

Association between lifestyle factors and semen parameters: An overview of systematic reviews

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Abstract

Infertility, defined as inability of a couple to conceive after a year of unprotected regular intercourse, with third of cases due to suboptimal sperm quality. There are modifiable and nonmodifiable risk factors that can affect the quality and quantity of sperm and hence fertility. Several separate systematic reviews exist on this topic and clinicians are often faced with a plethora of reviews with variable quality giving conflicting advice. Therefore, we summarized the current available data by conducting a systematic review of systematic reviews on risk factors such as coffee/caffeine, body mass index (BMI)/obesity, cigarette smoking, and paternal age, on sperm parameters of count, motility, and morphology so that all evidences are present together, at one place. Embase, OVID MEDLINE(R), and Cochrane central database of systematic review were searched for relevant publications between 2010 and present. Search terms were: smoking, obesity, obese, BMI, caffeine, paternal age, advanced paternal age, male infertility, male fertility, sperm motility, sperm quality, and sperm analysis. Systematic reviews that met the criteria were retrieved and the relative reference lists were searched. All included studies were quality assessed using the AMSTAR checklist tool. Electronic and manual hand search yielded a total of 318 studies, of which 11 were excluded after removing duplicates and a further 286 excluded based on titles and abstract. Full-text screening of 21 articles, excluded 10 further studies. Eleven publications were finally included. Obesity and smoking were associated with decline in sperm count and morphology, age with decline in motility and morphology. Caffeine consumption was not associated with changes in any of the three parameters. Obesity and smoking are modifiable risk factors impacting on the semen parameters; caffeine consumption may not have any adverse effects on sperm parameters. This overview was limited by the quality of included reviews which in turn were limited by observational nature of the included studies, small numbers, and heterogeneity of the population. Further prospective data collection is needed to have good quality evidence. In conclusion, high BMI, smoking, and advanced paternal age were found to be associated with decline in one or more parameters of semen quality in males, albeit the evidence is of varying strength. Caffeine was not associated with any deterioration.

Keywords: BMI, caffeine, male fertility, paternal age, semen parameters, smoking

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INTRODUCTION

Infertility is defined as inability of a couple to conceive after 12 months of regular unprotected intercourse. One in seven couples is affected across the world. Contributing factors to infertility could be male, female, or combined factors. Approximately 30% of the causes are attributed to the male partner.^[1] Semen analysis is a basic and first investigation used to evaluate male fertility. Parameters of semen analysis used to assess sperm are count, motility, and morphology,^[2-4] as per strict World Health Organization (WHO) criteria.^[5,6]

There are various lifestyle factors that can affect the quality and quantity of sperm.^[7,8] The modifiable risk factors include obesity/body mass index (BMI), smoking, and caffeine intake, whereas nonmodifiable includes paternal age. Several studies have studied the impact of these modifiable risk factors on sperm count, motility, and morphology.^[9]

Overweight and obesity are associated with excess fat accumulation, which can be measured using the BMI, where 25 to 29.9 is overweight and >30 is obese. There are several risks and complications to obesity and reduced fertility is now recognized as one of them.^[10] Some studies have found an association between high BMI and low semen volume with no other semen parameters affected.^[10-13]

Smoking cigarettes has been associated with a deterioration of sperm quality. Although the etiology is not fully understood, it is suggested that toxins from cigarette smoke can decrease sperm mitochondrial activity and damage the chromatin structure in human sperm.^[9] However, the evidence is controversial, and some studies have found no effect on semen quality.^[14-16]

Coffee consumption, on the other hand, has been hypothesized to influence not only semen parameters, but also sperm DNA integrity. However, most studies have failed to find an association between amount of caffeine consumption and male fertility.^[9]

Finally, as more couples are choosing to delay pregnancy to later stages of life,^[17] it is important to understand the impact of advanced paternal age on fertility outcomes. Although increasing maternal age has been established as a factor for fertility,^[18] the influence of paternal age is poorly understood. Nevertheless, Johnson *et al.* report that several studies suggest advanced paternal age is associated with declines in fertility.^[19]

Various systematic reviews exist on these topics, some with conflicting conclusions. Hence, clinicians are increasingly faced with difficulties in decision making. Systematic reviews (or overviews) of reviews are a logical and appropriate next step, allowing the findings of separate reviews to be compared, providing clinical decision makers with the evidence they need. Therefore, we summarized the current available data and conducted an overview of systematic reviews on the association between risk factors such as coffee/caffeine, BMI/obesity, cigarette smoking, and advanced paternal age, on semen count, motility, and morphology so that all evidences are present together at one place.

