Systematic Review and Meta-Analysis

Medicine®

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Is low body mass index a risk factor for semen quality? A PRISMA-compliant meta-analysis

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Abstract

Background: Male infertility has become a worldwide public health problem. However, the effect of low body mass index (BMI) is still controversial.

Methods: Relevant articles in Pubmed, Embase, Web of science, and Wanfang database published until September 2017 were searched without language restriction. We performed a meta-analysis about low BMI and semen parameters containing total sperm count, concentration, semen volume, and sperm motility (overall and progressive), including 709 men with low BMI and 14,622 men with normal BMI.

Results: Thirteen studies were included in this meta-analysis and a total of 15,331 individuals were accumulated. We pooled data from these articles and found standardized weighted mean differences in semen parameters (total sperm count and semen volume) showed significant difference between low BMI and normal BMI.

Conclusions: This systematic review with meta-analysis has confirmed that there was a relationship between low BMI and semen quality, which suggesting low BMI may be a harmful factor of male infertility. Yet lacking of the raw data may influence the accuracy of the results. Further researches are needed to identify the role of underweight in male sterility.

Abbreviations: BMI = body mass index, SMD = standardized weighted mean differences, WHO = World Health Organization.

Keywords: low body mass index, meta-analysis, semen parameters, underweight

1. Introduction

As an important clinical characteristic, body mass index (BMI) indicates the state of body to some extent. Increasing evidence suggested that high BMI (overweight and obesity) is a risk factor for people, which contributes to the development of many diseases, such as diabetes, cardiovascular disease, cancers, as well as male infertility.[1–3] Male infertility is a multi-factorial diseases, which is affected by genetic factors, environmental exposure as endocrine disrupters,[4,5] lifestyle-related factors,[6] and obesity.[7,8] Currently, the effect of obesity on male fertility has attracted more attention since a large number of related studies have gradually emerged.[9] However, whether men with low BMI has normal fertility or not is still unknown. As a well-known health risk,[10,11] low BMI could increase the mortality risk in patients with schizophrenia,[3] as well as compromise live birth rate in fresh transfer in vitro fertilization cycles.[12] Thus, it is important to pay additional attention to the effect of low BMI on fertility body.

A meta-analysis[13] published in 2013 identified a J-shaped association between BMI categories and risk of oligozoospermia or azoospermia, which suggests that low BMI may impair semen quality. Some studies have also identified that low BMI was associated with reduced semen quality, even though the affected semen parameters were not precisely the same. Jensen et al[14] reported that low BMI could reduce total sperm count and sperm concentration, and Paasch and colleagues[15] found a similar result that sperm count was decreased in underweight group than normal-weight group. In additional to sperm count, Luque et al[16] also reported a lower motility of underweight men. The analogous result about semen volume was found by Qiu et al.[17]

However, many researches also reported that no relationship exists between low BMI and any semen parameters, such as studies conducted by Belloc et al,[9] Duits et al,[18] and Shayeb et al[19] with a large number of participants.

We summarized all these relevant studies and performed this meta-analysis to investigate the effect of low BMI on several semen parameters, so as to reveal the relationship between low BMI and semen quality.

2. Materials and methods

2.1. Ethics statement

This is a meta-analysis based on published studies only, ethical approval was not necessary.

Editor: Gunjan Arora.

DG and MX contributed equally to the study and they should be regarded as joint first authors.

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

The authors have no conflicts of interest to disclose.

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Medicine (2019) 98:32(e16677)

Received: 3 January 2019 / Received in final form: 3 July 2019 / Accepted: 8 July 2019

