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Is There a Correlation Between Impaired Sperm Quality and Overweight/Obesity?: A Review

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Obesity is associated with significant disturbance in the hormonal status that can affect the reproductive system. In recent decades, an increasing interest in related to the association between high BMI levels, obesity and decreased sperm quality, which could also lead to a decrease in male reproductive potential. The aim of the present work is to identify the basic mechanisms of impaired sperm quality due to overweight and obesity. Sedentary lifestyle and work, as well as age of men are defined as possible ways to elevated BMI levels. Both inflammation and oxidative stress (as related pathophysiological processes) are considered as basic mechanisms, which could be found in the pathogenesis of male infertility caused by high BMI levels and obesity.

Key words: body mass index (BMI), sperm quality, sedentary lifestyle, age, inflammation, oxidative stress

Introduction

One of the most interesting periods in human ontogenesis is associated with the rapid processes of growth, development and sexual maturation. Thus, phenotypic traits are formed and the body reach the reproductive maturity.

The main goal of the experts in the biomedical sciences is to improve the system for assessment and prevention of adolescent health issues [23]. In this regard, for each new generation, the dynamics and completion of the physical and sexual maturation is associated with physical development during growth. Moreover, to achieve the correct

determination of the physical development it is not enough to take into consideration only the quantitative morphofunctional changes, but also the qualitative changes that occur at certain stages of development should be followed. Thus, these changes are the basis of the adult individual formation [4, 5].

It is therefore necessary to study the body composition and type. In this regard, different studies showed the physical development and indicators of the body composition and type [26, 27, 29].

The present review aims to study the pathophysiological mechanisms of male infertility associated with high BMI levels and obesity based on literature data.

Body weight and overweight – an important part of the processes of growth and sexual development: Many studies also report that various diseases and increased mortality in adulthood are associated with abnormalities in normal body weight, especially during the accelerated morphological development during the adolescence. Furthermore, body weight is measured as the main indicator of overweight, which could serve as environmentally sensitive indicator during the individual development. However, data on the body weight cannot be used alone as a direct indicator for determining overweight without considering its relationship to height. The most commonly used type of connection between the two traits is the body mass index (BMI). Thus, research is focused on this integral physical characteristic, which is related to the variations from healthy body weight [6, 24, 25, 28, 30, 43]. In this regard, in recent years studies indicate a deviation from healthy body weight with frequent achievement of high BMI levels (BMI>25.0 kg/m^2) and obesity (BMI $\geq$ 34.9 kg/m^2). In addition, the obesity is becoming a global health problem, reaching epidemic levels in recent years [1, 18]. In general, the obesity impairs the body health and the potential to maintaining the balance in metabolic processes and homeostasis. As a result, the obesity could lead to pathophysiological processes in the organism, which affect the cardiovascular, nervous and endocrine systems, as well as reproductive system and sperm quality. Obesity-induced high levels of BMI can also be due to various factors, such as sedentary lifestyle and work, men age, etc.

Association between elevated BMI levels and sperm quality: In recent decades, there has been an increasing interest in research related to the association between elevated BMI levels and decreased sperm quality, which could also lead to a decrease in male reproductive potential. Studies published in databases such as PubMed, Embase, Scopus, Web of Science, and Wanfang are related to the impact of the overweight and obesity on sperm quality. In parallel, opposite data are found regarding the relationship between elevated levels of BMI and decreased sperm quality [1, 17, 21, 40].

Hammoud et al. [15] and Sermondade et al. [39, 40] reported that overweight and obesity were associated with an increased prevalence of azoospermia or oligozoospermia. In addition, Ramaraju et al. [34] found oligozoospermia and asthenozoospermia in men with obesity. Jensen et al. [17] established that men with BMI<20.0 kg/m^2 and BMI >25.0 kg/m^2 had reduced sperm concentration and total sperm count, respectively, compared to men with BMI between 20.0 – 25.0 kg/m^2. Moreover, the percentage of normal spermatozoa was also reduced, among men with high levels of BMI. According to the authors, sperm volume and percentage of motile spermatozoa were not affected by elevated BMI levels. Kort et al. [19] studied 520 men and found significant (p<0.05) and negative relationship between BMI and the total number of normal-motile sperm cells. In addition, a significant difference (p<0.05) was

found in the total number of normally motile sperm among the different BMI groups. According to a new retrospective study of 9 464 patients, Ramírez et al. [35] found that elevated BMI levels affect first sperm concentration and total sperm count, which is confirmed by applying logistic predictions analysis.

