrine hormonal disturbances.

More studies are recommended to find out the correlation of weight gain and the genetic liability of food consumption behaviors.

References

- [1] Chen Y, Peng Q, Yang Y, Zheng S, Wang Y. The prevalence and increasing trends of overweight, general obesity, and abdominal obesity among Chinese adults: a repeated cross-sectional study. BMC Public Health. 2019; 19(1):1293. doi: 10.1186/s12889-019-7633-0.
- [2] Jiménez EG, Cordero MA, García CG, López PG. Prevalence of nutritional overweight and obesity and hypertension as well as their relationship with anthropometric indicators in a population of students in Granada and its provinces. Nutr Hosp. 2011; 26(5):1004-10. doi: 10.1590/S0212-16112011000500013.
- [3] Bentham J, Di Cesare M, Bilano V, Bixby H. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017; 390:2627–2642. doi: 10.1016/S0140-6736(17)32129-3
- [4] Ernst ND, Obarzanek E, Clark MB, Briefel RR, Brown CD, Donato K. Cardiovascular health risks related to overweight. J Am Diet Assoc.1997; 97(7): S47-S5. https://doi.org/10.1016/S0002-8223(97)00729-3.
- [5] Harris MI, Flegal KM, Cowie CC. et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults. Diabetes Care.1998; 21:518-524. https://doi.org/10.2337/diacare.21.4.518.
- [6] Bliddal H, Leeds AR, Christensen R. Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons a scoping review. Obes Rev. 2014; 15(7): 578–586. doi: 10.1111/obr.12173/
- [7] Corral RA, Caples SM, Jimenez LF, Somers VK. Interactions Between Obesity and Obstructive Sleep Apnea. Chest. 2010 Mar; 137(3): 711–719.

- [8] Kruijsdijk RC, Wall E, Visseren FL. 2009. Obesity and cancer: the role of dysfunctional adipose tissue. Cancer Epidemiol. Biomark. Prev. 18:2569–78. doi: 10.1158/1055-9965.EPI-09-0372.
- [9] Wilding J. Are the causes of obesity primarily environmental? Yes. BMJ 2012; 345:e5843. doi: https://doi.org/10.1136/bmj.e5843
- [10] Silva M, Weiderpass E, Licaj I, Lissner L, Excess body weight, weight gain and obesity-related cancer risk in women in Norway: the Norwegian Women and Cancer study. Br J Cancer. 2018; 119(5): 646–656. doi: 10.1038/s41416-018-0240-5.
- [11] Lakka TA, Bouchard C. Physical activity, obesity and cardiovascular diseases. Handb Exp Pharmacol. 2005;(170):137-63. doi: 10.1007/3-540-27661-0_4.
- [12] King BM, Ivester AN, Burgess PD. Adults with Obesity Underreport High-calorie Foods in the Home. Health Behavior and Policy Review. 2-16;33(55): 439-443.doi: 10.14485/HBPR.3.5.4.
- [13] Block NE, Buse MG: Effects of hypercortisolemia and diabetes on skeletal muscle insulin receptor function in vitro and in vivo. Am. J. Physiol. 1989; 256: 39–48. doi: 10.1152/ajpendo.1989.256.1.E39.
- [14] Wang L, Wang H, Zhang B., Popkin BM, Du S. Elevated Fat Intake Increases Body Weight and the Risk of Overweight and Obesity among Chinese Adults: 1991–2015 Trends. Nutrients. 2020; 12 (11): 3272.
- [15] Rolls BJ, Hammer VA. Fat, carbohydrate, and the regulation of energy intake. Am J Clin Nutr 1995; 62(5 suppl):1086S-1095S. doi: 10.1093/ajcn/62.5.1086S.
- [16] Frank BHu, Tricia YLi, Graham AC, Walter CW, JoAnn EM. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. JAMA. 2003; 289(14):1785-91. doi: 10.1001/jama.289.14.1785.
- [17] World Health Organization. "Global Report on Diabetes." Isbn. vol. 978. pp. 6–86. 2016.
- [18] Røder ME, Porte D, Schwartz RS, Kahn SE. Disproportionately elevated proinsulin levels reflect the degree of impaired B cell secretory capacity in patients with noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab. 1998;83(2):604–608. doi: 10.1210/jcem.83.2.4544.
- [19] Wajchenberg BL, Bosco A, Marone MM et al.: Estimation of body fat and lean tissue distribution by dual energy x-ray absorptiometry and abdominal body fat evaluation by computed tomography in Cushing's disease. J. Clin. Endocrinol. Metab. 1995; 80(9), 2791–2794. doi: 10.1210/jcem.80.9.7673425.
- [20] Krotwiesky M: Thyroid hormones in the pathogenesis and treatment of obesity. Eur. J. Pharmacol. 2002; 440(3), 85–98. doi: 10.1016/s0014-2999(02)01420-6.
- [21] Pasquali R, Casimirri F: The impact of obesity on hyperandrogenism and polycystic ovary syndrome in premenopausal women. Clin. Endocrinol. (Oxf.). 1993; 39: 1–16 (1993). doi : 10.1111/j.1365-2265.1993.tb01744.x
- [22] Dietz J, Schwartz J: Growth Hormone alters lipolysis and hormone-sensitive lipase activity in 3T3-F442A adipocytes. Metabolism. 1991; 40 (8): 800–806. doi: 10.1016/0026-0495(91)90006-i.
- [23] Rosen T, Bosaeus I, Tolli J, Lindstedt G, Bengtsson BA: Increased body fat mass and decreased extracellular fluid volume in adults with growth hormone deficiency. Clin. Endocrinol. (Oxf.). 1993 38(1): 63–71. doi: 10.1111/j.1365-2265. 1993.tb00974. x.
- [24] Bhasin S, Woodhouse L, Storer TW: Androgen effects on body composition. Growth Horm. IGF Res. 2003; 13(Suppl.): 63–71. doi: 10.1016/s1096-6374(03)00058-3.
- [25] Kapoor D, Goodwin E, Channer KS, Jones TH: Testosterone replacement therapy improves insulin resistance, glycemic control, visceral adiposity and hypercholesterolaemia in hypogonadal men with Type 2 diabetes. Eur. J. Endocrinol. 2006; 154(6): 899–906. doi: 10.1530/eje.1.02166.
- [26] WPA. A Reorientation on Obesity. N Engl J Med. 1953; 248(23):959–964. doi: 10.1056/NEJM195306042482301.
- [27] Vidhu V. Thaker, GENETIC AND EPIGENETIC CAUSES OF OBESITY. Adolesc Med State Art Rev. 2017; 28(2): 379– 405.
- [28] Stunkard AJ, Sørensen TI, Hanis C, et al. An adoption study of human obesity. N Engl J Med. 1986; 314(4):193–8. doi: 10.1056/NEJM198601233140401.

