J Surg Med. 2023;7(10):694-699.
DOİ: 10.28982/josam.7978

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

Self-reported occupational exposure and its association with sperm DNA fragmentation in infertile men

Zeynep Caliskan [1], Canan Kucukgergin [2], Gulsan Aktan [3], Nurgul Bulut [4], Gul Ozdemirler [1]

[1] Department of Medical Biochemistry, Istanbul Yeni Yuzyil University, Istanbul, Turkey
[2] Department of Medical Biochemistry, Istanbul University, Istanbul, Turkey
[3] Department of Andrology, Istanbul University, Istanbul, Turkey
[4] Department of Biostatistics and Medical Informatics, Istanbul Medeniyet University, Istanbul, Turkey

ORCID ID of the author(s)

ZC: 0000-0001-8165-2024
CK: 0000-0002-1797-5889
GA: 0000-0003-2382-7927
NB: 0000-0002-7247-6302
GO: 0000-0001-8891-6387

Corresponding Author
Zeynep Caliskan
Istanbul Yeni Yuzyil University, Maltepe Mahallesi, Yılanlı Ayazma Cd., No: 26, 34010 Zeytinburnu, İstanbul, Turkey
E-mail: z.sezginn@gmail.com

Ethics Committee Approval
Ethical approval was obtained from the Istanbul Yeni Yuzyil University Ethics Committee (Date: October 3, 2022, No: 2022/0710-922).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2023 October 24

Abstract

Background/Aim: Sperm quality has experienced a decline in recent years, with this issue being particularly pronounced in industrialized nations, suggesting a potential link to occupational exposures. Evaluating sperm DNA fragmentation can yield valuable insights into male fertility, although its association with occupational exposures remains less well-established. Our study aimed to investigate the relationship between self-reported occupational exposures and sperm DNA fragmentation in infertile men.
Methods: This retrospective cohort study involved 391 infertile men who sought fertility treatment at a university clinic between 2017 and 2020. A brief questionnaire was administered to collect data on patients' demographic characteristics, medical history, occupation, and exposure types. In this comparative study, patients were categorized into two groups based on their occupational exposures (the unexposed and exposed groups). The exposed group was further sub-grouped according to their specific exposure types, which included cement, solvents, metals, pesticides, mechanical vibration, and heat. The primary outcome in this study was assessed using the terminal deoxynucleotidyl transferase-mediated nick end-labeling test (TUNEL), with results expressed as the sperm DNA fragmentation index (DFI).
Results: Patients in the exposed group exhibited a significantly higher sperm DFI compared to those in the unexposed group (14 [17] vs. 8 [9], $P<0.001$). After accounting for potential confounding factors, our results demonstrated that several occupational exposure factors significantly increased the risk of elevated sperm DFI (>15%) levels, including solvents (odds ratio (OR) 8.2, 95% confidence interval (CI) 3.6–18.5, $P<0.001$), metals (OR: 2.2, 95% CI: 1.0–4.7, $P=0.048$), pesticides (OR: 14.6, 95% CI: 1.6–130.7, $P=0.016$), mechanical vibration (OR: 2.6, 95% CI: 1.5–4.6, $P<0.001$), and heat (OR: 6.4, 95% CI: 1.7–23.5, $P=0.005$).
Conclusion: The findings of our study corroborate earlier research suggesting that occupational exposures may have adverse effects on sperm DNA fragmentation in men. The identification and management of such exposures as part of routine clinical practice could offer a complementary approach to enhancing infertility treatment outcomes.

Keywords: male infertility, occupational exposure, sperm DNA fragmentation

How to cite: Caliskan Z, Kucukgergin C, Aktan G, Bulut N, Ozdemirler G. Self-reported occupational exposure and its association with sperm DNA fragmentation in infertile men. J Surg Med. 2023;7(10):694-699.

Introduction

Infertility affects approximately 15% of couples, with the male factor being responsible, either partially or solely, in one out of every two cases. Male infertility has been attributed to various etiologies, with particular attention given to sperm DNA damage, which has been extensively studied for its impact on the structural and functional characteristics of sperm. Numerous studies have reported elevated levels of sperm DNA fragmentation in infertile men [1]. Sperm DNA fragmentation refers to the integrity of the genetic material contained within sperm and serves as an indicator of the quality of sperm DNA. The integrity of sperm DNA plays a critical role in transmitting genetic information that influences fertilization, embryo development, implantation, and pregnancy. Sperm DNA damage can arise from defective spermatogenesis, abnormalities in chromatin remodeling, incomplete apoptosis, and heightened testicular and post-testicular oxidative stress [2]. Moreover, various external factors can compromise chromatin integrity, leading to gradual DNA damage over time.