Ramaraju et al. [34] conducted a retrospective cohort of 1 285 men with CASA analysis. The authors found that obesity (BMI≥30kg/m^2) was associated with lower volume, sperm count and concentration, progressive motility andtotal. After an analysis of 30 publications and a total of 115. 158 participants, we can conclude that obesity is associated with reduced reproductive potential. As a proof of the statement, Campbell et al. [8] found that the obesity-induced male infertility (OR = 1.66, 95% CI 1.53-1.79) and the rate of live birth per cycle of Assisted Reproduction Technology (ART) was reduced (OR = 0.65, 95.0% CI 0.44-0.97). In addition, according to the authors men had an increased percentage of spermatozoa with low mitochondrial membrane potential (MMP), DNA fragmentation and abnormal morphology.

Many studies showed changes in the main sperm parameters, along with the sperm chromatin, DNA fragmentation, mitochondrial damage, apoptosis processes, serum reproductive hormone levels, etc. Oliveira et al. [31] investigated 1 824 men and found that elevated BMI levels negatively affected the sperm concentration, motility and morphology ($p<0.05$). In contrary, elevated BMI levels were not associated with impaired sperm DNA integrity, which was assessed by DNA fragmentation using TUNEL assays test, sperm chromatin protamination using chromomycin A3 staining and apoptosis of the spermatozoa using annexin V staining ($p<0.05$). However, elevated BMI levels were associated with increased mitochondrial damage in the sperm cells detected by applying Mito Tracker Green test ($p<0.05$). Chavarro et al. [9] found that BMI was positively related to estradiol levels and inversely related to total testosterone and sex hormone-binding glogulin (SHBG) levels. The authors also found a strong inverse relationship between BMI and inhibin B levels and a lower testosterone: LH ratio among men with a BMI> = 35 kg/m^2, as well as between BMI and inhibin B levels and a lower testosterone: LH ratio among men with a BMI> = 35 kg/m^2. In addition, the authors found that men with obesity had a lower total sperm count (concentration x volume) than men with normal weight. Chavarro et al. [9] stated that sperm cells with elevated DNA damage were significantly increased in men with obesity.

High BMI levels and impaired sperm quality related to sedentary lifestyle and work: The relationship between overweight, obesity and sedentary occupations, as well as sedentary lifestyles in the male population were also studied. Sedentary jobs, such as long-haul driving, desk work, call center operators, computer-based work lead to immobilization and weight gain. That suggests elevated BMI levels and obesity, which in turn affects spermatogenesis. According to Brownson et al. [7] and Stamatakis et al. [42] the sedentary behavior became an increasing part of modern life, including transportation, work and leisure time. Sharpe [41] also proved the negative effects of the sedentary lifestyle and obesity on testicular function (testosterone levels and sperm production). According to Magnusdottir et al. [22] poor sperm quality was associated with sedentary work and obesity but not with plasma levels of persistent organochlorines. Priskorn et al. [33] found that men who watch television more than 5 hours/day had total sperm count 104 million and an adjusted sperm concentration of 37 million/mL versus 158 million and 52 million/mL, among men who did not watch

television that long on a regular basis. Furthermore, an increase in follicle-stimulating hormone and decreases in testosterone and the testosterone/luteinizing hormone ratio were detected in men who watched television for a long time.

After the analysis of spermograms (according to the WHO, 2010) of 159 men who visited a clinic for ART, we found the highest levels of overweight and obesity in the group of men who work in a sitting position and at the same time they had reduced sperm quality (unpublished data). Further research is needed to clarify the importance of a sedentary lifestyle, obesity and sperm quality.