http://dx.doi.org/10.1097/MD.0000000000016677

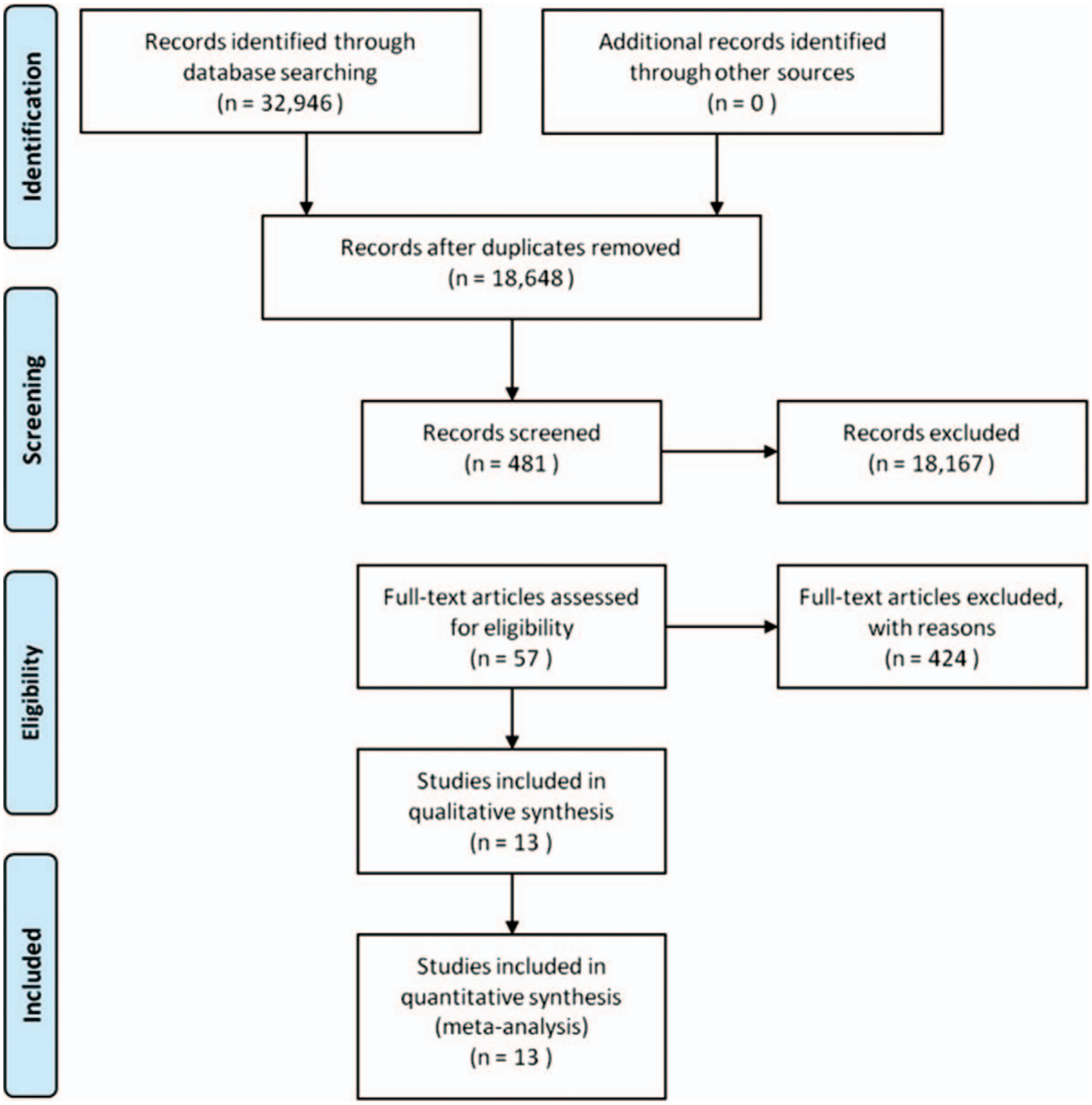

Figure 1. Flow chart of study selection.

2.2. Search strategy and selection criteria

Relevant studies about BMI and semen parameters published until September 2017 from PubMed, Web of Science, Embase, and Wanfang database were searched regardless of language used. We performed a basic screen of these studies by browsing titles from databases, and removed duplicates and irrelevances. Then, articles that are reviews, or without data about the relationship between BMI and semen parameters, or irrelevances through viewing the abstracts were also excluded. Afterwards, we also excluded articles with no available data, articles could not be included in the analysis, and articles without data about underweight group. The references of the pivotal studies screened out were also searched to find out other relevant articles. At last, regardless of the origin, age, size, or ethnicity of participants, the eligible ones were incorporated into our study. The information about study characteristics and semen parameters of underweight and normal weight of these articles were extracted. The above work was completed by 2 authors independently. After discussion, they reached agreement.

The search strategy is taken as follows: (overweight OR weight OR obesity OR BMI OR body fat OR body weight OR body mass index OR adiposity OR IBW OR ideal weight) AND (sperm OR semen OR spermatozoa OR sperm count OR sperm concentration OR semen quality OR semen parameters OR sperm quantity OR total sperm count OR oligozoospermia OR azoospermia OR semen volume OR sperm motility OR spermatids OR spermatocytes OR spermatogonia).

2.3. Data synthesis and analysis

We performed this meta-analysis using articles including data about any 1 of semen parameters (total sperm count, sperm concentration, semen volume, sperm motility, or sperm progressive motility) in underweight and normal weight. In order to facilitate the calculation, we converted all data extracted to the

Table 1

Summary of characteristics of observational studies included in this review.