Studies on occupational exposure have suggested that work-related activities involving chemical and physical exposures can potentially impact male reproductive function, potentially leading to infertility [3]. Occupational tasks often expose individuals to a multitude of physical and chemical hazards. Among the physical hazards are excessive heat, mechanical vibrations, ionizing radiation, and, more recently, electromagnetic fields, which have been linked to disruptions in spermatogenesis and alterations in sperm characteristics [4]. In addition to physical hazards, chemical hazards like pesticides, solvents, and heavy metals have been associated with compromised semen quality and elevated abortion rates, as indicated by numerous studies [5,6]. However, the complexity of occupational exposure scenarios, compounded by various confounding factors such as smoking, alcohol consumption, body mass index, dietary habits, and socioeconomic status, has made it challenging to unequivocally attribute the significance of a single workplace hazard to date [3,7].

Numerous studies have established a connection between occupational exposure to specific harmful substances and an increased incidence of sperm DNA damage, resulting in reduced fertility. Sperm DNA fragmentation has emerged as a sensitive biological marker for detecting exposure to occupational toxicants [8]. While most epidemiological investigations into occupational exposure have traditionally focused on conventional semen parameters, such as sperm concentration, motility, and morphology, there remains a limited understanding of the link between occupational exposure and sperm DNA fragmentation. Gathering general occupational exposure data through self-reported questionnaires can be a valuable means of identifying occupational risk factors associated with elevated levels of sperm DNA fragmentation in clinical settings. Despite its limitations, this approach offers accuracy and reliability comparable to other widely used exposure assessment techniques, such as quantitative exposure measurement [9]. The present study was undertaken to explore the relationship between exposure to occupational risk factors (as reported in the questionnaire) and the extent of sperm DNA fragmentation in infertile men, with the aim of comprehending the extent to which occupational exposure influences sperm quality.

Materials and methods

Study population

We conducted a retrospective cohort study involving 391 infertile men who had sought fertility treatment at Istanbul University Andrology Clinic between 2017 and 2020. Data for this study were obtained from a questionnaire regarding their occupations. Prior to accessing patient information and initiating the research, we obtained permission from the Istanbul Yeni Yuzyil University Ethics Committee on October 3, 2022 (No: 2022/0710-922). The study was carried out in compliance with the Helsinki Declaration.

Inclusion criteria for the study encompassed male patients diagnosed with infertility, with ages ranging from 20 to 53 years. Comprehensive medical histories were collected for all participating patients. Exclusion criteria comprised individuals with infertility due to female factors, men with anatomical anomalies, varicocele, genetic or endocrine factors, genitourinary inflammation, or infection.

The database contained various patient details, including names, ages, medical histories regarding prior conditions that could impact sperm DNA fragmentation, smoking status (yes/no), alcohol consumption (yes/no), occupation (job title), and the type of exposure encountered in their work. Occupational exposure data were utilized to classify patients into two distinct groups: the unexposed group, comprising men who did not report any exposure and whose professions did not involve contact with any of the agents mentioned above, and the exposed group.

The unexposed group consisted of individuals such as policemen, businessmen, traders, civil servants, teachers, and students. In contrast, the exposed group encompassed cement industry workers, hairdressers, painters, printers, carpenters, cleaners, chemical and textile workers, metal workers, goldsmiths, electricians, welders, farmers, machine operators, mechanical engineers, mechanics, forklift drivers, cooks, bakers, taxi drivers, couriers, and software developers.

Additionally, the exposed group was further subdivided into six categories based on their specific type of exposure, namely: cement, solvents, metals, pesticides, heat (prolonged sitting or excessive heat), and mechanical vibrations (Table 1).

Table 1: Classifications of occupational exposure groups based on a questionnaire

Groups		Occupation
Unexposed group		Policemen, businessmen, traders, civil servants, teachers, and students
Exposed group	Cement	cement industry workers
	Solvents	hairdressers, painters, printers, carpenters, cleaners, chemical and textile workers
	Metals	metal workers, goldsmiths, electricians, welders
	Pesticides	farmers
	Mechanical vibrations	machine operators, mechanical engineers, mechanics, forklift driver
	Heat (prolonged sitting or excess heat)	cooks, bakers, taxi drivers, couriers, software developers

Sperm DNA Fragmentation Index

Semen samples were collected via masturbation and placed into sterile containers, following a period of 3-4 days of abstinence. Spermatozoa were then subjected to direct swim-up preparation, and sperm DNA fragmentation was evaluated using the TUNEL method, as outlined in our prior study [10]. The

primary objective of this study was to measure sperm DNA Fragmentation Index (DFI).