- [29] Herle M, Smith A, Kininmonth A, Llewellyn C. The Role of Eating Behaviours in Genetic Susceptibility to Obesity. Curr Obes Rep. 2020; 9(4):512-521. doi: 10.1007/s13679-020-00402-0.
- [30] Huvenne H, Dubern B Karine, C, Poitou Ch. Rare Genetic Forms of Obesity: Clinical Approach and Current Treatments in 2016. Obes Facts. 2016; 9(3): 158–173. doi: 10.1159/000445061.
- [31] Wang T, Xu M, Bi Y, Ning G. Interplay Between Diet and Genetic Susceptibility in Obesity and Related Traits. Front Med. 2018; 12(6):601–7. doi: 10.1007/s11684-018-0648-6.
- [32] Krude H, Biebermann H, Schnabel D, Tansek MZ, Theunissen P, Mullis PE, Grüters A: Obesity due to proopiomelanocortin deficiency: three new cases and treatment trials with thyroid hormone and ACTH4-10. J Clin Endocrinol Metab 2003; 88:4633-4640. doi: 10.1210/jc.2003-030502.
- [33] Asai, M, Ramachandrappa S, Joachim M, Shen Y. Loss of function of the melanocortin 2 receptor accessory protein 2 is associated with mammalian obesity. Science. 2013; 341, 275–278. doi: 10.1126/science.1233000.
- [34] Anke Hinney and Johannes Hebebrand. Polygenic Obesity in Humans. Obes Facts. 2008; 1(1): 35-42. doi: 10.1159/000113935.
- [35] Chami, N., Preuss, M., Walker, R. W., Moscati, A. & Loos, R. J. F. The role of polygenic susceptibility to obesity among carriers of pathogenic mutations in MC4R in the UK Biobank population. PLoS Med. 2020; 17, e1003196. doi: 10.1371/journal.pmed.1003196.
- [36] Geets E, Meuwissen MC, Van HW. Clinical, molecular genetics and therapeutic aspects of syndromic obesity. Clin Genet. 2019; 95:23–40. https://doi.org/10.1111/cge.13367.
- [37] Laura Machado Lara Carvalho, Carla Sustek D'Angelo, Darine Villela, Silvia Souza da Costa, Alexander Augusto de Lima Jorge. Genetic investigation of syndromic forms of obesity. International Journal of Obesity. 2022; 46(1):1582–1586. I: 10.1038/s41366-022-01149-5
- [38] Czajkowski P, Adamska-Patruno E, Bauer W, Fiedorczuk J, Krasowska U, Moroz M, et al. The Impact of FTO Genetic Variants on Obesity and Its Metabolic Consequences Is Dependent on Daily Macronutrient Intake. Nutrients. 2020; 12(11):3255. doi: 10.3390/nu12113255.
- [39] Clement K, Vaisse C, Lahlou N et al.: A mutation in the human leptin receptor gene causes obesity and pituitary dysfunction. Nature 392, 398–401 (1998).
- [40] Burman P, Ritzen EM, Lindgren AC: Endocrine dysfunction in Prader–Willi syndrome: a review with special reference to GH. Endocr. Rev. 2001; 22, 787–799 (2001). doi: 10.1210/edrv.22.6.0447.