High BMI levels and impaired sperm quality related to men age: Concerning man age and fertility, some evidence showed a decrease in reproductive potential with increased age, as presented in assisted reproductive technology outcomes. Nevertheless, further consensus remains to be achieved regarding male aging impact on sperm quality. In addition, some studies showed an association between age and sperm quality, others reported no relationship between them [44]. According to Sallmén et al. [36], the association between BMI and infertility was similar regarding men of different ages.

Based on our study (unpublished data), BMI showed a significant correlation only with the age of the patients regarding to the conventional sperm parameters. Moreover, impaired sperm parameters due to obesity factors were more significant in younger men (25-30 years).

WHO [45] reported worldwide obesity has nearly tripled since 1975. In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 650 million were obese. 39.0% of adults aged 18 years and over were overweight in 2016, and 13.0% were obese. Most of the world‘s population lives in countries where overweight and obesity kill more people than underweight. Approximately 39 million children under the age of 5 were overweight or obese in 2020. Over 340 million children and adolescents aged 5-19 were overweight or obese in 2016.

Association between elevated BMI levels and sperm quality - basic mechanisms: Based on the studied literature concerning the mechanisms of reduced reproductive potential caused by obesity and high BMI levels, we could conclude that these mechanisms are mainly related to the expression of inflammation and oxidative stress. Impaired sperm quality in men is furthermore associated with the impact of endogenous and exogenous factors. Multifarious male infertility impair male reproductive functions via the common mechanisms of inflammation andoxidative stress, where both are related pathophysiological processes. Moreover, occurrence of one the above processes induced the other. Inflammation and oxidative stress could be found in the pathogenesis of male infertility. Inflammatory mechanisms activate specific pattern recognition receptors (PRRs) in testicular and epididymal cells, leading to activation of transcription factors. On the other hand, reactive oxygen species (ROS) production cause oxidation of membrane phospholipids and intracellular proteins, which can activate the PRRs-inflammatory pathway as well. In addition, according to Dutta et al. [13] the activated transcription factors supported the expression of inflammatory mediators, which caused exaggerated inflammation and could also act as oxidative stress, creating a vicious feedback loop.

However, the relation between the obesity and sperm parameters is not sufficiently studied, as well as its mechanism of action and the expression of the impaired sperm parameters. Sengupta et al. [38] found that obesity caused systemic inflammation

associated with a chronic inflammation dependent on T-helper 1 (TH-1) T-lymphocytes. Several pro-inflammatory mediators, including the cytokines [16], interacted with the complex reproductive regulations of the hypothalamic-pituitary-gonadal (HPG) axis, resulting in changes in the spermatogenesis [11]. According to the authors, impaired steroidogenesis or spermatogenesis resulted in hypogonadotropic hypogonadism, as well as decreased sperm parameters. In addition, inflammation could result in the excessive production of ROS and induced oxidative stress [12]. As stated Sengupta et al. [37] oxidative stress caused disruption of the functions and morphology of the sperm cells. Sperm DNA damage, deformation, and compromised plasma membrane integrity were observed by Alahmar et al.[2, 3]. ROS induced sperm motility led to altered sperm mitochondrial activities and reduced energy production in the spermatozoa.

According to Du Plessis et al. [10], Liu and Ding [20] changes, such as induced sleep apnea, alterations in the hormonal profiles (reduced inhibin B and androgen levels, elevated estrogen levels) and increased scrotal temperatures were expressed as impaired sperm parameters (decreased total sperm count, concentration and motility; increased DNA fragmentation index). Hakonsen et al. [14] and Palmer et al. [32] stated that that weight loss, lifestyle changes or bariatric surgery, can efficiently result in increased serum testosterone levels and sperm count, suggesting benefits for a possible weight loss on male fertility. Moreover, clinicians should consider the men obesity before applying assisted reproduction. More exercise is recommended, as well as increased movement in order to reduce the body weight and to therefore improve sperm parameters and have better performance in ART.