Sample size

The sample size was determined by considering the number of eligible patients without missing data for the period spanning from 2017 to 2020. For a retrospective comparative study, the sample size was computed using the standard method. With a test power of 95% and a type I error rate of 0.05, the minimum required sample size in each group was calculated to be 71, assuming an effect size of 0.6.

Statistical analysis

Descriptive statistics were used to summarize the data, including median values, minimum and maximum ranges, as well as counts and percentages (% frequencies). To assess the normality of the data distribution, the Kolmogorov-Smirnov test was employed. Given that the numerical characteristics exhibited non-normal distributions, comparisons between the unexposed and exposed groups were conducted using the Mann-Whitney U test. Comparisons involving more than two groups were assessed using the Kruskal-Wallis test, with Bonferroni adjustment applied for multiple comparisons.

For categorical characteristics, group data were analyzed using the Pearson Chi-square test. After dividing participants into two groups based on their sperm DNA Fragmentation Index (DFI) levels, specifically above and below 15 (as per our previous study), odds ratios (OR) and their respective 95% confidence intervals for the risk factors were computed through multiple logistic regression analysis. This analysis was adjusted for the participants' exposure status, accounting for smoking, age, and alcohol variables.

All calculations were performed using the SPSS 22.0 program, with a selected statistical significance level of *P*-value <0.05.

Results

The study recruited 391 infertile men aged between 20 and 53 years. The mean age of the participants was 32. The largest age group, comprising 55.75% of the population, fell between 30 and 39 years old, while the smallest age group, consisting of 12.28%, was over 40 years old. Most participants exhibited high sperm DNA Fragmentation Index (DFI) levels (<15%) (66.5%). The median sperm DFI among the participants was 10 (14).

Based on the information gathered from the questionnaire, infertile men were divided into two groups according to their exposure status: the unexposed group (n=199) and the exposed group (n=192). Solvent exposure was the most prevalent risk factor among the exposed population (42.2%), followed by exposure to metals (19.3%), heat (17.7%), and cement (12.0%). Only 5.7% and 3.1% of men were exposed to mechanical vibrations and pesticides in their occupational settings, respectively. The differences in mean age, smoking, and alcohol consumption between the unexposed and exposed groups were found to be statistically insignificant (*P*=0.112, *P*=0.550, *P*=0.506, respectively). However, there was a significant difference in the median distribution of sperm DFI between the exposed and unexposed groups (14 [17] vs. 8 [9], *P*<0.001).

Upon conducting multiple comparisons, it was observed that the median sperm DFI value in the group exposed to solvents was significantly higher than that in the non-exposed group (*P*<0.001). Additionally, the sperm DFI median value showed a significant increase in men who were exposed to pesticides (*P*=0.008), vibration (*P*=0.037), and heat (*P*=0.035) (Table 2).

Logistic regression was employed to assess the correlation between occupational exposure type and sperm DFI. Table 3 presents the adjusted ORs, with the unexposed group serving as the reference group with an OR of 1. Notably, individuals exposed to solvents had an 8.2-fold higher likelihood of having a sperm DFI >15% (OR: 8.197 [3.628–18.520], *P*<0.001). Exposure to metals was associated with a 2.2-fold higher risk of having a sperm DFI value above 15 (OR: 2.169 [1.008–4.670], *P*=0.048), while those exposed to pesticides had a substantially higher risk, with a 14.6-fold increase (OR: 14.642 [1.640-130.747], *P*=0.016). Exposure to mechanical vibration was estimated to elevate the risk by 2.6 times (OR: 2.573 [1.452–4.559], *P*<0.001). Men exposed to heat exhibited a 6.4-fold higher sperm DFI value compared to those in the unexposed group (OR: 6.411 [1.747–23.521], *P*=0.005). However, there was no statistically significant association between sperm DFI value and exposure to cement (*P*=0.059).

