Tobacco smoking and semen quality in infertile males: a systematic review and meta-analysis

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Abstract
Background: Nowadays, the total number of couples visiting an infertility clinic is on the rise. Tobacco smoking is considered one of the major factors leading to male infertility. In this study, we aimed to systematically investigate the impact of tobacco smoking on semen quality in infertile male participants.

Methods: Online databases (Cochrane Central database of Randomized Controlled Trials and the databases of MEDLINE and EMBASE respectively) were searched for relevant English publications that satisfied the inclusion and exclusion criteria of this analysis. The clinical endpoints which were assessed included semen parameters (oligozoospermia, asthenozoospermia, teratozoospermia, and azoospermia), morphological defects of spermatozoa and the hormones involved in reproduction. RevMan 5.3 software was used to analyze the data whereby mean difference (MD) and risk ratios (RR) with 95% confidence intervals (CI) were generated to represent the results.

Results: Sixteen studies with a total number of 10,823 infertile male participants (5257 smokers and 5566 non-smokers) were included. Results of this analysis showed oligozoospermia to be significantly higher in smokers (RR: 1.29, 95% CI: 1.05–1.59; P = 0.02). Morphological defect of spermatozoa (MD: 2.44, 95% CI: 0.99–3.89; P = 0.001) was also significantly higher in smokers whereby significant head (MD: 1.76, 95% CI: 0.32–3.20; P = 0.02), neck (MD: 1.97, 95% CI: 0.75–3.18; P = 0.002) and tail (MD: 1.29, 95% CI: 0.35–2.22; P = 0.007) defects were observed. However, smoking did not affect the pH (MD: 0.04, 95% CI: [−0.03–0.11]; P = 0.30) and motility (RR: 1.42, 95% CI: 0.97–2.09; P = 0.07) of spermatozoa. Additionally, tobacco smoking did not cause any dis-balance in hormones which were involved in reproduction.

Conclusions: In conclusion, with reference to the clinical endpoints which were studied in this analysis, tobacco smoking was associated with a lower sperm count and an increase in the number of morphological defects of spermatozoa. However, the pH and motility of spermatozoa as well as the production of hormones which were involved in reproduction were not affected in this population of infertile males.

Keywords: Smoking, Infertile men, Semen, Oligozoospermia, Asthenozoospermia, Teratozoospermia, Azoospermia

Background
Tobacco smoking among the young generation is becoming worse day by day [1]. The effect of tobacco smoking on lung cancer is already well-known [2]. However, other serious health hazards of smoking have not often well

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(30 to 50 years old) in the United Kingdom to be impotent due to this bad habit. Male infertility (approximately 50% of the cases of infertility among couples [7]) is gradually leading to depression and other psychological outcomes, and this might be potential signs of serious future consequences.

The impact of tobacco smoking on semen quality has seldom been systematically studied. Therefore, by comparing semen parameters between smokers and non-smokers, we aimed to systematically investigate the impact of tobacco smoking on semen quality in infertile male participants.

Methods

Electronic databases and searched strategies

An electronic search was carried out for English language publications through the Cochrane Central database of Randomized Controlled Trials, the databases of MEDLINE (Medical-related publications) and EMBASE respectively. The terms ‘smoking and infertility’, ‘smoking and male infertility’, ‘smoking and semen’, ‘smoking and sperm’, ‘smoking and young males’, ‘infertility and tobacco smoking’, ‘smoking and male health’, ‘smoking, males and impotence’, ‘smoking and infertile men’, ‘smoking and sperm morphology’, ‘smoking and sex’, ‘smoking and sperm count’, ‘smoking and testosterone’, ‘smoking and LH’, ‘smoking and FSH’, ‘smoking and prolactin’ and ‘smoking and sperm motility’ were used to find relevant publications.

To improve this search process, the terms ‘males, men, cigarettes, nicotine, tobacco and non-fertile’ were also included one at a time during the search process. In addition, reference lists of suitable articles were also reviewed for relevant publications.