METHODS

The electronic databases Embase, OVID MEDLINE(R), and Cochrane central database of systematic review were searched to identify relevant systematic reviews published from 2010 to October 2020, so only articles post-WHO criteria update were included. Studies prior to this update would have reported semen characteristics of patients as abnormal, whom will now be reclassified as normal based on the new reference values.^[6] Search terms used were caffeine OR smoking OR obesity OR BMI OR paternal age AND male (in)fertility OR sperm OR sperm/seminal motility OR sperm/seminal count/sperm concentration OR sperm/seminal morphology. Search was limited to only studies in humans, males, and systematic reviews but no language restriction applied.

Titles and abstracts of all articles retrieved using above-mentioned search terms from the database search were screened. The inclusion criterion was systematic reviews assessing the impact of lifestyle factors such as “smoking,” “obesity,” “BMI,” “advanced paternal age,” “caffeine”/“coffee” on semen parameters of “sperm count,” “sperm motility,” and “sperm morphology.” The studies were excluded if they were not performed on humans and if they mentioned about interventions/treatments/*in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI)/supplements.

Full texts of selected abstracts matching inclusion criteria were obtained. In addition, reference lists of included articles were hand searched. Studies were analyzed for inclusion independently by two of the authors (BA and SF). Any discrepancies were resolved by discussion with AM or SV. Articles were included only if full texts were available. The author(s), publication year, aim of study, search strategy, number of studies included, study

characteristics, and result outcomes were carefully extracted. The quality of each of the included studies was assessed according to the criteria set by A MeaSurement Tool to Assess Systematic Review (AMSTAR).

RESULTS

The search strategy identified a total of 318 articles, including 121 from Cochrane database of systematic reviews, 113 from Embase, 83 from OVID MEDLINE(R), and 1 article from manual searches of references. However, 11 of these studies were duplicates. After reviewing studies based on titles and abstracts, as they had no relevance to the primary research question, 286 studies were excluded. Twenty-one full text articles were assessed for eligibility. Among the full text articles,

further studies were eliminated because of no access to full text ($n=1$); only conference abstract ($n=8$); outcomes on DNA fragmentation ($n=1$) only.

Finally, 11 studies which met all the inclusion and exclusion criteria were included in this present study [Figure 1]. Five were on of BMI, two for smoking, one for advanced paternal age, another one for coffee/caffeine intake, and two with multiple exposure/risk factor groups.

A total number of 438 likely overlapping observational studies were included in this analysis. The scope of the original reviews is summarized in Table 1. The study aims, search strategy, characteristics, quality assessment, and study outcomes are listed in Table 1.