Table 3: Logistic regression analysis of association between sperm DFI and occupational exposures

	Sperm DFI >15	
	OR (%95 CI)	***P*-value**
Unexposed	1.00	0.001
Cement	2.509 (0.965-6.521)	0.059
Solvents	8.197 (3.628-18.520)	0.001
Metals	2,169 (1.008-4.670)	0.048
Pesticides	14.642 (1.640-130.747)	0.016
Mechanical vibration	2.573 (1.452-4.559)	0.001
Heat	6.411 (1.747-23.521)	0.005

OR: Odds ratio

Discussion

Male infertility is a substantial health concern characterized by numerous contributing factors. Among these factors, industrialization and economic growth have emerged as significant contributors due to heightened exposure to hazardous substances, leading to a detrimental impact on sperm quality. Consequently, it is imperative to gain a comprehensive understanding of how occupational factors can influence sperm quality. This study aimed to investigate the correlation between sperm DNA fragmentation (SDF) and self-reported occupational exposures using a questionnaire specifically designed for routine consultations.

Table 2: Demographic characteristics and sperm DFI levels of exposure groups

					Exposed group					
		Unexposed group (n=199)	**Exposed group (n=192)**	***P*-value**	**Cement (n=23)**	**Solvents (n=81)**	**Metals (n=37)**	**Pesticides (n=6)**	**Mechanical vibration (n=11)**	**Heat (n=34)**
Age (years), mean (SD)		32 (8)	33 (8)	0.112*	30 (7)	31.5 (7)	33 (10)	36 (7)	33 (8)	34 (4)
Sperm DFI, median (IQR)		8 (9)	14 (17)[a]	0.001*	11 (12)	20.5 (14.8)[a]	10 (12)	35 (25)[a]	13 (14)[a]	16 (30)[a]
Smoking n (%)	**No**	119 (59.8)	101 (52.6)	0.550**	10 (41.7)	21 (61.8)	18 (48.6)	3 (50.0)	43 (52.4)	6 (54.5)
	Yes	80 (40.2)	91 (47.4)		14 (58.3)	13 (38.2)	19 (51.4)	3 (50.0)	39 (47.6)	5 (45.5)
Alcohol consumption n (%)	**No**	163 (81.9)	166 (86.5)	0.056**	16 (66.7)	32 (94.1)	31 (83.8)	6 (100.0)	74 (90.2)	9 (81.8)
	Yes	36 (18.1)	26 (13.5)		8 (33.3)	2 (5.9)	6 (16.2)	0 (0.0)	8 (9.8)	2 (18.2)

SD: standard deviation, IQR: inter quartile range, *Kruskal-Wallis, **Pearson Chi-Square, [a] *P*<0.001 compared with the unexposed group.

The findings revealed a notable association between self-reported occupational exposure to solvents, metals, pesticides, mechanical vibration, and heat and an elevated risk of experiencing high levels of SDF. These associations remained significant even after adjusting for confounding variables such as smoking and alcohol consumption.

Exposure to solvents emerged as the most prevalent occupational factor within our study population, affecting 42.2% of participants. Previous research has extensively documented the potential impact of solvent exposure on male infertility and semen quality [9,11,12]. For instance, De Fleurian et al. [11] investigated the influence of self-reported physical or chemical occupational exposures on semen quality and found a significant association between solvent exposure and semen impairment (adjusted OR: 2.5; 95% CI: 1.4–4.4). However, studies specifically addressing sperm DNA damage have primarily focused on distinct solvent exposures, yielding inconsistent results.

Occupational exposure to benzene, for example, has been linked to DNA damage in immature germ cells in men, resulting in compromised sperm DNA integrity [13]. A recent study even highlighted the heightened risk of DNA fragmentation in fertile men exposed to paint thinners containing toluene, polyurethane, butyl carbitol, and numerous other components [14]. Moreover, workplace styrene exposure was associated with increased sperm DNA damage, as assessed through the Comet assay [15]. Furthermore, a study on coke oven workers exposed to polyaromatic hydrocarbons revealed significantly elevated levels of bulky DNA adducts and 8-oxo-7,8-dihydro-2’-deoxyguanosine compared to the control group, indicating potential sperm DNA damage and subsequent loss of integrity [16].

In contrast, Jurewicz et al. [17] reported no discernible correlation between occupational solvent exposure and SDF Index (DFI). However, our study findings indicate that the percentage of DNA fragmentation observed in the spermatozoa of the unexposed group was notably lower than that of workers exposed to solvents. Moreover, individuals with occupational solvent exposure faced an eight-fold higher risk of experiencing elevated levels of sperm DFI (>15%). It is plausible to hypothesize that this increased sperm DFI may be linked to the heightened production of reactive oxygen species (ROS) triggered by exposure to various solvents in occupational settings.