Study	Location	Study group	Ascertainment of BMI	Repeated semen collection	BMI distribution	Total sperm count	Sperm concentration	Semen volume	Sperm motility	Sperm motility (progressive)
						Mean ± SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Belloc et al (2014)	France	5826 men referred in the course of a couple infertility evaluation of any origin	Self-reported	Once	<18.5 (n = 27)	133±104	49.5±49.0	3.0±1.3	38.3±13.9	35.1±13.8
					18.5–24.9 (n = 5799)	171±170	56.4±54.9	3.3±1.6	39.7±16.7	36.9±16.8
Wang et al (2017)	China	1466 male partners in subfertile couples visited a reproductive medical center	Measured on site	Once	<18 (n = 68)	126.8±33.5		3.4±1.1	50.1±13.5	39.8±11.2
					18–25 (n = 1398)	124.1±34		3.5±1.2	48.9±14.1	39.5±8.3
Luque et al (2015)	Argentina	1384 male partners of couples attending the laboratory named LAR	Measured on site	Once	<20 (n = 45)	103.3±11.4*		2.8±0.3*	41.8±2.5*	
					20–24.9 (n = 1339)	157.9±3.6*		3.3±0.1*	47.8±0.5*	
Jensen et al (2004)	Denmark	1259 men attending a compulsory physical examination for military service	Measured on site	Once	<20 (n = 217)	105 (47–240)†	40.0 (17–75)†	3.0±1.5	63.7±14.5	
					20–25 (n = 1042)	138.0 (59–259)†	46.0 (23–84)†	3.2±1.4	65.4±12.4	
Paasch et al (2010)	Germany	1102 patients attending the clinic examining the factors affecting semen quality	NA	Once	≤20 (n = 99)	154.8±16.8*			45.8±3.70*	
					20–25 (n = 1003)	159.2±5.51*			40.9±1.01*	
Aggerholm et al (2008)	Denmark	1053 general participants from 5 separate occupational or environmental semen studies	Self-reported	Once	<20.0 (n = 67)	165 (86–351)†	67 (25–102)†			39 (19–66)†
					20.0–25.0 (n = 986)	161 (77–309)†	55 (9–99)†			40 (19–66)†
Bandel et al (2015)	Sweden	932 men from a general population of 4 cohorts	Measured on site or self-report	Once or twice	<18.5 (n = 27)		76±55	2.8±1.5		52±17
					18.5–24.9 (n = 905)		72±63	3.5±1.6		53±18
Shayeb et al (2011)	United Kingdom	857 male partners of couples attending for infertility investigations at the Aberdeen Fertility Clinic	NA	Once	<18.5 (n = 18)	147.2 (70.8–266.3)‡	45.9 (31.9–98.5)‡	3.2±1.9	40.8 (26.0–51.0)‡	
					18.5–24.99 (n = 839)	144.0 (61.1–290.8)‡	47.9 (22.0–84.3)‡	3.5±1.8	45.0 (29.4–59.0)‡	
Duits et al (2010)	the Netherlands		Self-reported	At least twice	<20 (n = 35)	149.5 (50.8–88.8)†	60 (34.4–78.8)†	3.2±1.5		33.7±17.4

(*continued*)

Table 1

(continued).

Study	Location	Study group	Ascertainment of BMI	Repeated semen collection	BMI distribution	Total sperm count	Sperm concentration	Semen volume	Sperm motility	Sperm motility (progressive)
						Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
		668 men visiting the Centre for Reproductive Medicine as part of a subfertile couple								
					20.1–25 (n = 633)	174.3 (50.2–219.6)[†]	53.3 (18.0–89.0)[†]	3.7 ± 2.5		31.1 ± 15.9
Xiao et al (2013)	China	418 men attending the infertility clinic	Measured on site	Once	<18.5 (n = 17)	156 (93.3–219.6)	61 (39.5–116)[†]	2.5 (1.9–3)[†]		42 (32.5–55.0)[†]
					18.5–23.9 (n = 401)	166.5 (70.4–298)	71 (27–111)[†]	2.5 (2–3.5)[†]		48 (28.0–60.0)[†]
Qiu et al (2017)	China	52 infertile patients and 115 normal men	NA	NA	<18.5 (n = 52)		36.5 ± 6.8	3 ± 1.9	49.6 ± 7.6	
					18.5–23.9 (n = 115)		40.8 ± 8.9	3.2 ± 0.6	51.2 ± 4.3	
Koloszar et al (2005)	Hungary	125 normozoospermic male patients attending infertility clinic	Measured on site	NA	≤20 (n = 29)		38 ± 14			
					20.1–25 (n = 96)		39 ± 14			
Hajshafiha et al (2013)	Iran	74 male patients living as a partner in an infertile couple	Measured on site	Twice	≤20 (n = 8)	119.37 ± 76.8			45.25 ± 21.8	
					20.1–25.0 (n = 66)	115.84 ± 65.1			47.56 ± 18.2	

BMI = body mass index, SD = standard deviation, SE = standard Error, IQR = interquartile range.
[*] Mean ± SE.
[†] MEDIAN (IQR).
[‡] Mean (IQR).

