Overweight and seminal quality: a study of 794 patients

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Objectives: To evaluate sperm quality, levels of markers of epididymal and accessory gland function, and T in semen from men grouped according to their body mass index (BMI).
Design: Blind prospective study.
Setting: Andrology and reproduction laboratory in Cordoba, Argentina (2006–2007).
Patient(s): Seven hundred ninety-four men.
Intervention(s): None.
Main Outcome Measure(s): In semen samples, sperm quality (volume, density, motility, morphology, viability, hypoosmotic swell test, and nuclear maturity) and levels of neutral alpha-glucosidase, fructose, citric acid and T.
Result(s): Multivariate analysis showed a negative association between BMI and motility, rapid motility and neutral alpha-glucosidase levels, and a positive association between BMI and seminal fructose levels. No associations were found among BMI and sperm concentration, the other parameters evaluated, or seminal T levels.
Conclusion(s): Results found in our study support a deleterious effect of obesity on seminal quality, probably by alterations in the function of the epididymis (i.e., in epididymal maturation). (Fertil Steril® 2009;■:■–■. ©2009 by American Society for Reproductive Medicine.)

Key Words: Overweight, obesity, sperm quality, epididymis, seminal T, neutral alpha-glucosidase, fructose, citric acid

For more than a decade, various studies have alerted researchers about a diminution in male fertility (i.e., sperm quality) in patients consulting for infertility and the overall population (1–3). The etiology of this adverse trend in male reproductive health is unknown; nevertheless, environmental factors are suspected to contribute because of the rapid increase in the frequency of these reproductive problems (4). Among these environmental factors, nutritional habits are crucial, including diet composition (5).

Obesity is a condition that has doubled in the past decade and is reaching epidemic proportions in several countries, including the United States, where 22% of the population has a body mass index (BMI) ≥ 30 kg/m^2 (6). Although overweight and obesity have been demonstrated to affect female fertility (7), there is no consensus on the effect of BMI on male fertility and seminal parameters (4, 8–10). As Hammoud et al. (11) elucidated in a notable critical review, the epidemiologic studies performed at the population level and in infertile couples during recent years suggest that obesity is associated with reduced male fertility, although this effect seems to be modest. Nevertheless, whether overweight or obesity affect the functional activity of spermatozoa is not well established, because results reported by different authors conflict or do not exhibit a clear dose-response character.

Obesity and nutritional habits are mainly associated with significant disturbance in the plasma hormonal milieu, such as a decrease in total and free T levels, decreased gonadotropin levels, decreased binding capacity of sex hormone-binding globulin, and hyperestrogenemia (5, 6, 8, 11–13). Undoubtedly, all these alterations might affect the male reproductive system and gamete quality. In support of this idea, some studies have documented a decrease in sperm quality associated with increased BMI (4, 10, 14). Despite the fundamental contribution of the epididymis, seminal vesicles, and prostate to fertility and their secretory activity being androgen-dependent, we found no studies assessing the effect of overweight on male accessory gland function.

The objectives of this article are to evaluate semen from patients grouped by their BMI: [1] sperm quality parameters such as volume, concentration, motility, morphology, viability, membrane integrity, functionality, and nuclear maturity; [2] levels of functional markers of epididymis and male accessory glands (seminal vesicles and prostate); and [3] T concentration.

MATERIALS AND METHODS

Semen samples were obtained from the male partner of couples being studied for infertility who attended the Andrology and Reproduction Laboratory in Córdoba, Argentina. This prospective study was performed during 2006–2007, and written informed consent was obtained from all participants.

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Because our study includes noninvasive procedures, and the semen samples were voluntarily provided by patients and kept rigorously anonymous, institutional review board approval was unnecessary. From the 1,758 patients who were asked to participate in the present study, 45.2% were finally included; the final number of semen samples evaluated (one sample per patient) was 794 (Fig. 1). The patients' height and weight were measured in the andrology laboratory on the same day that their semen sample was obtained and processed. All patients completed a form containing data on age, abstinence period, toxic exposure, and genitourinary and other diseases that can alter the hypothalamic-hypophyseal-testicular axis. According to their BMI (BMI = weight [kg] / height^2 [m^2]), patients were classified into three groups: normal ($18.5 \leq$ BMI < 25), overweight ($25 \leq$ BMI < 30), and obese ($30 \leq$ BMI ≤ 50).