Inclusion criteria

Inclusion criteria were based on the following features:

(a) Studies based strictly on infertile male participants;
(b) Studies that compared respective semen parameters in smokers versus non-smokers;
(c) Studies that reported the following endpoints: semen parameters, pH of semen, morphological defects of spermatozoa, types of abnormal structural defects, and hormones which were involved in the functioning of the male reproductive system.

Exclusion criteria

Exclusion criteria were based on the following features:

(a) Studies that consisted of fertile/normal male participants;
(b) Studies that did not compare respective semen parameters in smokers versus non-smokers;
(c) Studies that did not report the above-mentioned endpoints;
(d) Duplicated studies.

Endpoints

Selective endpoints included:

- Oligozoospermia;
- Asthenozoospermia;
- Teratozoospermia;
- Azoospermia;
- Morphological defects of spermatozoa: head, neck or tail defects;
- pH of semen;
- Testosterone level;
- Follicle stimulating hormone (FSH) level;
- Luteinizing hormone (LH) level;
- Prolactin level.

The endpoints have been listed in Table 1.

| Study          | Selective endpoints reported                                      |
|----------------|------------------------------------------------------------------|
| Al-Turki2014   | pH of semen, testosterone level, FSH level, LH level, prolactin level |
| Al-Turki2016   | Serum testosterone, semen pH                                       |
| Anifandis2014  | Sperm immotility                                                 |
| Caserta2012    | Oligozoospermia, asthenozoospermia, teratozoospermia, FSH level, LH level |
| Cui2016        | Abnormal sperm head, abnormal sperm body, abnormal sperm tail     |
| Gaur2007       | Oligozoospermia, asthenozoospermia, teratozoospermia              |
| Meri2013       | Serum pH                                                          |
| Mital2012      | Asthenozoospermia (reduced motility), oligozoospermia (low sperm count), teratozoospermia (sperm with abnormal morphology), azoospermia (no sperm count), immotility, sperm head defect, sperm tail defect |
| Trummer2002    | Asthenozoospermia, oligozoospermia, teratozoospermia, testosterone, FSH level, LH level, prolactin level |
| Mostaf2006     | Amorphous sperm head, pathological sperm midpiece, pathological sperm tails |
| Os2019         | Amorphous sperm head, pathological sperm midpiece, pathological sperm tails |
| Yu2013         | Sperm immotility                                                 |
| Zhang2013      | Semen pH, sperm head defects, sperm neck defect, sperm tail defect |
| Zhang2015      | FSH level, LH level, testosterone level                           |
| Dikshit1987    | Immotility of sperms and abnormal morphology                     |
| Kunzle2003     | pH, immotility of sperms and abnormal morphology                 |

Abbreviations: FSH follicle stimulating hormones, LH luteinizing hormone
Data extraction and review
The search of studies was carried out with reference to the PRISMA guideline [8]. Six authors (PKB, GJ, AB, ART, MZSS and MP) independently reviewed the articles which were considered relevant to this analysis and data were extracted appropriately. The authors’ names, year of publication, the study design, the endpoints which were reported, the total number of smokers and non-smokers respectively, age of patients, and the total number of events which were reported in each study were carefully extracted.

Any disagreement which was raised was spontaneously resolved by the seventh author (FH).

With the exception of the mean age of the participants, other data at baseline were not included in this analysis for two main reasons:

- Many original studies did not include risk factors and co-morbidities at baseline;
- Baseline features which were reported in certain studies were different from those reported in other studies and a comparison would not have been possible.

Statistical analysis
The latest version of RevMan software (5.3) was used to analyze the data. This analysis involved both continuous and dichotomous data. Mean and standard deviation (SD) were used during subgroup analysis whereby pooled mean difference (MD) was calculated for the continuous data. For dichotomous data, risk ratios (RR) and 95% confidence intervals (CI) were generated to represent the results.

The statistic Q test and statistic $I^2$ test were used to evaluate heterogeneity [9]. During the subgroup analysis, statistical significance was set at a $P$ value $\leq 0.05$. A fixed effects model ($I^2 < 50\%$) or a random effects model ($I^2 > 50\%$) was used based upon the $I^2$ value which was obtained during each subgroup analysis.