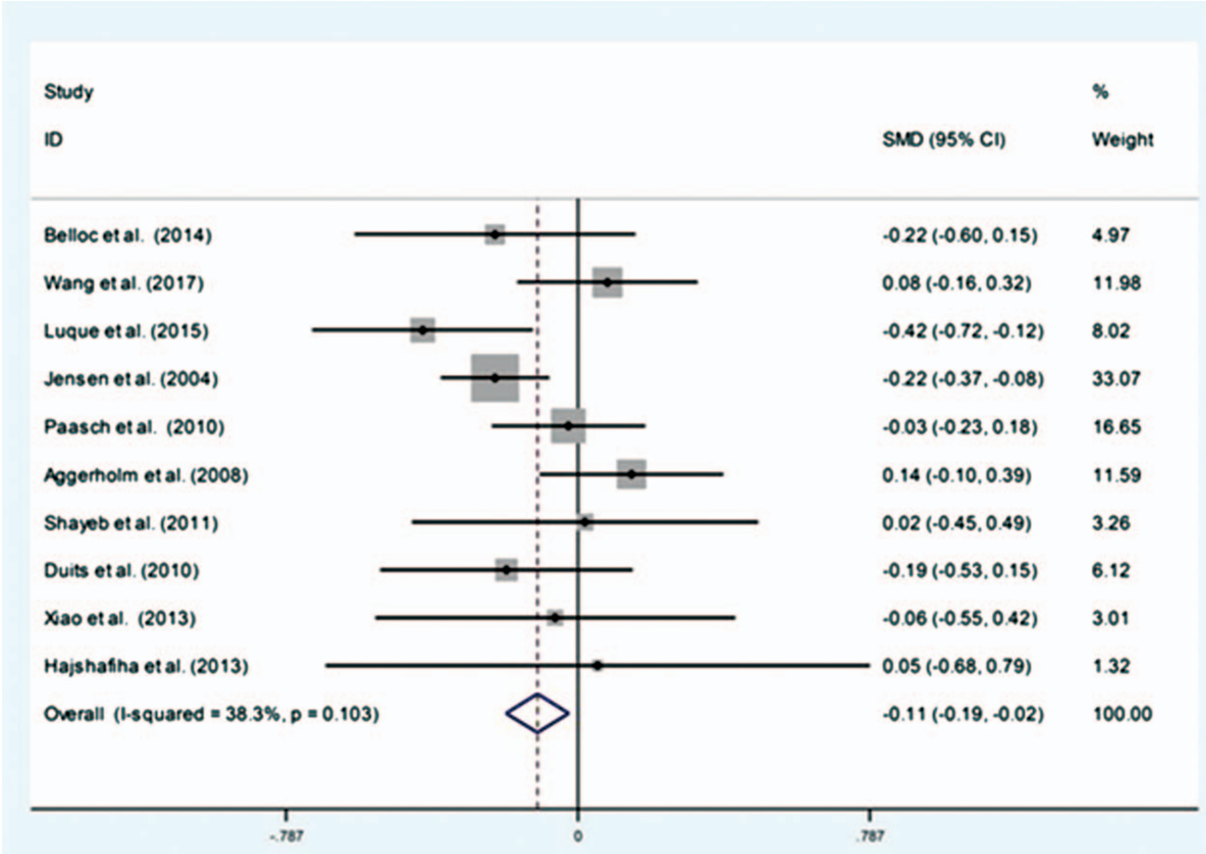

Figure 2. Forest plot of total sperm count of low body mass compared with normal body mass. Each point represents a separate study for the indicated association.

form of mean and standard deviation. BMI was divided into 2 levers by World Health Organization (WHO) criteria: under 18.5 (underweight) and 18.5 to 24.9 (normal weight) kg/m^2, except in some ones classifying according to their own standard. Group with a BMI between 18.5 and 24.9 was defined as the reference group. SMD was used as the effect scale index that calculated by mean, standard deviation and sample size using Stata version 12.0.