Samples

After abstinence of 2–10 days, semen samples were collected by masturbation in sterile containers or by natural coitus with special silastic condoms (Male Factor Pak; Apex Medical Technologies, San Diego, CA). When necessary, samples were transported to the laboratory maintained at approximately 37°C. Samples were analyzed within 1 hour after collection in all cases.

Seminal Parameters Evaluated

After liquefaction, semen analysis was performed according to the World Health Organization (WHO) recommendations (15), and sperm morphology was assessed by Kruger's strict criteria (16). Seminal volume was determined in a graduated conic tube. Sperm concentration and motility were assessed by conventional methods in a Makler counting chamber (Sefi-Medical Instrument, Haifa, Israel). Sperm viability was determined with a supravital eosin Y technique. The hypoosmotic swelling test (HOS) evaluated incubating spermatozoa in a hypoosmotic solution, and sperm chromatin condensation was evaluated with the aniline blue technique. Sperm morphology was assessed using Papanicolaou staining and according to Kruger's strict criteria. Finally, using colorimetric techniques, seminal plasma concentrations of neutral α-glucosidase (NAG), fructose, and citric acid were assessed as functional markers of epididymis, seminal vesicles, and prostate, respectively and expressed in relation to semen volume. Seminal total T levels were assayed using a commercial RIA kit (DSL 4000; Diagnostic Systems Laboratories, Webster, TX) with a sensitivity of 0.08 ng/mL. Results were adjusted according to seminal volume.

Statistical Analysis

Results were expressed as mean ± SEM only for descriptive purposes. Data were analyzed using multivariate regressions (linear regression), with BMI, age, and abstinence as independent variables. The level of significance used was 5%. In all cases, *n* represents the number of samples evaluated.

RESULTS

Some characteristics of the patients included in the present study are shown in Table 1. It is important to note that 77.4% of our obese patients had a BMI between 30 and 35, corresponding to the subcategory named *obesity I*, and 16.8% a BMI between 35 and 40 (obesity II). Only 5.8% of the obese patients from the present study exhibited morbid obesity ($40 <$ BMI ≤ 50).

Sperm quality results after semen processing and multivariate regression analyses are shown in Table 2. As can be seen, there is a negative association between BMI and total motility or rapid motility (grade A). A similar profile was obtained for NAG levels (functional marker of epididymis, where motility is acquired) and BMI. Alternatively, a positive association was detected between BMI and seminal fructose levels. No association was found between BMI and sperm concentration or with other parameters evaluated in the present study. Finally, no significant differences were detected in seminal T levels between groups (normal, 1.41 ± 0.13 ng/mL ejaculate, n = 27; overweight, 1.47 ± 0.12 ng/mL ejaculate, n = 27; obese, 1.97 ± 0.29 ng/mL ejaculate, n = 26).

DISCUSSION

In a large sample of men attending an andrology laboratory, we evaluated the possible deleterious effect of an elevated BMI on different parameters reflecting semen quality, such as sperm quality, levels of functional markers of the epididymis and male accessory glands, and T concentration.

Although the impact of obesity upon sperm parameters is still a controversial issue (9, 12, 13), several authors have detected deleterious effects with sperm density and motility being more affected (4, 17, 18). Accordingly, Jensen et al. (4) reported that, in a large sample study performed in healthy volunteers (n = 1558), men with BMI >25 kg/m^2 had an approximately 20% reduction in sperm

FIGURE 1

Status of the patients who attended the Andrology and Reproductive Laboratory in Córdoba, Argentina, between 2006-2007. (**A**) The percentage of patients who refused to participate in the study, the percentage of patients that agreed to participate but were excluded by researchers, and the percentage of patients finally included in the study. (**B**) Reasons for exclusion.