Each study was excluded one by one and a new analysis was carried out each time to observe any significant difference compared to the main results which were obtained (sensitivity analysis).

Ethical approval or board review approval was not required for this type of research articles.

Results
Search outcomes
Electronic search resulted in a total number of 342 articles. After a proper assessment of the titles and abstracts, we excluded 285 studies. Fifty-seven (57) full-text articles were assessed for eligibility. Among the full-text articles, further studies were eliminated because:

- They included fertile/normal male participants (8);
- They involved infertile couples without specifying the gender (3);
- They reported endpoints which were not considered relevant specifically for this analysis (9);
- They were duplicated studies (21).

Finally, 16 studies [10–25] which satisfied all the inclusion and exclusion criteria of this research were included in this analysis (Fig. 1).

Basic features of the studies which were included in this analysis
A total number of 10,823 infertile male participants (5257 smokers and 5566 non-smokers) were included in this analysis.

The main features of the original studies have been summarized in Table 2. The study design, the participants’ enrollment periods (1985–2015), the mean age (26.5–40.5 years old), and the total number of smokers (5257 participants) and non-smokers (5566 participants) have been listed in Table 2.

Other characteristics of the participants and the reasons for exclusion have been summarized in Table 3. Majority of the patients did not consume alcohol and the minority who consumed alcohol were only moderate consumers. Participants with varicocele, cryptorchidism, aspermia, chronic diseases, genital infections, genital trauma, chromosomal abnormalities were excluded from this analysis (Table 3).

Oligozoospermia and teratozoospermia
Results of this analysis showed oligozoospermia to be significantly higher in smokers (RR: 1.29, 95% CI: 1.05–1.59; $P = 0.02$) whereas teratozoospermia was not significantly different (RR: 1.22, 95% CI: 0.96–1.56; $P = 0.10$) between the smokers and the non-smokers as illustrated in Fig. 2.

Asthenozoospermia and azoospermia
Asthenozoospermia (RR: 1.42, 95% CI: 0.97–2.09; $P = 0.07$) and azoospermia (RR: 3.02, 95% CI: 0.23–40.01; $P = 0.40$) were not significantly different between the smokers and non-smokers (Fig. 3).

Impaired motility of spermatozoa and pH of semen (continuous data)
The motility of sperms was not impaired between the smokers and non-smokers (MD: 1.26, 95% CI: [-0.64–3.17]; $P = 0.19$). In addition, pH of semen was also similarly observed (MD: 0.04, 95% CI: [-0.03–0.11]; $P = 0.30$) [Fig. 4].
Table 2  General features of the studies

| Studies     | Study design | Year of patients' enrollment | No of infertile smokers (n) | No of infertile non-smokers (n) | Age (years) S/NS |
|-------------|--------------|------------------------------|-----------------------------|---------------------------------|------------------|
| Al-Turki2014| Retrospective| 2010–2012                    | 90                          | 168                             | 34.2/34.1        |
| Al-Turki2016| Retrospective| 2008–2013                    | 194                         | 322                             | 34.6/34.3        |
| Anifandis2014| Prospective   |                            | 33                          | 98                              | 37.9/37.1        |
| Caserta2012 | Cross sectional| 2006–2011                  | 200                         | 448                             | 38.3/38.5        |
| Cui2016     | Prospective   | 2013–2015                    | 920                         | 298                             | –                |
| Gaur2007    | Retrospective | 2001–2004                    | 100                         | 100                             | –                |
| Men2013     | Retrospective | 2010–2011                    | 396                         | 564                             | –                |
| Mita2012    | Cross sectional|                            | 178                         | 126                             | 40.5/35.0        |
| Trummer2002 | Prospective   | 1993–2000                    | 478                         | 517                             | 31.5/33.4        |
| Mostafa2006 | Prospective   | –                            | 20                          | 20                              | –                |
| Osser1992   | Retrospective | –                            | 186                         | 164                             | –                |
| Yu2013      | Cross sectional| 2011–2012                   | 147                         | 175                             | 35.6/33.6        |
| Zhang2013   | Retrospective | 2007–2010                    | 737                         | 775                             | 29.6/29.9        |
| Zhang2015   | Retrospective | 2013–2014                    | 704                         | 372                             | 29.9/30.4        |
| Dikshit1987 | Prospective   | 1985–1986                    | 219                         | 288                             | 26.7/26.5        |
| Kundze2003  | Retrospective | 1991–1997                    | 655                         | 1131                            | 32.3/33.2        |