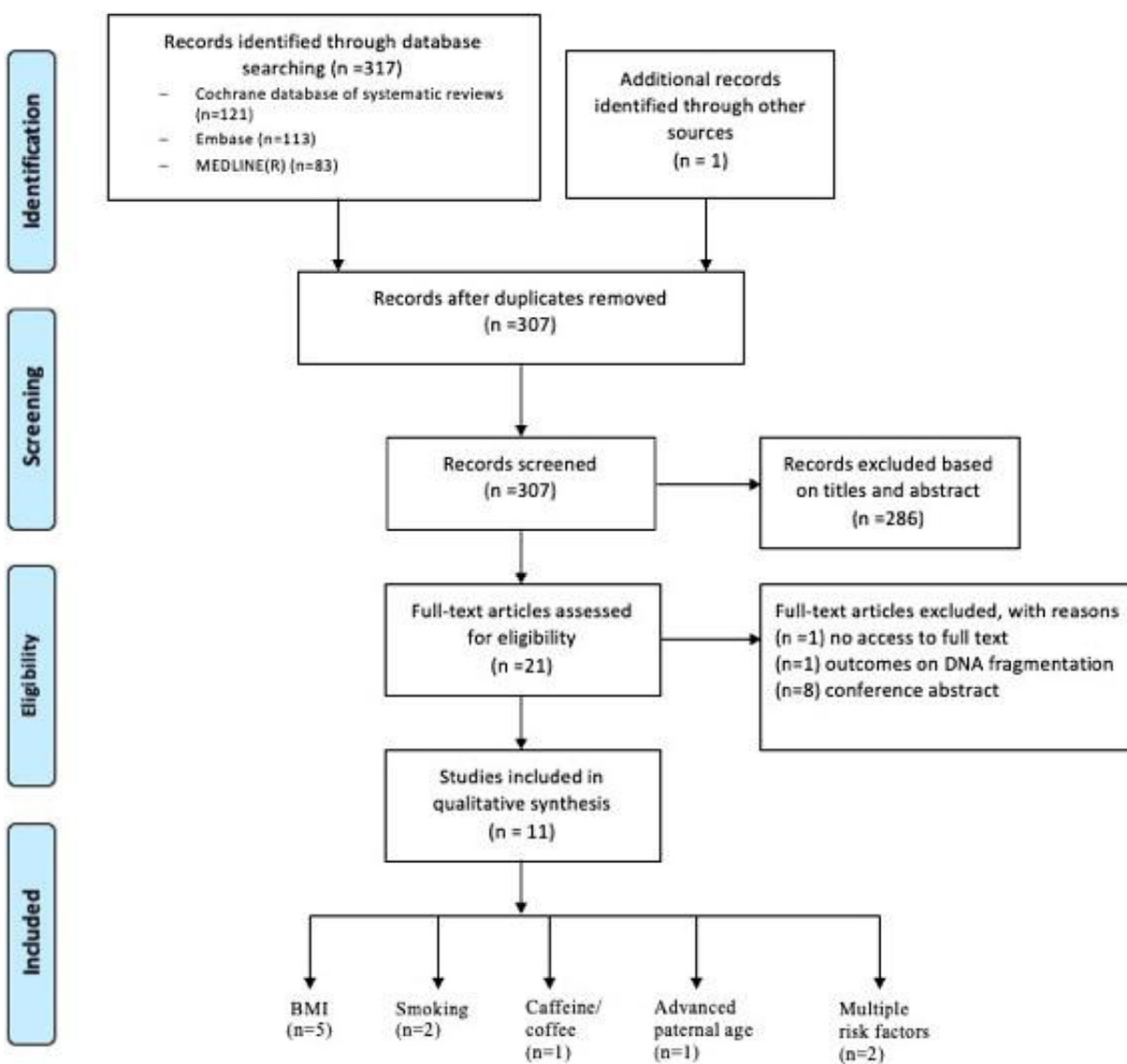


Figure 1: The flow diagram depicts the flow of information through the different phases of PRISMA literature search. It maps out the number of records identified, included, and excluded and the reasons for exclusion.

Table 1: Scope of included studies, main outcomes, and quality assessment

Study	Aim/objective	Search strategy and methodology	No. of studies included	Study characteristics	Main outcomes	Quality assessment
Bundhun <i>et al.</i> (2019)	Systematically investigate the impact of tobacco smoking on semen quality in infertile male participants	Cochrane central database of RCT, MEDLINE, Embase between 1985 and 2015 English language restriction. Participants with varicocele, cryptorchidism, aspermia, chronic diseases, genital infections, genital trauma, and chromosomal abnormalities were excluded. Meta-analysis of retrospective, prospective, cross-sectional study	16	10,823 infertile participants (5257 smokers and 5566 nonsmokers) the age range (26.5–40.5 years old)	<ul style="list-style-type: none"> Tobacco smoking was associated with a lower sperm count and an increase in the number of morphologic defects of spermatozoa The motility of sperms was not impaired between the smokers and nonsmokers (MD: 1.26, 95% CI: [-0.64–3.17]; $P=0.19$). 	Critically low quality
Campbell <i>et al.</i> (2015)	Critically evaluate and synthesize the current evidence on the effects of paternal obesity on male reproductive potential	PubMed, OVID, Web of Science, Scopus, Cinahl, and Embase English language restrictions. Studies were retrieved up to March 2013, with an updated search performed in April 2015. Meta-analysis of cross-sectional and longitudinal studies	30	Total of 115,158 males aged >18 years without history of reproductive disorders. Participants from clinical ART & general population	<ul style="list-style-type: none"> No significant differences were found for sperm concentration overall (clinical ART & general population) or in either of the subgroups on the effect of male obesity A nonsignificant decrease in the percentage of sperm with normal morphology was found for obese men compared with normal weight men, but a statically significant decrease was found when analysis was restricted to the clinical ART population A small but significant decrease in motility for obese men overall (WMD = -3.72%, 95% CI -7.11 to -0.33) No significant differences in ejaculate volume for obese men overall or in the subgroup analyses 	Critically low quality
Durai Rajanayagam (2018)	To examine the effect of key lifestyle factors that are associated with male infertility such as smoking cigarettes, alcohol intake, use of illicit drugs, obesity, psychologic stress, advanced paternal age, dietary practices, and coffee consumption	PubMed database and manual additional searches within 10 years. Beyond 10 years at authors discretion English language	74	N/A	<ul style="list-style-type: none"> Smoking: no concrete potential relationship between smoking and male infertility as of yet. Obesity is linked to low ejaculate volume, low sperm concentration, and low total-sperm count. The severity obesity consequences on semen parameters may be varied due to comorbidities Caffeine: no firm potential relationship between caffeine intake and male infertility *No clear conclusion on advanced paternal age effect on fertility 	Critically low quality
Guo <i>et al.</i> (2017)	Investigate the effect of overweight and obesity on several sperm parameters	PubMed, Web of Science, Embase, and Wanfang databases. Published until June 2015 without language restriction. Meta-	24 and "personal data" from fertility clinic - 2106 patients from own	26,814 participants from general and infertile population. Participants	<ul style="list-style-type: none"> Overweight decreased the quality of total sperm count and semen volume ($P = 0.000$ and 0.002) 	Moderate quality