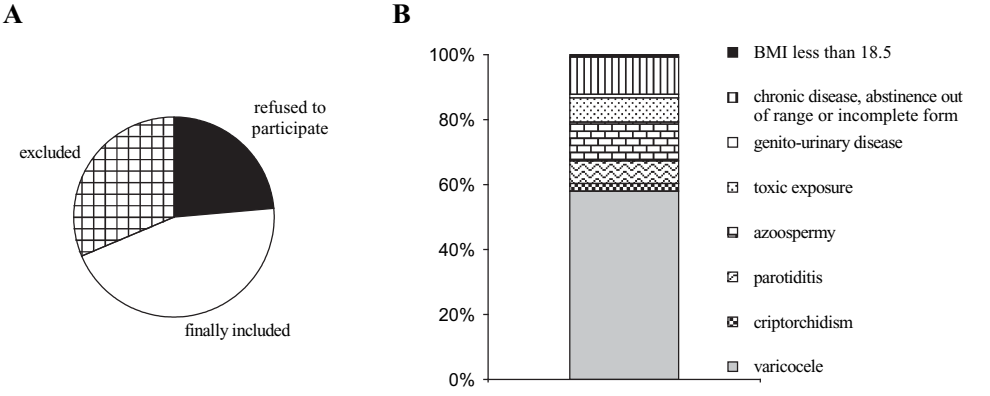

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TABLE 1

Characteristics of the patients enrolled in the present study.

Parameter	Total patients, n = 794 *(range)*	Patients grouped by BMI		
		Normal (n = 251)	Overweight (n = 388)	Obese (n = 155)
Patients included in each category (%)	100.0	31.6	48.9	19.5
BMI (kg/m^2)	27.2 ± 0.1 (18.6–46.8)	23.4 ± 0.1	27.3 ± 0.1	33.2 ± 0.3
Age (years)	34.9 ± 0.2 (20–65)	34.1 ± 0.4	35.1 ± 0.3	36.0 ± 0.5
Abstinence period (days)	4.0 ± 0.1 (2–10)	3.9 ± 0.1	4.1 ± 0.1	4.1 ± 0.1

Note: Men enrolled in this study attended the Andrology and Reproductive Laboratory in Córdoba, Argentina. Patients were classified into three groups by BMI: normal (18.5 ≤ BMI < 25), overweight (25 ≤ BMI < 30), and obese (30 ≤ BMI ≤50). Values are expressed as mean ± SEM. *n* = number of seminal samples evaluated (one per patient).

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concentration and total sperm count, compared with men classified as normal. Similarly, Koloszar et al. (17) found that patients with normozoospermia with a higher BMI (i.e., 30.1–39) had a significantly lower sperm concentration than those with a BMI <30. Therefore, and because both sperm morphology and gamete density reflects spermatogenesis (19–21), the reported results could be attributed to alterations in this androgen-dependent process.

In our study, we failed to find a significant association between BMI and sperm concentration. Furthermore, we did not find alterations in sperm morphology, evaluated either in accordance with WHO 1992 or with Kruger's strict criteria. In agreement with our results, Qin et al. (13) determined that, in a study of 990 fertile males classified according to their BMI, sperm quantity and morphology were not modified in obese volunteers; on the contary, they detected significant alterations only in underweight men (BMI < 18.5). A similar trend was previously reported (4). In fact, Qin et al. (13) stated that "being overweight may be a protective factor for low sperm concentration and low total sperm count;" they argued that the association between BMI and sperm density does not depend on reproductive hormones plasma levels (T, FSH, LH, E_2) (13). In agreement with this proposal, Strain et al. (8) reported that alterations in reproductive hormones in obese men (diminution in free and total T and FSH) did not affect spermatogenesis.

It is important to highlight that in our study, 94.2% of the patients had a BMI <40 (obesity I plus obesity II), and only 5.8% presented morbid obesity (40 < BMI < 50). Discrepancies between our results and those of other authors could be attributed to differences in volunteers' BMI range or distribution in the obese group. In this respect, Pasquali et al. (22) reported that reduced spermatogenesis is a consequence of hypotestosteronemia found in "massively" obese individuals. We did not find differences in the diminution trend between patients with obesity II or morbid obesity with respect to obesity I (linear regression analysis). It is also important to note that the population enrolled in our study comprised men who attended an andrology laboratory (members of a couple with fertility problems) and not healthy volunteers.

In addition, we found a negative association between BMI and sperm motility (total and rapid motility) and between BMI and

TABLE 2

Slope of BMI and *P* value of linear multivariate regressions on seminal parameters from patients attending an andrology laboratory.