Total no of patients (n) 5257 5566

Abbreviations: S smokers, NS non-smokers
There was a significant increase in the morphological defects of spermatozoa (MD: 2.44, 95% CI: [0.99 – 3.89]; \(P = 0.001\)) including head (MD: 1.76, 95% CI: 0.32 – 3.20; \(P = 0.02\)), neck (MD: 1.97, 95% CI: 0.75 – 3.18; \(P = 0.002\)) and tail (MD: 1.29, 95% CI: 0.35 – 2.22; \(P = 0.007\)) defects as shown in Figure 5.

Hormones which were involved in reproduction
This analysis did not show any significant difference in testosterone level (MD: 0.18, 95% CI: -1.26 – 1.63; \(P = 0.80\)), LH level (MD: 0.18, 95% CI: -0.47 – 0.83; \(P = 0.58\)) and prolactin level (MD: 1.79, 95% CI: -5.78 – 9.36; \(P = 0.64\)) between smokers and non-smokers as shown in Fig. 6. FSH level was also not significantly decreased (MD: 0.12, 95% CI: -0.41 – 0.64; \(P = 0.66\)) [Fig. 7].

Table 4 has summarized the results of this analysis. Sensitivity analysis showed that in the subgroup analyzing for teratozoospermia, excluding study Mostafa2002 showed a statistically significant result (RR: 1.32, 95% CI: 1.03–1.70; \(P = 0.03\)). Otherwise, consistent results were obtained throughout all the other subgroups.
Discussion

As expected, this analysis showed smoking to have a significant impact on the quantity and quality of sperms in the infertile male participants. Tobacco smoking was associated with a lower sperm count and an increase in the number of morphological defects including head, neck and tail defects of spermatozoa. However, the pH and motility of spermatozoa as well as the hormones which were involved in reproduction were not affected in this population of infertile males.

A recent meta-analysis which assessed human semen showed tobacco smoking to have a negative impact on semen parameters [26]. The analysis which consisted of a total number of 5865 fertile and infertile men showed a reduced sperm count and impaired motility in semen samples of these young men. Even though the results

![Fig. 2 Oligozoospermia and teratozoospermia observed in smoking and non-smoking infertile male participants](image)

![Fig. 3 Asthenozoospermia and azoospermia observed in smoking and non-smoking infertile male participants](image)
### Fig. 4: Impaired motility of spermatozoa and pH of semen observed in smoking and non-smoking infertile male participants

| Study or Subgroup | smokers Mean | smokers SD | smokers Total | non-smokers Mean | non-smokers SD | non-smokers Total | Mean Difference IV, Random, 95% CI | Mean Difference IV, Random, 95% CI |
|-------------------|-------------|------------|---------------|------------------|----------------|------------------|-----------------------------------|-----------------------------------|
| 1.1.1 pH of semen |             |            |               |                  |                |                  |                                   |                                   |
| Al-Turki2014      | 7.43        | 0.3        | 90            | 7.37             | 0.43           | 168              | 19.3% 0.06 [0.03, 0.15]            |                                   |
| Al-Turki2016      | 7.4         | 0.4        | 194           | 7.4              | 0.2            | 322              | 21.2% 0.00 [0.06, 0.06]            |                                   |
| Kunze2003         | 7.5         | 0.3        | 655           | 7.4              | 0.2            | 1131             | 22.7% 0.10 [0.07, 0.13]            |                                   |
| Zhang2013         | 7.12        | 0.24       | 737           | 7.13             | 0.23           | 775              | 22.7% -0.01 [0.03, 0.01]           |                                   |
| Subtotal (95% CI) | 1676        |            | 2396          | 85.9%            |                |                  |                                   |                                   |