Current research regarding the impact of metal exposure on sperm DNA integrity in humans presents a challenge due to inconsistent findings. Non-essential heavy metals, encompassing but not limited to lead, cadmium, arsenic, mercury, and barium, have the potential to adversely affect male fertility and sperm quality. The detrimental effect of heavy metals on male fertility is attributed to their capacity to stimulate the production of ROS, leading to lipid peroxidation and damage to sperm DNA [18]. A comprehensive study conducted on infertile men in China aimed to explore the relationship between urinary metal concentration and sperm DNA damage. Their findings suggest that exposure to mercury (Hg), nickel (Ni), and manganese (Mn) may potentially result in increased sperm DNA damage [19].

In vitro research has revealed that lead can compete with or replace zinc in human protamine P2 (HP2), a zinc-containing protein crucial for binding to sperm DNA during spermatogenesis. Exposure to lead led to a dose-dependent reduction in HP2-DNA binding, potentially affecting sperm DNA and contributing to sperm DNA damage [20]. Conversely, a study involving coke oven workers exposed to metal mixtures did not observe a significant correlation between SDF and either metal mixtures or individual metals [21].

In our study, while we did not find a significant difference in SDF Index (DFI) between the group with metal exposure and the unexposed group, we did identify an increased risk of high DFI associated with metal exposure.

Various pesticides, encompassing pyrethroids, organophosphates, phenoxyacetic acids, carbamates, organochlorines, and combinations thereof, have undergone examination concerning their impact on male fertility [22]. Notably, exposure to organophosphates has been associated with abnormal semen characteristics, including reduced sperm counts, motility, viability, density, abnormal morphology, and increased DNA damage [23]. Individuals exposed to insecticides in their occupational settings, particularly fenvalerate or carbaryl, have displayed a notable induction of DNA damage in spermatozoa [24,25]. In fact, Xia et al. [25] suggested that carbaryl may function as a genotoxic agent due to its ability to cause DNA fragmentation and numerical chromosomal abnormalities during spermatogenesis.

In our study, we observed a significant association between pesticide exposure and high SDF Index (DFI). It is worth noting, however, that this association may be influenced by the relatively small proportion of participants (3.1% of our study population) who reported such occupational exposures.

Physical factors, such as mild heat stress, have the potential to disrupt sperm DNA integrity. It’s crucial to recognize that the optimal temperature for spermatogenesis is slightly lower than the body’s core temperature, typically differing by approximately 1–2°C. Consequently, germ cells become susceptible to localized heating of the testes. A prior study conducted in Poland reported that sedentary work associated with heat stress (where individuals spent ≥ 50% of their work time in a sedentary position) can double the risk of sperm DNA damage while not altering conventional semen parameters. This phenomenon may be attributed to the sedentary work style leading to an increase in testicular temperature, thereby resulting in failure in sperm chromatin remodeling during spermiogenesis [26]. Furthermore, heat stress amplifies the generation of ROS, leading to additional damage to mature sperm DNA [27]. Occupations involving prolonged sitting or daily commutes, such as driving, are more likely to raise scrotal temperatures, which have been linked to increased sperm DNA damage [28] and reduced sperm motility [11].

Additionally, previous studies have indicated that infertile males with varicocele tend to exhibit higher scrotal temperatures than expected, and this elevated testicular temperature has been shown to impact sperm DNA integrity. Our findings align with these observations, as we discovered that individuals working in roles such as software developers, drivers, or cooks were at an increased risk of experiencing elevated SDF due to extended periods of sitting and exposure to excessive heat. However, it is crucial to acknowledge that the limited number of subjects in the heat-exposed group underscores the need for longitudinal studies to validate our findings.

Research into the potential hazards of mechanical vibrations on the male reproductive system primarily relies on empirical, clinical, and epidemiological analyses involving both laboratory animals and male individuals working in the industrial and transportation sectors. These investigations also explore the repercussions of such vibrations on libido. Notably, it has been observed that mechanical vibrations are associated with conditions like oligospermia and teratozoospermia, whereas exposure to elevated temperatures and extended periods of sitting has been linked to reduced sperm motility [11].