In order to evaluate the possible heterogeneity between articles, we accessed the I^2 statistic. The random-effect model was used to assess standardized weighted mean differences (SMD) under the condition that P value for heterogeneity was $\leq .10$ or $I^2 \geq 50\%$, which indicates a lack of high heterogeneity.[20] Additionally, we conducted sensitive analyses and subgroup to evaluate the effect of single literature and the ethnicity of study participants on the overall outcome, respectively. Egger test and Begg funnel plot were further calculated to show a diagnosis of publication bias. All statistical were performed with Stata version 12.0. $P < .05$ was defined as statistically significant.

3. Results

3.1. Result of search

We found a total of 32,946 articles, including 10,306, 11,712, 9568, and 1360 articles from PubMed, Web of Science, Embase, and Wanfang, respectively. Then, we excluded 32,465 studies including 14,298 duplicates and other irrelevances. After review of 481 abstracts, 57 studies were selected for further screening, which were potentially appropriate to be included in this meta-analysis. Finally, after excluding 7 ones without available data, 12 could not be included in the calculation, and 25 without data about underweight group, 13 articles studying the effect of low BMI on semen parameters were incorporated into our meta-analysis (Fig. 1).

3.2. Description of studies and participants

After a layer of screening, 13 articles (Table 1) with a total of 15,331 participants (709 belonging to underweight group, and 14,622 belonging to the reference group) were included in our meta-analysis. Six of these studies included more than 1000 participants, which constituted the main component of this meta-analysis. There are 3 articles that used 18.5 and 25.0 as the boundaries of BMI as prescribed by WHO, while 7 used 20.0 and 25.0, 1 used 18.5 and 24.0, and 1 used 18.0 and 25.0, respectively. All participants collected at least 1 semen sample for testing, who recruited from either a general population or subfertile couples, with 1 exception that from physical examination of conscription. Among these articles, researched outcomes including each semen parameters were as follows: total sperm count (10/13), concentration (10/13), volume (9/13), motility (8/13), and progressive motility (6/13). Data of height and weight used in these studies were all measured by professional researches except 4 self-reported and 3 without mention. Except for 2 case–control articles, a prospective cohort,