Conclusion

Based on the present review, we could conclude that obesity and high BMI levels could possibly lead to male infertility. Sedentary lifestyle and work, as well as age of men are defined as possible ways to elevated BMI levels and obesity, which induced basic mechanisms such as inflammation and oxidative stress. Such experiments need to be further performed in order to gain more thorough knowledge on the pathophysiological mechanisms of male infertility associated with high BMI levels and obesity.

References

1. **Aggerholm, A. S., A.M. Thulstrup, G. Toft, C. H. Ramlau-Hansen, J. P. Bonde.** Is overweight a risk factor for reduced semen quality and altered serum sex hormone profile? – *Fertility and Sterility*, **90(3)**, 2008, 619-626.
2. **Alahmar, A. T., A. E. Calogero, R. Singh, R. Cannarella, P. Sengupta, S. Dutta.** Coenzyme Q10, oxidative stress, and male infertility: A review. – *Clinical and Experimental Reproductive Medicine*, **48**, 2021a, 97-104.
3. **Alahmar, A. T., P. Sengupta.** Impact of Coenzyme Q10 and Selenium on seminal fluid parameters and antioxidant status in men with idiopathic infertility. – *Biological Trace Element Research*, **199**, 2021b, 1246-1252.
4. **Andreenko, E., M. Nikolova.** Age features in the development of the subcutaneous fat tissue, muscularity and muscle-fat rations in men with different physical activity. – *Glasnik, Antropološkog društva Srbije*, **43**, 2008, 478-487.

5. Andreenko, E., M. Nikolova. Topical distribution of the subcutaneous fat tissue on some parts and regions of the body in children and adolescents from south Bulgaria. – *Biotechnology and Biotechnological Equipment*, **24**, 2010, 342-346.
6. Boukov, Y., M. Nikolova, G. Baltadgiev, T. Matev. Basic somatometric indices in three generations of children from Plovdiv. – *Journal of Anthropology*, **3**, 2000, 41-49.
7. Brownson, R. C., T. K. Boehmer, D. A. Luke. Declining rates of physical activity in the United States: what are the contributors? – *Annual Review of Public Health*, **26**, 2005, 421-443.
8. Campbell, J. M., M. Lane, J. A. Owens, H. W. Bakos. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. – *Reproductive BioMedicine Online*, **31(5)**, 2015, 593-604.
9. Chavarro, J. E. , Th. L Toth, D.L Wright, J. D Meeker, R. Hauser. Body mass index in relation to semen quality, sperm DNA integrity, and serum reproductive hormone levels among men attending an infertility clinic. – *Fertil. Steril*, **93(7)**, 2010, 2222-2231.
10. Du Plessis, S. S., S. Cabler, D. A. McAlister, E. Sabanegh, A. Agarwal. The effect of obesity on sperm disorders and male infertility. – *Nature Reviews Urology*, **7**, 2010, 153-161.
11. Dutta, S., A. Biswas, P. Sengupta. Obesity, endocrine disruption and male infertility. – *Asian Pacific Journal of Reproduction*, **8**,2019a, 195-201.
12. Dutta, S., A. Majzoub, A. Agarwal. Oxidative stress and sperm function: A systematic review on evaluation and management. – *Arab Journal of Urology*, **17**, 2019b, 87-97.
13. Dutta, S., P. Sengupta, P. Slama, S. Roychoudhury. Oxidative stress, testicular inflammatory pathways, and male reproduction. – *International Journal of Molecular Sciences.*, **22**, 2021, Article ID10043.
14. Hakonsen, L. B., A. M. Thulstrup, A. S. Aggerholm, J. Olsen, J. P. Bonde, C. Y. Andersen, M. Bungum, E. H. Ernst, M. L. Hansen, E. H. Ernst, C. H. Ramlau-Hansen. Does weight loss improve semen quality and reproductive hormones? Results from a cohort of severely obese men. – *Reproductive Health*, **8**, 2011,24.
15. Hammoud, A. O., N. Wilde, M. Gibson, A. Parks, D. T. Carrell, A. W. Meikle. Male obesity and alteration in sperm parameters. – *Fertility and Sterility,* **90(6),** 2008, 2222-2225.
16. Irez, T., S. Bicer, S. Sahin, S. Dutta, P. Sengupta. Cytokines and adipokines in the regulation of spermatogenesis and semen quality. – *Chemistry and Biology Letters*, **7**, 2020, 131-139.
17. Jensen, T. K., A.-M. Andersson, N. Jørgensen, A.-G. Andersen, E. Carlsen, J. H. Petersen, N. E. Skakkebæk. Body mass index in relation to semen quality and reproductive hormones among 1,558 Danish men. – *Fertility and Sterility*, **82(4)**, 2004, 863-870.
18. Kasman, A., F. Del Giudice, E. Shkolyar, A. Porreca, G. M. Busetto, Y. Lu, M. L. Eisenberg. Modeling the contribution of the obesity epidemic to the temporal decline in sperm counts. – *Archivio Italiano Di Urologia E Andrologia*, **92(4),** 2020.
19. Kort, H. I., J. B. Massey, C. W. Elsner, D. Mitchell-Leef, D. B. Shapiro, M. A. Witt, W. E. Roudebush. Impact of body mass index values on sperm quantity and quality. – *Journal of Andrology*, **27(3)**, 2006, 450-452.
20. Liu, Y., Ding Z. Obesity, a serious etiologic factor for male subfertility in modern society. – *Reproduction*, **154(4)**, 2017, 123-131.
21. MacDonald, A. A., G. P. Herbison, M. Showell, C. M. Farquhar. The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis. – *Human Reproduction Update*, **16**, 2010, 293-311.