Heterogeneity: Tau^2 = 0.00; Ch^2 = 39.74, df = 3 (P < 0.00001); I^2 = 92%

Test for overall effect: Z = 1.04 (P = 0.30)

### Fig. 5: Morphological defects of spermatozoa observed in smoking and non-smoking infertile male participants

| Study or Subgroup | smokers Mean | smokers SD | smokers Total | non-smokers Mean | non-smokers SD | non-smokers Total | Mean Difference IV, Random, 95% CI | Mean Difference IV, Random, 95% CI |
|-------------------|-------------|------------|---------------|------------------|----------------|------------------|-----------------------------------|-----------------------------------|
| 1.2.1 Abnormal forms of sperm |             |            |               |                  |                |                  |                                   |                                   |
| Dikshit1987       | 20.24       | 0.61       | 219           | 19.35            | 0.57           | 288              | 10.4% 0.89 [0.76, 1.02]            |                                   |
| Kunze2003         | 78.8        | 14.6       | 655           | 76.3             | 15.5           | 1131             | 3.2% 2.50 [1.06, 3.94]            |                                   |
| Mei2013           | 73          | 11.7       | 396           | 60.7             | 11.7           | 564              | 3.0% 12.30 [10.80, 13.80]         |                                   |
| Mostafa2006       | 14.4        | 3.59       | 20            | 13.5             | 3.28           | 20               | 1.7% 0.90 [1.23, 3.03]            |                                   |
| Osseo1992         | 49.6        | 1.1        | 186           | 49.9             | 1.2            | 164              | 10.0% -0.30 [0.04, 0.06]           |                                   |
| Trummer2002       | 56.1        | 17.9       | 478           | 57.8             | 17.6           | 517              | 1.6% -1.70 [3.91, 0.51]           |                                   |
| Subtotal (95% CI) | 1954        |            | 2684          | 29.9%            |                |                  |                                   |                                   |

Heterogeneity: Tau^2 = 2.76; Ch^2 = 313.45, df = 5 (P < 0.00001); I^2 = 98%

Test for overall effect: Z = 3.29 (P = 0.0010)

| 1.2.2 Head defects |             |            |               |                  |                |                  |                                   |                                   |
|--------------------|-------------|------------|---------------|------------------|----------------|------------------|-----------------------------------|-----------------------------------|
| Cui2016            | 88.38       | 15.11      | 920           | 82.5             | 11.66          | 298              | 2.6% 5.88 [4.24, 7.52]            |                                   |
| Osseo1992          | 47.2        | 1          | 186           | 47               | 1.2            | 164              | 10.0% 0.20 [0.03, 0.43]           |                                   |
| Zhang2013          | 88.32       | 4.3        | 562           | 87.81            | 3.78           | 615              | 8.5% 0.51 [0.05, 0.97]            |                                   |
| Subtotal (95% CI)  | 1668        |            | 1077          | 21.2%            |                |                  |                                   |                                   |

Heterogeneity: Tau^2 = 1.41; Ch^2 = 45.46, df = 2 (P < 0.00001); I^2 = 96%

Test for overall effect: Z = 2.40 (P = 0.02)

| 1.2.3 Neck defect  |             |            |               |                  |                |                  |                                   |                                   |
|--------------------|-------------|------------|---------------|------------------|----------------|------------------|-----------------------------------|-----------------------------------|
| Cui2016            | 49.32       | 14.43      | 920           | 41.38            | 8.58           | 298              | 3.5% 7.94 [6.59, 9.29]            |                                   |
| Osseo1992          | 1.8         | 0.1        | 186           | 1.8              | 0.1            | 164              | 16.6% 0.00 [0.02, 0.02]           |                                   |
| Zhang2013          | 2.15        | 2.02       | 562           | 2.34             | 2.29           | 615              | 9.9% -0.19 [-0.44, 0.06]          |                                   |
| Subtotal (95% CI)  | 1668        |            | 1077          | 24.0%            |                |                  |                                   |                                   |