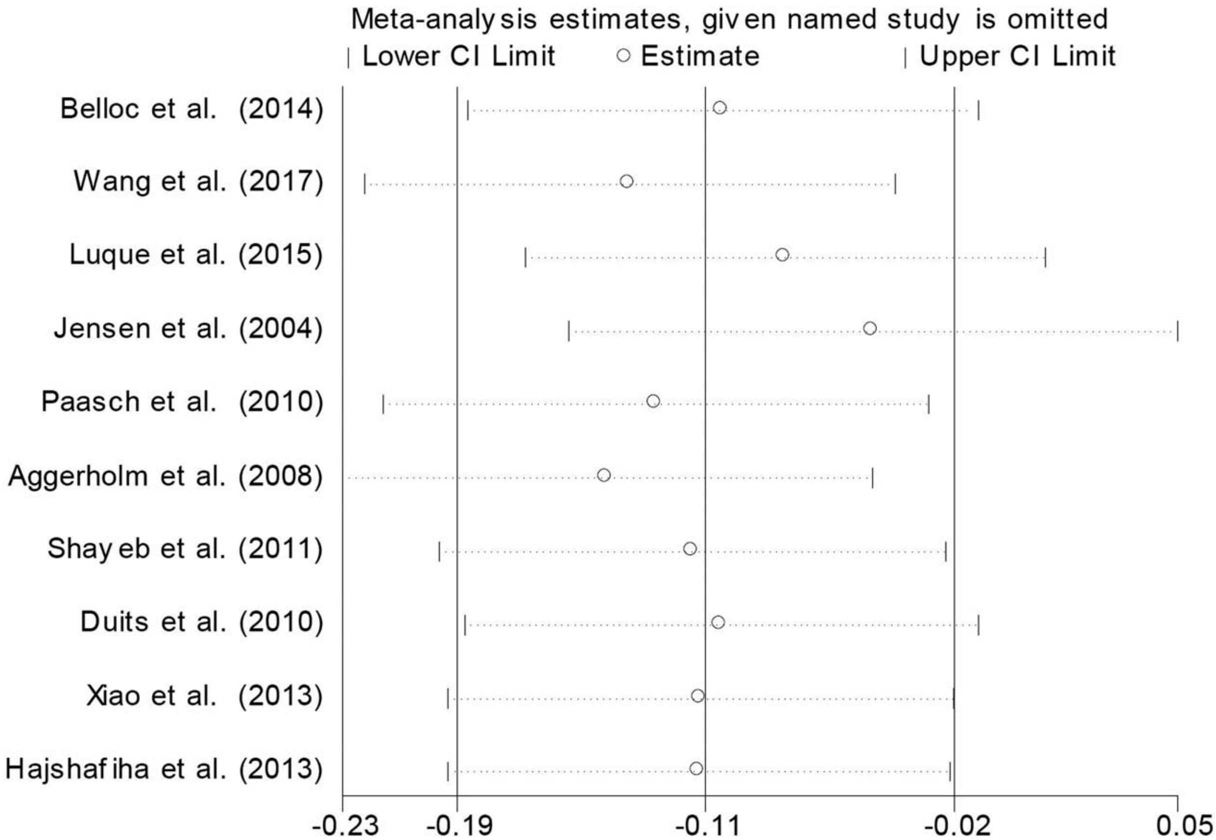

Figure 3. Sensitivity analysis about total sperm count.

and a retrospective study that reported cross-sectional data, all others were cross-sectional studies.

3.3. Impact of BMI on semen parameters

Data from 13 articles were used to perform the meta-analysis in this review. After calculated the SMD of semen parameters in low BMI group compared with normal BMI group, the results showed that underweight decreased the level of total sperm count (P = .001) (Fig. 2) and semen volume (P = .001). At the same time, no significant statistical difference about changes of sperm concentration and sperm motility was observed. We only showed the result of total sperm count in this meta-analysis, while the results of other semen parameters did not show in any special figure.

3.4. Sensitivity analyses

The sensitivity analyses were conducted to evaluate the effect of a special study on the whole outcome. The results showed that the SMD of total sperm count changed after removing data from Luque et al[16] or Jensen et al,[14] and the SMD of motility changed when excluding data from Wang et al[21] or Paasch et al,[15] while the results of others were not qualitatively altered with or without any article (Fig. 3).

3.5. Subgroup analyses

Given the effect of the ethnicity of population on the outcome, we conducted subgroup analyses. The results provided evidence that the total sperm count and semen volume were different in the Caucasian and Colored populations (Fig. 4).

3.6. Assessment of publication bias

We performed the Egger test and Begg funnel plot to assess the publication bias, and the results showed no evidence in each semen parameter (Fig. 5).

4. Discussion

As a worldwide health problem, infertility has drawn widespread attention in recent decades. Many studies have investigated the effect of low BMI on female reproductive capacity. Veleva et al[22] established a positive relationship between low BMI and miscarriage. Cai et al[12] found low BMI compromised live birth rate in fresh transfer in vitro fertilization cycles. These results indicate that low BMI is a risk factor for female fertility. However, there is no relevant report about the effect of low BMI on male reproductive capacity. This meta-analysis showed that low BMI decreased semen parameters such as total sperm count, semen volume rather than sperm concentration and motility (overall or progressive motility), suggesting that low BMI is a risk for semen quality.

The result of this meta-analysis is consistent with several studies that recruited more than 1000 participants,[14,15] although they showed impact of low BMI on different semen parameter. While 2 meta-analysis[13,23] about the influence of BMI on total sperm count or sperm concentration showed no