22. **Magnusdottir, E. V., T. Thorsteinsson, S. Thorsteinsdottir, M. Heimisdottir, K. Olafsdottir.** Persistent organochlorines, sedentary occupation, obesity and human male subfertility. – *Human Reproduction*, **20(1)**, 2005, 208-215.
23. **Mitova, Z.** Distribution of subcutaneous fat tissue in 9-15 year-old schoolchildren from Sofia. – *Acta Morphol. et Anthropol.*, **10**, 2005, 234-238.
24. **Mladenova, S., M. Nikolova, D. Boyadzhiev.** Body mass index, some circumference indices and their ratios for monitoring of physical development and nutritional status of children and adolescents. – *Acta Morphol. et Anthropol,* **10**, 2005, 226-229.
25. **Mladenova, S., M. Nikolova.** Components of body mass and their relations during the growth period of the boys. – *Proceedings from Balkan Scientific Conference of Biology*, *Plovdiv University Press*, 2005, 138-150.
26. **Nikolova, M., S. Mladenova.** Anthropometric indicators for assessment of body composition. – *Acta Morphol. et Anthropol*, **10**, 2005, 218-225.
27. **Nikolova, M., S. Sivkov, V. Akabaliev, S. Mladenova.** Body composition of children and adolescents in Plovdiv. – *Proceedings from Balkan Scientific Conference of Biology, Plovdiv University Press*, 2005, 150-159.
28. **Nikolova, M., E. Godina, D. Mollova.** A comparison of Plovdiv and Moscow children's height,weight and BMI values. – *Acta morphologica et anthropologica*, **15**, 2010, 212-216.
29. **Nikolova, M., D. Mollova, Sl. Tineshev**. Pecullarities in body composition of children. Comparison of Anthropometric and Bioelectrical impedance methods. – *Journal of Biomedical & Clinical Research*, **2**, 2009, 121-126.
30. **Nikolova, M., S. Tineshev.** Comparison of the body mass index to other methods of body fat assessment in bulgarian children and adolescent. – *Biotechnology and Biotechnological Equipment*, **24**, 2010, 329-337.
31. **Oliveira, J. B. A., C. G. Petersen, A. L. Mauri, L. D. Vagnini, A. Renzi, B. Petersen, M. Mattila, F. Dieamant, R. L. R. Baruffi, J. G. Franco Jr.** Association between body mass index and sperm quality and sperm DNA integrity. A large population study. – *Andrologia*, **50(3)**, 2018.
32. **Palmer, N. O., H. W. Bakos, J. A. Owens, B. P. Setchell, M. Lane**. Diet and exercise in an obese mouse fed a high-fat diet improve metabolic health and reverse perturbed sperm function. – *American Journal of Physiology-Endocrinology and Metabolism*, **302**, 2012, 768-780.
33. **Priskorn, L., T. K. Jensen, A. K. Bang, L. Nordkap, U. N. Joensen, T. H. Lassen, I.A. Olesen, S. H. Swan, N.E. Skakkebaek, N. Jørgensen**. Is sedentary lifestyle associated with testicular function? A cross-sectional study of 1,210 Men. – *American Journal of Epidemiology*, **184(4)**, 2016, 284-294.
34. **Ramaraju, G. A., S. Teppala, K. Prathigudupu, M. Kalagara, S. Thota, M. Kota, R. Cheemakurthi**. Association between obesity and sperm quality. – *Andrologia*, **50(3)**.
35. **Ramírez, N., G. Estofán, A. Tissera, R. Molina, E. M. Luque, P. J. Torres, A. Mangeaud, A. C. Martini**. Do aging, drinking, and having unhealthy weight have a synergistic impact on semen quality?. – *Journal of Assisted Reproduction and Genetics*, **38(11)**, 2021, 2985-2994.
36. **Sallmén, M., D. P Sandler, J. A Hoppin, A. Blair, D. D. Baird**. Reduced fertility among overweight and obese men. – *Epidemiology*, **17(5)**, 2006, 520-523.
37. **Sengupta, P., K. Bhattacharya, S. Dutta**. Leptin and male reproduction. – *Asian Pacific Journal of Reproduction*, **8**, 2019, 220-226.
38. **Sengupta, P., S. Dutta, U. D'Souza, A. Alahmar**. Reproductive tract infection, inflammation and male infertility. – *Chemistry and Biology Letters*, **7**, 2020, 75-84.