Heterogeneity: Tau^2 = 1.03; Ch^2 = 135.47, df = 2 (P < 0.00001); I^2 = 96%

Test for overall effect: Z = 3.17 (P = 0.002)

| 1.2.4 Tail defect  |             |            |               |                  |                |                  |                                   |                                   |
|--------------------|-------------|------------|---------------|------------------|----------------|------------------|-----------------------------------|-----------------------------------|
| Cui2016            | 11.64       | 12.77      | 920           | 6.23             | 7.19           | 298              | 4.2% 5.41 [4.25, 6.57]            |                                   |
| Osseo1992          | 3           | 0.2        | 186           | 3.1              | 0.3            | 164              | 10.6% -0.10 [-0.15, -0.05]        |                                   |
| Zhang2013          | 2.3         | 2.21       | 562           | 2.24             | 1.71           | 615              | 10.0% 0.06 [0.17, 0.29]           |                                   |
| Subtotal (95% CI)  | 1668        |            | 1077          | 24.8%            |                |                  |                                   |                                   |

Heterogeneity: Tau^2 = 0.59; Ch^2 = 87.92, df = 2 (P < 0.00001); I^2 = 96%

Test for overall effect: Z = 2.71 (P = 0.007)

| Total (95% CI)     | 1668        |            | 1077          | 24.8%            |                |                  |                                   |                                   |

Heterogeneity: Tau^2 = 0.23; Ch^2 = 756.45, df = 14 (P < 0.00001); I^2 = 98%

Test for overall effect: Z = 7.65 (P < 0.00001)

Test for subgroup differences: Ch^2 = 1.93, df = 3 (P = 0.59), I^2 = 0%
which were obtained were almost similar with respect to this current analysis, the other analysis included studies which were published between the years 2010 to 2015, whereas our current analysis included studies which were published even before the year 2010. Another difference with respect to the current analysis was the fact that there was no language barrier in the other analysis. Moreover, the other analysis also assessed results with reference to the total number of cigarettes which were consumed daily. In contrast to the other analysis, this current meta-analysis assessed specific morphological defects, as well as any dis-balance of the hormones which were involved in reproduction.

Another study evaluating the effect of cigarette smoking on vital seminal parameters which influence fertility showed smoking to cause impaired motility to a higher extent in comparison to the impairment in sperm count [27]. Men with primary infertility aged between 25 to 40 years were included and a follow-up period of less and above 5 years were considered.

A case control study also showed smoking to be associated with a lower semen concentration, impaired motility of spermatozoa and an increased morphology defect [28] in part reflecting the results of this current analysis. Additionally, an article published by the Canadian Society of Clinical Chemists showed that abnormal structural defects of spermatozoa, especially round head defects, were associated with tobacco smoking which might be attributed to increased oxidative stress and insufficient scavenging antioxidant enzymes in the seminal fluids of infertile men [29]. Other studies have shown zinc to contribute to this unwanted mechanism in...
infertile smokers [30]. Other mechanisms have well been explained in previously published reviews [31, 32].

Briefly, the possible mechanisms which might be involved with the effect of cigarette smoking on semen parameters are: toxic contents found in cigarette smoking might have harmful effects on male germ cells and their developmental processes [33]. Negative effects of nicotine on semen parameters have also previously been reported [34]. Other possible mechanisms might be related to the negative impact of smoking on the 8 nAChR subunits found in human spermatozoa, resulting in smoking-related sperm damage [35]. In addition, different proteins (Aldoa, ATP5a1, Gpx4, Cs) expressed in sperms were significantly altered in smokers [36]. Cigarette smoking was found to also affect Ca2+ - ATPase activity of the spermatozoa as well [37].

However, even though clinical research has shown smoking to have an adverse effect on the progressive sperm motility irrespective of the total number of cigarettes smoked daily [38, 39], other studies showed no relationship between smoking and male infertility [40].

This current analysis showed no significant influence of smoking on testosterone, prolactin and LH levels. To support this point, Wang et al. showed smoking not to be an independent predictor of sex-hormone binding globulin even though a relation or linked was observed between increasing packets of cigarette and sex-hormone binding globulin [41]. Similarly, another study conducted in Taiwan showed no significant difference in LH and FSH levels between smokers and non-smokers [42] showing smoking to have a much higher impact on semen compared to the production of hormones which were involved in the functioning of the male reproductive system.

Several alternative methods to stop smoking have been suggested [43–46]. However, apart from smoking, other factors such as regular heavy alcohol consumption [47], certain medications, co-morbidities, autoimmune diseases and other environmental factors might also contribute to abnormalities in semen parameters, morphology and impaired motility and should further be investigated [48].

This interesting research should inspire other scientists to investigate more about the mechanisms, the factors associated with a poor semen quality in smokers; in order for proper actions to be taken in a timely manner to reduce this serious dilemma faced by several young men and couples in our society.

This meta-analysis should be considered new for the following reasons: it is among the only few meta-analyses to systematically show the impact of smoking on the quality of semen in infertile males. This article might be considered new on the basis of the total number of participants and the number of different endpoints which were analyzed in one particular study.

**Limitations**

Limitations might be the fact that a high level of heterogeneity was observed among several of the subgroups analyzing the different endpoints. This could be due to the inclusion of observational data. In addition, several endpoints were analyzed only using a small number of studies. Factors such as alcohol consumption could have had an influence on the main results. Moreover, the infertility duration, and other associated factors such as genital infections, varicocele, environmental factors were not clearly reported in several studies.

### Table 4 Results of this analysis

| Endpoints                          | No of studies involved (n) | RR or MD with 95% CI | P value | I² (%) |
|------------------------------------|---------------------------|----------------------|---------|--------|
| Oligozoospermia                    | 4                         | 1.29 [1.05–1.59]     | 0.02    | 0      |
| Teratozoospermia                   | 3                         | 1.22 [0.96–1.56]     | 0.10    | 0      |
| Asthenozoospermia                  | 4                         | 1.42 [0.97–2.09]     | 0.07    | 85     |
| Azoospermia                        | 2                         | 3.02 [0.23–40.01]    | 0.40    | 92     |
| pH of semen                        | 4                         | 0.04 [–0.03–0.11]    | 0.30    | 92     |
| Impaired motility of sperm (continuous data) | 4 | 1.26 [–0.64–3.17]    | 0.19    | 87     |
| Abnormal form of sperm             | 6                         | 2.44 [0.99–3.89]     | 0.001   | 98     |
| Head defects                       | 3                         | 1.76 [0.32–3.20]     | 0.02    | 96     |
| Neck defects                       | 3                         | 1.97 [0.75–3.18]     | 0.002   | 99     |
| Tail defects                       | 3                         | 1.29 [0.35–2.22]     | 0.007   | 98     |
| Testosterone level                 | 4                         | 0.18 [–1.26–1.63]    | 0.80    | 94     |
| LH level                           | 3                         | 0.18 [–0.47–0.83]    | 0.58    | 66     |
| Prolactin level                    | 2                         | 1.79 [–5.78–9.36]    | 0.64    | 95     |
| FSH level                          | 3                         | 0.12 [−0.41–0.64]    | 0.66    | 0      |

**Abbreviations:** MD mean difference, RR risk ratio, CI confidence intervals, LH luteinizing hormone, FSH follicle stimulating hormone


**Conclusions**

In conclusion, with reference to the clinical endpoints which were studied in this analysis, tobacco smoking was associated with a lower sperm count and an increase in the number of morphological defects of spermatozoa. However, the pH and motility of spermatozoa as well as the production of hormones which were involved in reproduction were not affected in this population of infertile males.

**Abbreviations**

CI: confidence intervals; FSH: follicle stimulating hormones; LH: luteinizing hormone; RR: risk ratios

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**Availability of data and materials**

All data and materials used in this research are freely available. References have been provided.

**Authors’ contributions**

PKB, U. MZSS, AB, ART, MP and FH were responsible for the conception and design, acquisition of data, analysis and interpretation of data, drafting the initial manuscript and revising it critically for important intellectual content. PKB wrote this manuscript. All authors read and approved the final manuscript as presented.

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**Ethics approval and consent to participate**

Ethical approval was not applicable for this systematic review and meta-analysis.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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