(Continued)

Table 1: (Continued)

Study	Aim/objective	Search strategy and methodology	No. of studies included	Study characteristics	Main outcomes	Quality assessment
Johnson et al. (2015)	Quantitatively synthesize the current state of knowledge on the effect of male age on seven ejaculate traits (semen volume, sperm concentration, total sperm count, morphology, total motility, progressive motility, and DNA fragmentation)	analysis of prospective, retrospective, case-controls and cross-sectional studies PubMed, Web of Science, Scopus, and Embase English language restriction. Excluded studies which did not provide statistical variables which would lead to calculating standardized effect sizes Meta-analysis	study Sperm analysis with 1999 and 2010 WHO criteria	from Europe, North and South America, and Asia	<ul style="list-style-type: none"> Obesity decreased the quality of total sperm count, sperm concentration, and semen volume ($P = 0.001$, 0.006, and 0.000, respectively) Changes of sperm motility (total or progressive) did not show significant statistical difference Every 5-unit increase in BMI, the SMD fell 2.4%, 1.3%, and 2.0% compared with normal weight Increase in male age negatively and significantly affected semen properties Male age is associated with a decrease in semen volume, a decrease in total sperm count, a decrease in percent motility, a decrease in percent progressive motility, a decrease in percent normal sperm Sperm concentration was unaffected 	Critically low quality
Li et al. (2011)	Review published data to identify and completely understand the effects of socio-psycho-behavioral risk factors on semen quality	Medline/PubMed, Embase, and China National Knowledge Infrastructure databases English language restriction Meta-analysis of cross-sectional, case-control, and cohort studies	57: systematic review 4: meta-analysis	29,914 male participants aged 13 years and older from fertile, infertile, and general population 26 countries/regions Males were without diseases influencing semen quality abstinence period of 2-7 days	<ul style="list-style-type: none"> Smoking was identified as a risk factor for all of the classic sperm parameters (pooled MDs are 0.25, 0.07, 0.20, 1.85, and 0.492 for semen volume, sperm density, total sperm count, the percentage of sperm progressive motility and normal sperm, respectively; the pooled MD is 0.72 for the percentage for abnormal sperm, $P < 0.05$) Higher age influences male semen volume significantly (pooled MDs, 0.57; $P = 0.01$) The effect of BMI and coffee consumption on the five sperm parameters were uncertain ($P > 0.05$) There was no evidence from this meta-analysis that there is a relationship between BMI category and mean sperm concentration, median sperm concentration, mean total sperm count, median total sperm count, mean semen volume, or average sperm motility 	Critically low quality
MacDonald et al. (2009)	Investigate the impact of BMI on semen parameters and reproductive hormones in men of reproductive age	MEDLINE, Embase, biologic abstract, PyscINFO, CINAHL No language limits Excluded - animal studies, experimental studies, studies < 100 participants Meta-analysis of cross-sectional, case-control, longitudinal, and interventional studies	31 in review 5 for semen parameters, 18 for hormone profile 5 in meta-analysis	Males from general and subfertile population Mean age between 12 and 60 Excludes men with disorders or the reproductive organs or had previous surgery in genital/pelvic area	<ul style="list-style-type: none"> There was no evidence from this meta-analysis that there is a relationship between BMI category and mean sperm concentration, median sperm concentration, mean total sperm count, median total sperm count, mean semen volume, or average sperm motility 	Critically low quality

(Continued)

Table 1: (Continued)

Study	Aim/objective	Search strategy and methodology	No. of studies included	Study characteristics	Main outcomes	Quality assessment
Ricci et al. (2017)	A systematic review of observational studies to summarize the relation between coffee/caffeine intake and parameters of male fertility including semen quality, sperm ploidy, sperm DNA integrity, and time to pregnancy	MEDLINE and Embase databases and human limitation 1966-2016 included abstracts. Retrospective, prospective, and cross-sectional studies	28	19,967, healthy and subfertile men. Across all continent except Antarctica	<ul style="list-style-type: none"> No relation was observed between coffee/caffeine consumption and total sperm count and morphology No study found a significant relation between coffee/caffeine intake and semen volume, except in cola consumers, as the higher the weekly cola intake, the lower sperm volume No significant difference was found in relation to coffee intake and sperm concentration No significant difference throughout the categories of coffee/caffeine consumption and sperm motility – two studies observed an increase in sperm motility No clear relationship between time to pregnancy and caffeine Compared to individual with normal weight Class I obesity and class II obesity had a lower semen volume Sperm count was lower in the cases of class II obesity and class III obesity categories Class III obesity had decreased sperm concentrations Overweight, class I obesity, and class III obesity categories had a decrease in sperm vitality percentages A decrease in total sperm motility in individuals with class III obesity In the case of progressive motility, no significant associations were found for any adiposity categories analyzed Individuals with underweight, class II obesity, and class III obesity were associated with a decrease in spermatozoa with normal morphology A J-shaped association was found between BMI and abnormal sperm count (<40 M/ ejaculate). 	Critically low quality
Salas-Huetos et al. (2021)	Summarized the evidence from published studies investigating the potential associations between WHO obesity categories and sperm quality/parameters and reproductive hormones	MEDLINE-PubMed, EmbaseManual searchEnglish languageHigh quality, human case-control, cross-sectional, and observational prospective and retrospective studiesQuality assessment performedMeta-analysis	60: systematic review28: meta-analysis	Fertile or infertile males with sperm disorders, sperm DNA damage or idiopathic infertilityAged 16-66Across all continents	<ul style="list-style-type: none"> Class III obesity had decreased sperm concentrations Overweight, class I obesity, and class III obesity categories had a decrease in sperm vitality percentages A decrease in total sperm motility in individuals with class III obesity In the case of progressive motility, no significant associations were found for any adiposity categories analyzed Individuals with underweight, class II obesity, and class III obesity were associated with a decrease in spermatozoa with normal morphology A J-shaped association was found between BMI and abnormal sperm count (<40 M/ ejaculate). 	Moderate quality
Sermondade et al. (2013)	Update the evidence on the association between BMI and sperm count	PubMed, Embase databasesNo language restrictions applied. Included unpublished	64: systematic review21: meta-analysis	13,077 participants from infertile and general population	<ul style="list-style-type: none"> Class III obesity had decreased sperm concentrations Overweight, class I obesity, and class III obesity categories had a decrease in sperm vitality percentages A decrease in total sperm motility in individuals with class III obesity In the case of progressive motility, no significant associations were found for any adiposity categories analyzed Individuals with underweight, class II obesity, and class III obesity were associated with a decrease in spermatozoa with normal morphology A J-shaped association was found between BMI and abnormal sperm count (<40 M/ ejaculate). 	Low quality

(Continued)

Table 1: (Continued)

Study	Aim/objective	Search strategy and methodology	No. of studies included	Study characteristics	Main outcomes	Quality assessment
Sharma <i>et al.</i> (2016)	Summarize the evidence of the effect of cigarette smoking on human semen characteristics in view of the new WHO criteria for the laboratory examination of human semen	through a systematic review with meta-analysis data from Meta-analysis of cross-sectional, prospective studies PubMed, Scopus, Saint Joseph's University Discover (SJUD), and Google Scholar. 2010-2015 Human studies only, no language restriction Meta-analysis of prospective, retrospective, case study, and cross-sectional studies	20	5865 males aged > 13 from infertile and general populations Moderate and heavy smokers had significantly lower counts. Sperm motility was decreased by moderate smoking and heavy smoking, albeit not significantly different in the latter. Sperm motility was higher in mild smokers than in moderate and heavy smokers. Sperm morphology was decreased by mild smoking, moderate smoking, and heavy smoking. The higher the cigarette consumption, the higher the magnitude of the effect size ($P < 0.0001$) Negative effect of smoking was more pronounced in infertile smokers than their counterparts from the general population	<ul style="list-style-type: none"> Compared with normal weight men, the ORs (95% CI) for oligospermia or azoospermia were 1.15 (0.93-1.43) for overweight men, 1.11 (1.01-1.21) for obese men, 1.28 (1.06-1.55) for morbidly obese men Underweight was associated with an increased but nonsignificant risk of abnormal sperm count, whereas overweight and obese men had a significantly elevated risk of abnormal sperm count compared with normal weight men Semen volume was not significantly affected by smoking Sperm counts were lower in smokers than in nonsmokers. Moderate and heavy smokers had significantly lower counts. Sperm motility was decreased by moderate smoking and heavy smoking, albeit not significantly different in the latter. Sperm motility was higher in mild smokers than in moderate and heavy smokers. Sperm morphology was decreased by mild smoking, moderate smoking, and heavy smoking. The higher the cigarette consumption, the higher the magnitude of the effect size ($P < 0.0001$) Negative effect of smoking was more pronounced in infertile smokers than their counterparts from the general population 	Moderate quality

BMI, body mass index; CI, confidence interval; MD, mean difference; SDM, standardized mean difference; OR, odds ratio; WMD, weighted mean difference.

Table 2: Summary outcomes of each review. Decrease-; Increase-; No change-

Study	Lifestyle	Count	Motility (progressive/total)	Normal morphology
Salas-Huetos <i>et al.</i> (2021)	Obesity			
Guo <i>et al.</i> (2017)	Obesity			N/A
Campbell <i>et al.</i> (2015)	Obesity	N/A		
Sermondade <i>et al.</i> (2013)	Obesity		N/A	N/A
MacDonald <i>et al.</i> (2009)	Obesity			N/A
Durairajanayagam (2018)	Obesity		N/A	N/A
Li <i>et al.</i> (2011)	Obesity			
Sharma <i>et al.</i> (2016)	Smoking			
Bundhun <i>et al.</i> (2019)	Smoking			
Durairajanayagam (2018)	Smoking			
Li <i>et al.</i> (2011)	Smoking			
Ricci <i>et al.</i> , 2017	Caffeine			
Li <i>et al.</i> (2011)	Caffeine			
Durairajanayagam (2018)	Caffeine			
Johnson <i>et al.</i> (2015)	Advanced male age			

The outcomes of the included studies are presented in Table 2.

Smoking

Four^[9,20-22] of the included 11 studies investigate smoking as a risk for infertility. The studies ranged in quality, one at moderate quality,^[20] whereas others^[9,21,22] had critically low quality.

The largest study^[21] had 29,914 participants from fertile, infertile, and general population. Participants were aged 13 or above without diseases. Bundhun *et al.*^[22] included 16 individual studies with a total number of 10,823 infertile male participants (5257 smokers and 5566 nonsmokers) and age between 26 and 40 years. Sharma *et al.*^[20] had 20 individual studies (*n* = 5865). Durairajanayagam^[9] had no information on study characteristics but reports the inclusion of 74 studies.

Three studies^[20-22] out of four reported that smoking was associated with decline in semen parameters. The fourth one^[9] concluded that tobacco smoking was associated with a lower sperm count and an increase in the number of morphologic defects of spermatozoa. However, motility of sperms was not impaired between the smoker and nonsmoker groups. Sharma *et al.*^[20] established exposure to cigarette smoking was associated with lower sperm counts and motility in moderate and heavy smokers compared to nonsmokers.

Proportion of normal morphology was decreased even in those who were classified as mild (1–10 cigarettes), moderate (10–20 cigarettes), or heavy (>20 cigarettes) smoking. The higher the cigarette consumption, the higher the magnitude of the effect size (*P* < 0.0001). Overall negative effect of smoking was more pronounced in infertile smokers than their counterparts from the

general population. Smoking was associated with reduced total sperm count, progressive motility, and normal morphology in study by Li *et al.*^[21] as well.

Furthermore, Sharma *et al.*^[20] found the overall effect on sperm count and motility remained similar when the 2010 and earlier WHO manuals were used, but it differed with regard to sperm morphology. Although the review set out to investigate the effect of the new criteria, some of the studies included were published prior to 2010 and the discrepancy was correlated to the length of time and compliance it takes to adopt guidelines into routine practice.