39. Sermondade, N., C. Faure, L. Fezeu, A. G. Shayeb, J. P. Bonde, T. K. Jensen, M. Van Wely, J. Cao, A. C. Martini, M. Eskandar, J. E. Chavarro, S. Koloszar, J. M. Twigt, C. H. Ramlau-Hansen, E. Borges Jr, F. Lotti, R. P. M. Steegers-Theunissen, B. Zorn, A. J. Polotsky, S. La Vignera, B. Eskenazi, K. Tremellen, E. V. Magnusdottir, I. Fejes, S. Hercberg, R. Lévy, S. Czernichow. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. – *Human Reproduction Update*, **19(3)**, 2013, 221-231.

40. Sermondade, N., C. Faure, L. Fezeu, R. Lévy, S. Czernichow. Obesity and increased risk for oligozoospermia and azoospermia. – *Archives of Internal Medicine*, **172(5)**, 2012, 440-442.

41. Sharpe, R. M. Environmental/lifestyle effects on spermatogenesis. – *Philosophical Transactions of the Royal Society B*, **365**, 2010, 1697-1712.

42. Stamatakis, E., N. Coombs, R. Jago, A. Gama, I. Mourão, H. Nogueira, V. Rosado, C. Padez. Type-specific screentime associations with cardiovascular risk markers in children. – *American Journal of Preventive Medicine*, **44(5)**, 2013, 481-488.

43. Tineshev, S., M. Nikolova. Anthropological characteristics of body composition in children and adolescents from Plovdiv. – *Biotechnology and Biotechnological Equipment*, **24**, 2010, 338-341.

44. Veron, G. L., A. D. Tissera, R. Bello, F. Beltramone, G. Estofan, R. I. Molina, M. H. Vazquez-Levin. Impact of age, clinical conditions, and lifestyle on routine semen parameters and sperm kinematics. – *Andrology*, **110(1)**, 2018, 68-75.

45. World Health Organization. Obesity and overweight, 2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight