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TESTOSTERONE LEVEL AND BODY MASS INDEX IN YOUNG PEOPLE IN YAKUTIA

DOI 10.25789/YMJ.2021.76.14

УДК 577.17

The aim of this study was to assess the levels of testosterone in serum as a function of body mass index (BMI, 15-30 kg/m2) in young men in Yakutia, aged 18 to 28. The total sample (n=87) was subdivided into three BMI groups: underweight (n=11), normal weight (n=64), and overweight (n=12). It was found that underweight in young men does not affect the level of testosterone in the blood. Thus, no significant differences in testosterone levels were found between the groups of men with underweight (23.06±5.66 nmol/L) and those with normal weight (22.9±8.24 nmol/L; p=0.703). In contrast, being overweight and obese led to lower testosterone levels. Thus, in overweight individuals, testosterone levels were significantly lower (18.54±5.73 nmol/L), compared with those who had an underweight (23.06±5.66 nmol/L; p=0.04) or the weight was normal (22.9±8.24 nmol/L; p=0.03). A comparative analysis of testosterone levels based on global data was conducted, including 1866 men. The age of the participants ranged from 18 to 30 years old. The control group comprised 528 men with normal body weight (18.5-24.99 kg/m2), and a group with an excess of overweight and obese (25-35 kg/m2) 1338 men were included. The results of testosterone level according to global data confirmed the inverse correlation of a decrease in testosterone levels with an increase in BMI (p<0.01). The assessment of heterogeneity of studies in the "Overweight/obese" subgroup was I2=46% (average heterogeneity), and in the "Normal weight" subgroup heterogeneity was I2=3% (unimportant heterogeneity), such insignificant heterogeneity in both subgroups may indicate a negative correlation of testosterone levels with BMI, regardless of race and ethnicity.

Keywords: testosterone, men, underweight, overweight, obesity.

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Introduction. According to the World Health Organization (WHO), many countries with low and middle income per capita face simultaneously several forms of malnutrition: undernutrition and overnutrition [9]. Undernutrition leads to wasting, stunting, and underweight, and overnutrition to energy imbalances and obesity develops because of this imbalance [9]. It is considered that being underweight can lead to osteoporosis [31], lowering of immune systems, muscle weakness, damage to the cardiovascular and nervous systems [10, 14]. Critical underweight can be fatal because of extreme wasting [15]. In turn, obesity is associated with an increased risk of cerebral ischemia of the heart, type 2 diabetes, and reproductive disorders [11, 12].

In recent years, obesity rates in men have increased, which can lead to long-term consequences for several homeostatic processes, including reproductive function [25]. In men, obesity negatively affects testosterone levels [23], sperm quantity, and quality [24], and is considered the most common cause of male hypogonadism [19]. In overweight the degree in men, the total testosterone decreases because of insulin resistance, which leads to a decrease in sex hormone-binding globulin [34]. More severe obesity is additionally associated with a decrease in the level of free testosterone because of the suppression of the steroid hormone-interrelated system: the hypothalamic-pituitary-testicular axis [34]. A decrease in testosterone in the blood itself leads to an increase in obesity, creating a self-reproducing cycle of metabolic complications [16].

There is currently very little research on the problems of undernutrition and underweight in men. Basically, such studies concern infants, children (under 5 years old), and women of reproductive age. Being underweight is not only related with several diseases [14, 25, 31] but is also a predictor of chronic energy deficit, which negatively affects people's ability to work [33]. There is also little research on the effect of being underweight on reproductive hormones in men, including testosterone. Basically, such studies on the effect of underweight on testosterone levels in the blood were conducted on samples of elderly men, as part of the therapy of age-related androgen deficiency [20, 21, 26].

The aim of this study is to assess the dependence of serum testosterone levels on body mass index (underweight, normal weight, overweight) in healthy young men in Yakutia, aged 18 to 28, in comparison with global data.

Materials and research methods. Sample. The present study included 87 men, whose average age was 20.15±2.15 years. All participants are Yakuts who were healthy during the study and were questioned about gender, nationality, and age. The participants in the study did not complain about their health condition and were not registered with the dispensary for chronic diseases. All subjects gave written informed consent to participate in the study and to process personal data. This work was approved by the local eth-

ical Committee on biomedical ethics at the YSC CMP (Yakutsk, Protocol № 16 of December 13, 2014).