Conversely, Durairajanayagam^[9] reported the lack of concrete significant evidence to support the potential relationship between smoking and male infertility. However, available evidence from previous studies support the recommendation of smoking cessation and minimizing exposure to tobacco smoke among couples who are trying to conceive.

Overall, a majority of these studies suggest a smoking history has a significant negative impact on semen parameters. Reduction in sperm count, motility, and normal morphology are associated with smoking, where the degree of abnormality is based on the smoking pack years.

Almost all individual studies included in these reviews were small; they were based on retrospective data collection of routinely collected data, hence limited by design.

Neither of them looked at newer methods of smoking such as vaping or e-cigarettes or use of nicotine patches.

Body mass index

Seven of the included 11 studies investigate BMI as a risk factor for infertility of which 2 were moderate quality, 1 was low, and 4 were critically low quality. Dates of publication ranged from 2011 to 2020.

Participants included general population and those attending infertility clinics^[21,23-26]; from only infertility clinic^[27] or were not clear.^[9] Number of included studies varied from 24 to 74 and population size varied from <100 to 115,158 but size was not reported in three studies.^[9,26,27] Campbell *et al.*^[24] had the largest population size ($n = 115,158$) where participants were aged 18 or above without history of reproductive disorders. In addition, a tenth of the data reported in Guo *et al.*^[25] and 5% in Sermondade *et al.*^[23] were data from unpublished studies.

Three studies^[23,25,26] used WHO criteria for obesity and further divided into three subgroups of 30.0 to 34.9 kg/m² (class I obesity), 35 to 39.9 kg/m² (class II obesity), and ≥ 40.0 kg/m² (morbid obesity, or class III obesity).

Campbell *et al.*^[24] divided participants into two groups: normal BMI and obese, but missed the overweight group. Macdonald *et al.*^[27] had three WHO categories of normal, overweight, and obese. BMI categories were uncertain in others.^[9,21] In addition, Durairajanayagam^[9] was a descriptive review with limited information about BMI categories.

Association of sperm count with high BMI was reported by all studies except one^[24]; with four^[9,23,25,26] suggesting reduction; and two^[21,27] reporting no difference. Association of sperm motility with high BMI was reported by five studies, with two studies^[24,26] suggesting reduction; and three^[21,25,27] reporting no difference. Reduction of normal morphology with high BMI was reported by two studies^[24,25] and one^[21] reporting no difference. None of the seven studies reported a relationship between a higher BMI and a worse decline in any of the semen parameters. As is visible from Table 2, there is consistent pattern of reduction in count and normal morphology but not in motility.

Coffee/caffeine

Three^[9,21,28] of the 11 included studies investigated the effect of caffeine on male fertility, and all three were of critically low quality published in 2011, 2017, and 2018.

Ricci *et al.*^[28] included fertile and subfertile males. This review included 28 individual studies ($n = 19,967$). The

individual studies varied in size from 41 to 4474 participants. Source of caffeine varied, so as the population studied. This review concluded that semen parameters did not seem to be affected by caffeine intake, at least caffeine from coffee, tea, and cocoa drink.

Advanced paternal age

Three of the included 11 studies^[9,19,21] explore the relation between advanced paternal age/aging on semen parameters. Of which, a study by Johnson *et al.*^[19] is the most comprehensive with 93,839 males, from 90 individual studies, population consisting of infertile and donors as well as volunteer population. Of the three, this is the only one^[19] with primary focus on age and semen quality. All three studies were of critically low quality.

All studies included in Li *et al.*^[21] were already included in Johnson *et al.*^[19] Li *et al.*^[21] only assessed semen volume and not count, motility or morphology. Review by Durairajanayagam^[9] was the latest publication of all the three and had systematic searches but had limited details about impact of age on semen parameters. It has description of few individual studies.

The meta-analysis in Johnson *et al.*^[19] suggests that increase in male age was found to be associated with a decrease in total and progressive motility, and percent normal sperm morphology but there was no impact on sperm concentration. All individual studies included in this review^[19] were small (range $n = 25-3669$). This is based on published retrospective data, hence unable to adjust for confounders or use age as a continuous variable. Hence, it was not possible to define a specific age where decline in motility happens or rate at which decline happens.