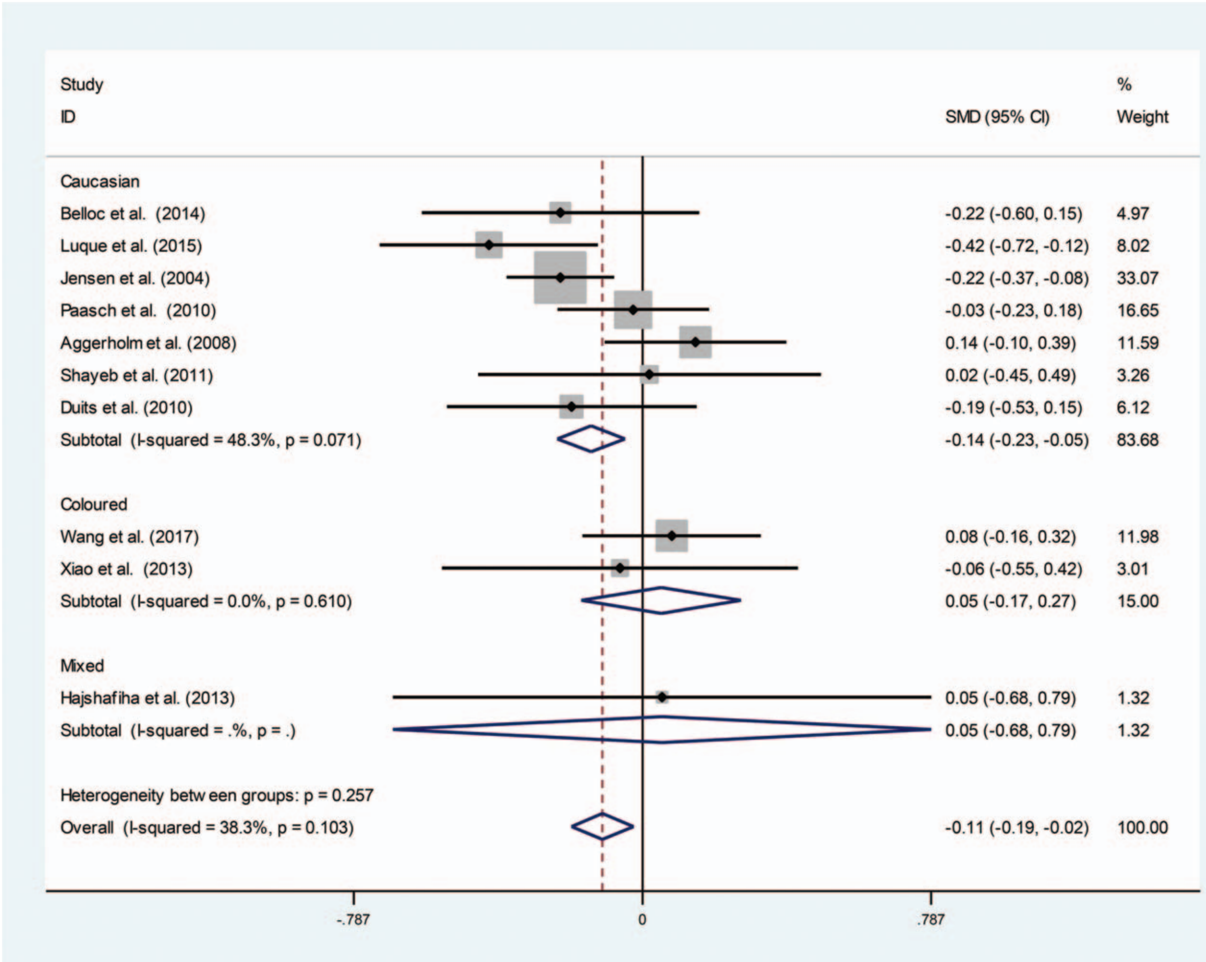

Figure 4. Subgroup analysis based on ethnicity about total sperm count.

relationship between them published in 2010 and 2013, respectively. MacDonald et al[23] found no relationship between BMI and total sperm count or sperm concentration, and Sermondade et al[13] found that sperm concentration showed no difference across different BMI categories. But researchers of the latter[13] found a J-shaped association between BMI categories and risk of abnormal sperm count, which suggests that low BMI may be a risk factor for semen quality. Differences in literatures included, sample size, method of statistical analysis may lead to the different result of our study and meta-analysis published before. And we guess sample size is the dominant one, since we updated new studies published in recent years. However, as the number of participant in low BMI group in included studies are relatively small, more relevant researches with a large sample size are needed to reveal the correlation between low BMI and semen parameters.

There are several mechanistic studies on the effects of obesity on semen quality yet. In general, it can be summarized as the following points:

(1) Hypothalamic-pituitary-gonadal axis disruption[24–26];
(2) Destruction of Sertoli and Leydig cells[27];
(3) Insulin resistance and hyperinsu linemia[28];
(4) Impairment of DNA integrity with increased level of oxidative stress[29];
(5) Erectile dysfunction and sexuality in a reverse fashion in obese men.[30]

However, few studies evaluated the mechanism low body weight on male reproductive capacity Limited by the number of related studies, the corresponding mechanism remains unclear. Analogous to obese men, some researchers[14] speculated that hormonal imbalance may be involved in reduced semen quality in men with low BMI. Additionally, men with low BMI may have unhealthy lifestyles, as well as slight malnutrition or subclinical adverse conditions, which could affect their reproductive health.[6] However, there is still lack of sufficient evidence, and more deeper studies are needed to show the precise mechanism.