Anthropometric measurements. Anthropometric indicators (body weight in kilograms, height in centimeters) were determined for all participants using standardized methods. BMI was calculated by dividing weight (kg) by height (cm) squared. According to the WHO classification [37], the sample was divided into 3 groups according to BMI: underweight (≤18.49 kg/m2), normal weight (18.5-24.99 kg/m2), overweight (≥25 kg/m2), and obesity (≥30 kg/m2).

Testosterone levels test. Venous blood for the study was taken in the morning after a 12-hour fast from all participants. To determine the level of testosterone circulating in the blood, an enzyme immunoassay kit "SteroidIFA-testosteron" (Company Alkor Bio, Russian Federation) was used. The testosterone concentration in the samples was measured at a wavelength of 450 nm in a VICTORX5 Multimode Plate Reader (Perkin Elmer Inc., USA).

Search criteria for publications for comparative analysis. For this analysis, they carried the main search for suitable studies out in the electronic databases PubMed-Medline and eLibrary.Ru. The following search strings were used: "testosterone AND men OR young men AND body mass index OR BMI". The last search was carried out on 10/04/2021. Details of each study included were collected in a pre-designed form. Thus, data were collected: first author, publication date, study location, sample size, age of participants, BMI (mean average), serum testosterone levels (mean average), methods for measuring testosterone levels (electrochemiluminescence immunoassay - ECLIA, enzyme immunoassay - ELISA, radioimmunoassay - RIA). The methodological quality of the included studies was assessed using the Newcastle-Ottawa scale. In total, 9 points were involved in this form. The final scores of the articles in this analysis ranged from 6 to 9 points. Comparative analysis was performed using The RevMan 5.3 software (The Cochrane Collaboration, UK). The difference in blood testosterone levels between obese and normal weight subjects was assessed using the total inverse variance. Heterogeneity was assessed using the Q-test based on the χ-square analysis and the I2 test (p<0.10 denoted significance). The inclusion criteria for studies in this analysis: studies were to be controlled, crossover, prospective, or clinical, studies were to investigate serum testosterone levels in men aged 18 to 30 with normal weight (<24.9 kg/m2) and/or overweight and obese (≥25 kg/m2). The exclusion criteria: uncontrolled studies, lack of sufficient information on testosterone concentrations, no data on BMI, duplicate study.

Literature search and relevant research. A literature search in electronic databases revealed 110118 publications (PubMed-Medline - 106644 and eLibrary.Ru - 3474). After applying different filters (sample age, gender, and unit of measurement of testosterone in the blood) 109882 articles were excluded. The full texts of 198 articles were reviewed, and this resulted in the exclusion of 186 articles. As a result, 12 publications [2, 3, 5-7, 13, 17, 18, 29, 30, 32, 35] met the inclusion criteria and were included in the final analysis (Figure 1).

Statistical analysis. The results were analyzed using a computer program for statistical data processing Statistica 13.5 (TIBCO Software Inc., USA). All results are expressed as mean (±)standard deviation, and p<0.05 were considered statistically significant. Comparative analysis between the three BMI groups was performed using the Mann-Whitney U-test.

Results and discussion. In the present study, the mean serum testosterone level in young men (18-28 years old) was 22.47±7.75 nmol/L. Earlier, serum testosterone levels were determined in Yakuts (18-25 years old), which varied from 12 to 30 nmol/L [1, 2, 4]. In general, the results of this study are consistent with earlier studies in which testosterone levels were studied in comparison with some parameters of male fertility (spermogram) [1], with the psycho-emotional state of athletes during breaks, during the competitive period [4] and depending on metabolic parameters [2].

Table 1 presents anthropometric characteristics and serum testosterone levels for the entire sample (n=87). Evaluation of the effect of BMI on testosterone levels showed that in the group of overweight men, the average testosterone level was statistically significantly lower – 18.54±5.73 nmol/L, than in the group