DISCUSSION

Main findings

This study reviewed all the available systematic reviews in last 10 years, which investigated the effect of four lifestyle risk factors on three sperm parameters using a systematic review approach. Three of these factors including BMI, smoking, and advanced paternal age were identified as significant risk factors for semen quality, but the effect of coffee/caffeine consumption on semen quality was not significant. BMI was the most studied lifestyle factor. Smoking has an adverse effect on semen parameters and fertility, where sperm count, motility, and normal morphology are significantly reduced. In addition, the amount of cigarette smoked is suggested to be related to the degree of semen parameter decline and male infertility. Advancing paternal age results in decline of sperm

parameters such as sperm count, total and progressive motility, and normal morphology. Increased BMI was associated with decreased total sperm count compared to normal weight men. A small significant decrease was found in sperm motility for obese men overall but no statistical difference for progressive motility. A statistical decrease was reported in the percentage of normal sperm morphology in obese subgroups, especially when restricted to the population undergoing assisted reproduction.

Strength

The main strength of this systematic review is its comprehensive literature search. It is also the first overview of systematic review to summarize all the available data. We also only included review studies published after the latest WHO criteria to reflect the best and most up to date result.^[6]

Limitations

Our study has few limitations. First, the extreme heterogeneity on exposure measurements, study populations, and outcomes make it difficult to draw concrete conclusions on the effects of lifestyle factors on fertility. Second, this systematic review of reviews found very few studies summarizing the relationship between risk factors and semen parameters, of which a majority were of poor quality. Over 70% of the included studies were of low or critically low quality when assessed. In addition, a significant number of the reviews failed to assess the risk of bias of the individual studies. Hence, the results should be interpreted with caution. Thirdly, the measurement of BMI and smoking was not ideal. These were self-reported that could be under- or overestimated, and the included reviews failed to quantify smoking. There were no reviews reporting on e-cigarettes or vaping. We have not looked at sperm DNA fragmentation. Although DNA fragmentation may show evidence of sperm damage, there is no evidence for its use as a routine diagnostic test in clinical practice. We have limited ourselves to three most important parameters of semen analysis as advocated by WHO. We appreciate that DNA fragmentation has been used widely especially in nonpublic sector; however, it is unclear whether it is a diagnostic or a prognostic test, there is a lack of gold standard, there is no consensus on its interpretation with multiple assays, let alone no treatment if sperm DNA fragmentation is identified. Hence, it was not appropriate to study the impact of lifestyle factors on sperm DNA fragmentation within this review.

The BMI was used in the systematic reviews as it is the conventional measure of obesity. However, it is an

imperfect and indirect measure of body fat, especially when the thresholds have been questioned^[29] and measure is based on self-reported height and weight^[30] as is the case in the included review of this present study.

This review concentrated on effect of lifestyle factor on semen parameters. Semen parameters do not automatically mean reduced male fertility as semen analysis as it is, has a very poor positive predictive value as a test of fertility.^[31]

CONCLUSION

In conclusion, high BMI, smoking, and advanced paternal age were found to be associated with decline in one or more parameters of semen quality in males, albeit the evidence is of varying strength. Caffeine was not associated with any deterioration.

Implications for policy and practice

Although there is association with decline in sperm count and motility with obesity, there are perceptions that as long as there are some motile sperms, assisted reproductive treatments such as IVF with addition of ICSI can be performed. Hence male age is not included in the access criteria. However, in addition to being expensive and invasive, these treatments are associated with complications such as ovarian hyperstimulation for women, increased risk of obstetric and perinatal complications when compared with those of spontaneous conception. Public funding of these treatments is limited as well across the world with most needing to pay themselves. Consequently, they should only be used when necessary and not to compensate for the lifestyle factors.

It is therefore really important that investment is carried out in education about the risk of these modifiable factors and their association with reduction in semen parameters. These could be one of few preventable causes of male infertility. Every opportunity for such education should be used.

Implications for future research

Seven out of 11 reviews are of critically low quality; others low or moderate quality. This is because of observational nature and routinely collected data. Randomized data will never be available to answer this question. To get high-quality observational data, well-designed studies with predefined criteria for semen analysis and for subject selection as well as clear definition of lifestyle factor are essential to reach a strong conclusion.

Prospective validated data need to be collected for all men undergoing semen analysis. There has to be international consensus for such data collection. It is only then we can assess the strength of association in large number and in different population. We also must be mindful that these data can only assess the association and not causation.

Authors' contributions

AM conceived the study, BA and SF did the searches, extracted data and quality assessments. BA wrote the first draft of the manuscript. All authors contributed to initial and final draft.

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Conflicts of interest

There are no conflicts of interest.

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