Seminal parameters	Normal (n = 251)	Overweight (n = 388)	Obese (n = 155)	BMI (slope)	P value
Seminal volume (mL)	3.2 ± 0.1	3.1 ± 0.1	3.1 ± 0.1	–0.01	0.526
Sperm concentration (× 10^6/mL)	43.7 ± 1.9	44.2 ± 1.8	43.0 ± 3.2	–0.45	0.162
Motility (% of total motile spermatozoa)	51.4 ± 1.2	50.2 ± 1.0	46.6 ± 1.7	–0.49	0.007
Rapid motility (% of rapid spermatozoa)	39.8 ± 1.2	38.8 ± 0.9	35.9 ± 1.6	–0.41	0.019
Viability (% of dead spermatozoa)	16.9 ± 0.6	17.8 ± 0.5	19.0 ± 1.0	0.10	0.321
Kruger's morphology (% of normal spermatozoa)	8.3 ± 0.4	8.4 ± 0.3	8.7 ± 0.5	0.001	0.973
OMS morphology (% of normal spermatozoa)	19.3 ± 0.7	19.7 ± 0.6	20.5 ± 1.0	0.06	0.552
HOS (% of reactive spermatozoa)	79.3 ± 0.9	78.1 ± 0.8	76.1 ± 1.7	–0.16	0.306
Nuclear maturity (% of mature nuclei sperm)	66.9 ± 1.2	66.8 ± 1.0	66.7 ± 1.5	–0.03	0.886
Alpha-glucosidase (mg%)	71.7 ± 3.5	65.0 ± 2.4	62.6 ± 3.5	–0.99	0.033
Fructose (mg%)	333.6 ± 8.1	329.4 ± 6.8	351.6 ± 9.6	2.27	0.049
Citric acid (mg%)	460.9 ± 10.4	443.9 ± 8.8	449.6 ± 12.1	–0.44	0.769

Note: Men enrolled in this study attended the Andrology and Reproductive Laboratory in Córdoba, Argentina. Values are shown as mean ± SEM. *n* = number of seminal samples evaluated (one per patient).

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NAG levels ($P < 0.05$). Concordantly, it has been reported that the number of normal motile spermatozoa differed statistically according to BMI, being significantly reduced in men with BMI higher than 30 vs. healthy men; however, these authors did not quantify the seminal levels of NAG (18). This substance is an enzyme secreted into the epididymal fluid that has been identified as modulator of epididymal maturation (23–26), a process involved in sperm motility acquisition (27). Accounting for the known androgen-dependency of NAG secretion (28) and the androgen level alterations reported in obese patients, the motility profiles and NAG levels found in our study support a possibly deleterious effect of obesity on epididymal function. Studies performed previously in our laboratory have linked epididymal function and NAG secretion with nutritional alterations (29).

Regarding androgen levels, and because several studies report that seminal T concentrations correlate better than plasma ones with testis function, germ cell viability, sperm quality, and sperm fertilizing capacity (30–32), we quantified total T concentration in seminal plasma; no differences were detected between groups.

Finally, we did not find an association between BMI and other seminal parameters such as sperm viability, membrane integrity and/or functionality (HOS), nuclear maturation, or seminal citric acid concentration.

As a final analysis it is important to remark that BMI, the most widespread parameter used to assess body composition, is possibly not the most accurate. Jensen et al. (4) claimed that BMI is a measure of weight in relation to height and does not directly reflect the percentage of body fat. In fact, it has been reported that plasma androgen levels are more closely associated with abdominal fat levels than with BMI. Likewise, differences in dietary proteins and fibers, but not fat or carbohydrates, are the major determinants of sex hormone binding globulin plasma levels (5). Divergences found between studies could be explained by differences in the life styles of the men enrolled in each study, as well as the previously mentioned differences in obesity ranges or their fertility status. Finally, the role of leptin levels in sperm quality pathogenesis provoked by obesity must be fully elucidated, because it has been recently demonstrated that serum leptin levels positively correlate with BMI and negatively correlate with sperm concentration, motility, morphology, and plasma T levels (33). Moreover, because leptin has been detected also in tubuli seminiferi and seminal plasma (34, 35), and the leptin receptor is expressed in testicular germ cells (36), it has been suggested that leptin mediates a link between obesity and male infertility (33).

In summary, our results support the idea of a deleterious effect of obesity on seminal quality, probably mediated by alterations in epididymal function. Nevertheless, further studies are needed to address this proposal fully. We believe that fertility decline in obese men could be the result of multiple factors, in which semen quality reduction has a documented effect. As Hammoud et al. (11, 37) stated, other factors such as accumulation of toxic substances and endocrine disruptors in the fatty tissue, life style, and/or sexual dysfunction must be taken into account. Because the incidence of obesity is growing, it is expected that the number of obese men with reduced fertility will increase as well (11).

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