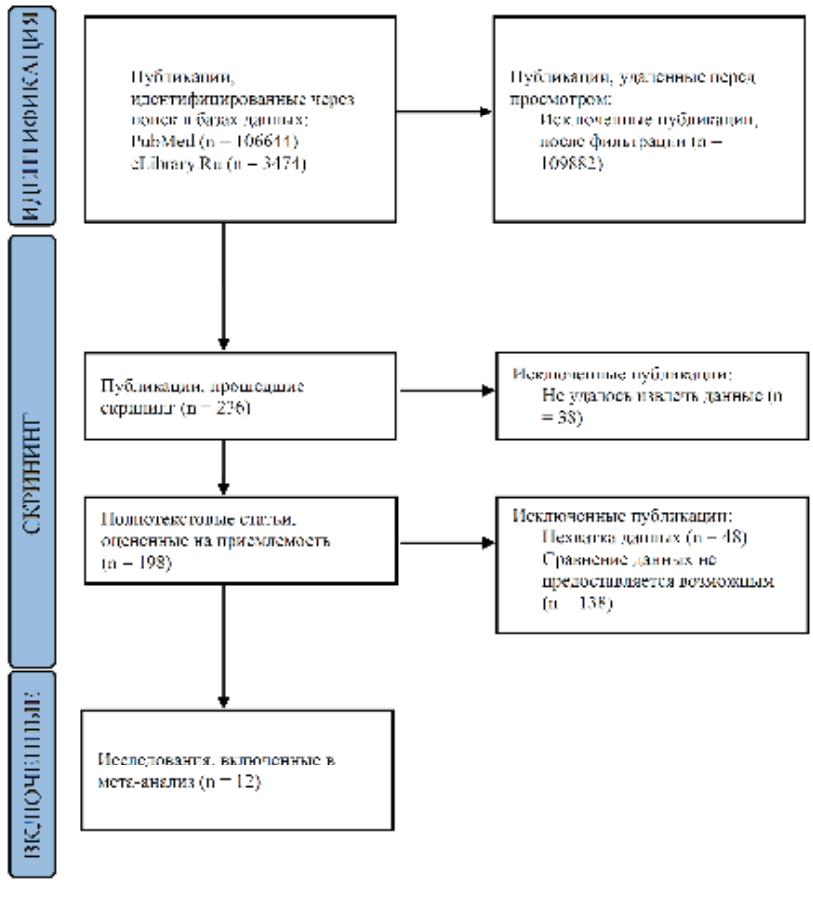

Fig 1. Block diagram of the selection of publications for comparative analysis.
Note: A representation of the process by which relevant studies were extracted from databases, selected or excluded. Preferable moments for presenting the results of systematic reviews and meta-analyses (PRISMA). From: Page M.J., McKenzie J.E., Bossuyt P.M., Boutron I., Hoffmann T.C., Mulrow C.D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.**n71**

Table 1

BMI and testosterone levels in young men (n=87)

Parameters	Underweight (n=11)	Normal weight (n=64)	Overweight (n=12)	Overweight and Underweight	Overweight and Normal weight	Normal weight and Underweight
Age (years)	18.91±0.83	20.25±2.26	20.75±2.05	p=0.01	p=0.231	p=0.09
Height (cm)	170.36±5.87	173.81±5.33	175.75±7.63	p=0.157	p=0.648	p=0.144
Weight (kg)	50.45±3.42	67.25±7.51	83.25±10.13	p<0.01	p<0.01	p<0.01
BMI (kg/m^2)	17.39±0.91	22.22±1.85	26.87±1.68	p<0.01	p<0.01	p<0.01
Testosterone (nmol/L)	23.06±5.66	22.9±8.24	18.54±5.73	**p=0.04**	**p=0.03**	p=0.703

Note: statistically significant differences are in bold.

of men with a underweight – 23.06±5.66 nmol/L (p=0.04) and with normal weight - 22.9±8.24 nmol/L (p=0.03) (Table 1). The results of the present study are consistent with those of Osadchuk et al., [2] where decreased testosterone levels were also found in overweight and obese men.

The average testosterone levels in the groups of men with normal weight and weight deficiency did not significantly differ from each other (p=0.703) (Table 1). In studies conducted in the United States and Germany, testosterone levels were lower in men with anorexia nervosa than in men of normal weight [8, 28, 36]. However, in anorexia nervosa, weight loss can be caused by excessive physical and mental stress, which leads to a violation of some reproductive and endocrine parameters [22]. It is possible that low testosterone levels may be associated with these disorders. In the present study, young men were relatively healthy, and it is possible that underweight in men, without increased physical activity, does not significantly affect testosterone levels in the blood.