Given that obesity is a potentially harmful factor in male infertility, many researchers have begun to study the effect of weight loss on semen quality through exercise interventions, dietary, or bariatric surgery.[31–33] Some researchers suggest that weight loss should be implemented in obese men for seeking fertility treatment,[34,35] In particular, bariatric surgery may gradually become a way for infertile men induced by obesity to improve their fertility in the circumstance that relevant studies have been springing out recent decades.[36,37] Our results have confirmed that low BMI is a pernicious factor for male fertility, which forced us to ponder the question that whether excessive weight loss affects semen quality in the opposite direction, and

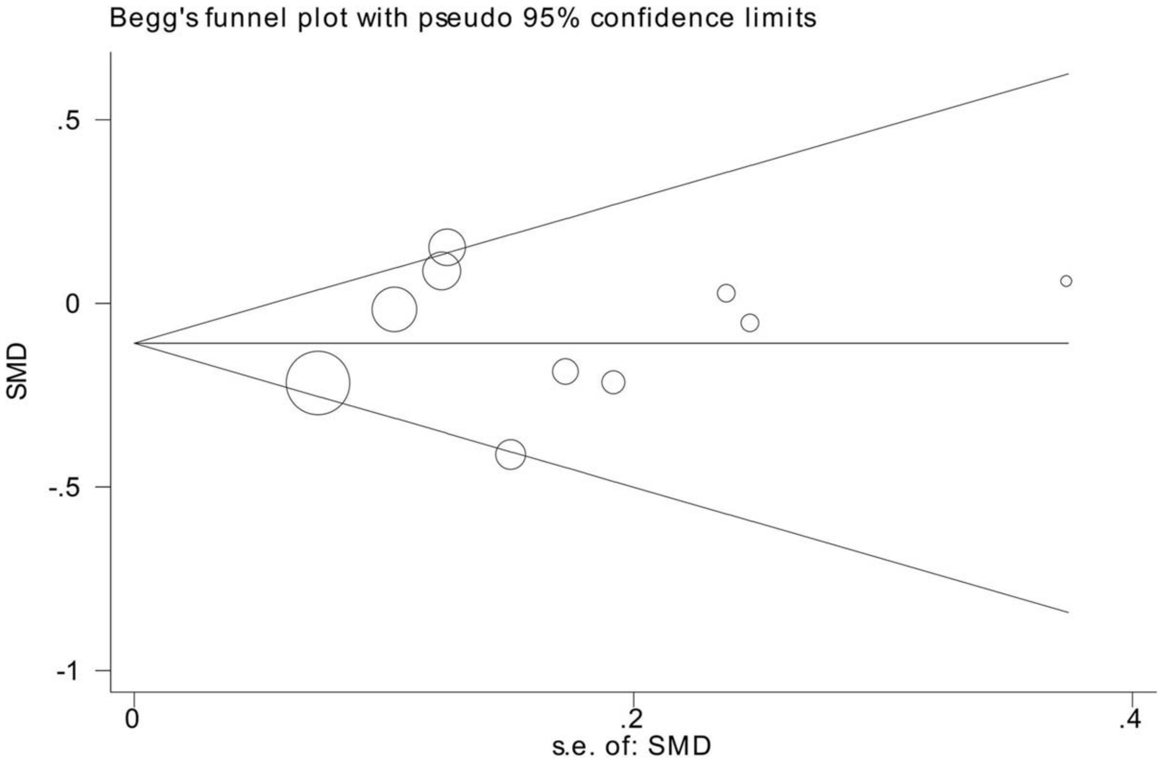

Figure 5. Funnel plot of observational studies about total sperm count.

whether weight loss treatment should be formulated a degree of restriction, especially about bariatric surgery. We expect more in-depth researches to answer these questions.

Because the original data could not be obtained from the corresponding authors, all information used in this meta-analysis was depended on published literatures only, which inescapably affected the authenticity and reliability of our results. We used SMD as the effect parameter, and converted data format through the acceptable formula to minimize effect as far as possible. Another problem is the inconsistent boundaries used to classify BMI in the included studies which could also influence the result, and we could not converted them into the standard criteria defined by WHO. Fortunately, the boundaries were only 4 types and were generally same that also explained the problem to a certain extent. Besides, taking the data processing into account, we kicked out some relevant articles that might provide useful information. And, the trial sequence analysis suggested that the number of participants included in our meta-analysis was small. Our study could serve as a reminder that calls for more attention to the content of this area.

According to this meta-analysis, men with low BMI have decreased parameters of semen, suggesting that underweight might be a risk factor of male infertility. We look forward to springing out large sample researches to identify the role of low BMI in male sterility.

Acknowledgment

The authors thank Na Qin for her support and guidance throughout the study.

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Writing – review and editing: Dan Guo, Jiazhen Dai.

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