Although the difference in serum testosterone levels in young men reached statistically significant differences (p<0.05), because of the small sample size, these differences were still on the level of error. To extrapolate this state-

Table 2

Publications included in the comparative analysis

Authors of the article and year of publication	Age	Methods for determining testosterone levels	Research location	n	BMI, kg/m^2	Testosterone, nmol/L
Subgroup 1. Overweight or obesity						
Abolovich et al., 1999	22-30	RIA	Argentina (Buenos Aires)	10	25.8	18.74±5.55
Kehinde et al., 2004	20-29	RIA	Kuwait (Kuwait City)	59	25	15.73±8.76
Gapstar et al., 2002	24-34	RIA	USA (Birmingham, Chicago, Minneapolis, Auckland)	482	25.8±4.7	22.55±6.94
Gapstar et al., 2002	24-34	RIA	USA (Birmingham, Chicago, Minneapolis, Auckland)	692	25±3.7	22.21±6.94
Velasco-Orjuela et al., 2018	21-28	ECLIA	Colombia (Bogota)	14	28.75±2.01	14.92±5.93
Roberts et al., 2013	20-23	ECLIA	USA (Los Angeles)	36	33.6 (31.2-34.7)	14.23±0.52
Popova et al., 2012	23-29	ELISA	Russia (Novosibirsk)	28	27.3±0.2	15.71±1.01
Popova et al., 2012	24-29	ELISA	Russia (Novosibirsk)	5	35.0±2	11.88±0.78
This work	18-30	ELISA	Russia (Yakutsk)	12	26.87±1.68	19.28±5.9
Total				**1338**		
Subgroup 2. Normal weight						
Sarita Sanke et al., 2016	19-30	ELISA	India (New Delhi)	32	21.1±2.4	20.57±4.93
Wright et al., 1995	25-29	RIA	USA (Raleigh)	16	24±1	23±2
Wright et al., 1995	26-28	RIA	USA (Raleigh)	17	24±1	22±1
Osadchuk et al., 2013	25-28	RIA	Russia (Syktyvkar)	39	22.8±0.2	25.85±1.21
Popova et al., 2012	23-24	ELISA	Russia (Novosibirsk)	50	22.1±0.2	23.35±1.04
Osadchuk et al., 2016	21-22	ELISA	Russia (Kemerovo)	54	23.04±0.4	22.59±0.93
Luisetto et al., 1995	19-31	RIA	Italy (Padua)	24	23±2.3	30.4±9.1
Pospísilová et al., 2012	23-34	RIA	Czech Republic (Prague)	232	22.5±2.79	18.5±6.05
This work	18-30	ELISA	Russia (Yakutsk)	64	22.22±1.85	22.9±8.24
Total				**528**		

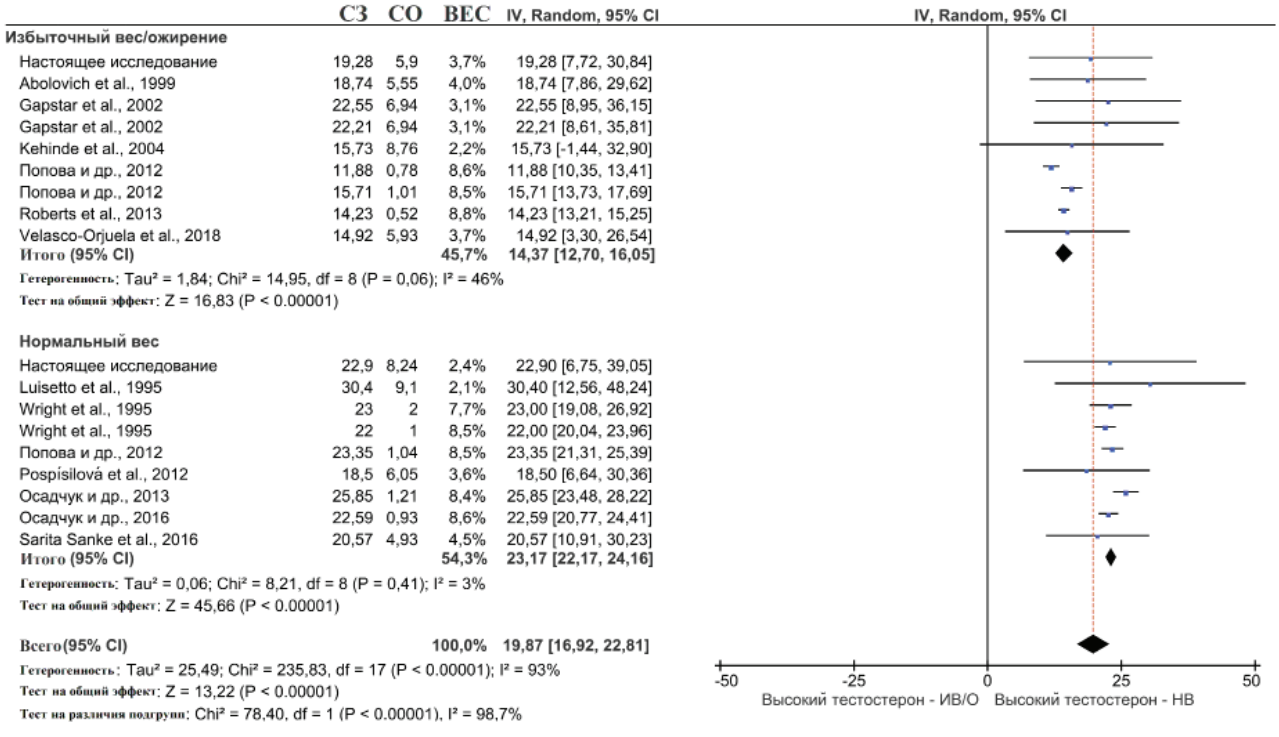

Fig 2. Comparative analysis of average serum testosterone levels in overweight/obese and normal-weight men (n=1866 men, 18-30 years old)

ment, we conducted additional research on the literature data on the effect of BMI on testosterone levels in men. A total of 1866 individuals were included in the comparative analysis, sample sizes varied from 5 to 692 in individual studies. All studies were published between 1995 and 2018. The age of the participants ranged from 18 to 30 years old. Detailed characteristics of these studies are shown in Table 2. The control group comprised 528 men with normal body weight (18.5-24.99 kg/m2), and a group with an excess of overweight and obese (25-35 kg/m2) 1338 men were included (total analysis 1866 people were included).

Comparative analysis of testosterone levels in men depending on BMI revealed statistically significant differences: in the "Overweight/obesity" subgroup, the average testosterone level (14.37; CI: 12.7-16.05 nmol/L) was significantly lower compared with subgroup "Normal weight" (23.17; CI: 22.17-24.16 nmol/L) (p<0.01) (Figure 2). This analysis showed that testosterone levels can depend on BMI: the higher the testosterone level, the lower the BMI. Assessment of heterogeneity of studies in the subgroup "Overweight/obesity" was I2=46% (average heterogeneity), and in the subgroup "Normal weight", heterogeneity was I2=3% (unimportant heterogeneity). The results got are consistent with previous studies [12, 23]. In an earlier meta-analysis [27] on the effect of racial differences on the concentration of sex steroid hormones found statistically significant differences between black and white men for free testosterone. Thus, in black men, the average levels of free testosterone were 2.5-4.9% higher than in white men. The authors believe that differences in lifestyle and anthropometry can explain these slight differences [27]. In the present study, no differences in average testosterone levels in men with normal weight from different populations of the world (21-24 kg/m2) were found (I2=3%, unimportant heterogeneity), which may indicate that there are no differences in testosterone levels depending on the racial and ethnic affiliation of the subjects. The average heterogeneity in overweight and obese men may be associated with a high variation in average BMI values (from 25 to 33 kg/m2), which shows a strong negative correlation of testosterone levels in the blood depending on BMI.

Conclusions

1. It was found that in young men (18-28 years old), underweight does not affect the level of testosterone in the blood, and the level of testosterone is more affected by overweight and obesity. So, we found that in a subgroup of overweight men, the average serum testosterone level was significantly lower compared to the subgroups of men with normal weight and weight deficiency, and in a subgroup of men with weight deficiency; the average testosterone level did not significantly differ from the subgroup of men with normal weight.

2. The results of a comparative analysis of average testosterone levels in 1866 men (18-30 years old) from different regions of the world indicate a negative correlation of testosterone levels with BMI, regardless of race and ethnicity.

The work was done within Yakutsk scientific center for complex medical problems "Study of the genetic structure and burden of hereditary pathology of populations of the Republic of Sakha (Yakutia)", the base part of a state assignment of the Ministry of Science and Higher Education of the Russian Federation (FSRG-2020-0016).

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