In a prospective cohort study conducted by Eisenberg et al. [29], 23% of participants were exposed to whole-body vibrations, and 27% encountered noise in their occupational environments. Parallel to our research, they reported that the mean ejaculate concentration, total sperm count, and DNA fragmentation index (DFI) were relatively lower in the control group. However, their results did not reach statistical significance. Our current study's findings also align with those of Jurewicz et al. [17], who identified a significant negative correlation between occupational exposure to vibrations, decreased sperm motility, and increased DNA fragmentation.

Daoud et al. [30] identified a statistically significant association between exposure to cement and an increased risk of oligozoospermia (adjusted OR: 1.1; 95% confidence interval [CI], 0.9–1.4) in their study. In contrast to the findings of De Fleurian et al. [11], who reported a nearly significant correlation between decreased semen quality and cement exposure, with an OR of 2.5 (95% CI, 0.95–6.5), we observed no statistically significant association between occupational cement exposure and SDF Index (DFI). Furthermore, no prior research has investigated the impact of occupational cement exposure on sperm DFI.

Even in individuals not exposed to occupational risk factors, there is a minimal occurrence of DNA fragmentation in spermatozoa. Several factors may contribute to this phenomenon, including but not limited to age, lifestyle choices, sedentary work habits, infections, and exposure to external factors such as air pollution, environmental contaminants, ionizing radiation, and ambient temperatures. The origin of DNA fragmentation in spermatozoa is nearly inevitable in our everyday lives. Hence, it is worth noting that DNA fragmentation in spermatozoa is a phenomenon that can manifest in males, albeit with varying degrees of prevalence.

Our research offers several notable advantages. Firstly, we conducted a comprehensive assessment of occupational exposure through a questionnaire. This knowledge regarding occupational risk factors can prove to be a valuable tool in clinical settings, aiding medical professionals in the diagnosis and treatment of infertile couples by contributing to a better understanding of the suboptimal SDF Index (DFI). Additionally, our results were adjusted for potential confounding factors that could have an association with sperm DFI. To minimize potential bias, the interviews were conducted in a way that ensured the interviewer had no prior knowledge of the sperm DFI results.

Furthermore, we recruited participants from the same center, collected semen samples consistently, and analyzed sperm DFI using a standardized protocol. The TUNEL method for assessing sperm DFI, based on our experience and the literature, is presented as a valuable tool and a superior fertility indicator compared to standard semen analysis. Lastly, our study holds significance due to the conflicting data in this area and the relatively large sample size.

Limitations

However, our research exhibits several limitations. Firstly, our study population consisted exclusively of infertile men, making it unfeasible to analyze a representative sample of the general male population. Given that these men represent only a subset of the population, it is crucial to exercise caution when interpreting the findings of such research. Additionally, the retrospective nature of the study, relying on data from a single institute's database, introduces the potential for selection bias and limits the generalizability of the results.

The second limitation stems from the use of a self-reported questionnaire as a qualitative measure of exposure and exposure type. Obtaining exposure data through participant interviews can be a challenging task, as their responses may not be reliable due to susceptibility to recall bias and exposure misclassification. As a result, this method is considered less precise compared to biological evaluations of exposure, which offer greater accuracy. However, we assumed that participants had adequate knowledge of their respective work environments.

Third, some of our sub-groups had relatively small sample sizes, leading to wide confidence intervals that could introduce observation bias.

Fourth, our research did not assess the duration or intensity of occupational exposure, which are crucial factors for evaluating their impact on reproductive function.

Finally, due to practical constraints, we were unable to comprehensively analyze the influence of other potential confounding variables, such as body mass index (BMI), education and income levels, physical activity, cell phone use, drug use, and coffee consumption, on sperm DNA damage.

Additional research is necessary to validate the observed associations in this study and implement relevant interventions based on these findings. To thoroughly investigate the link between occupational exposures and DNA fragmentation, comprehensive epidemiological studies should be undertaken. These studies should encompass measurements of bodily excretions, atmospheric specimens, and volatile organic compounds in the environment.

Conclusion

In summary, our research has successfully highlighted that occupational exposure to solvents, metals, pesticides, mechanical vibration, and heat may be considered risk factors associated with increased SDF. Consequently, occupational risk factors should be recognized as potential threats to sperm fertility and reproductive health. This study also reaffirms the utility of utilizing a questionnaire to assess occupational exposure, advocating for its integration into routine consultations to aid in the detection and management of occupational hazards among infertile men. Moreover, it can serve as a valuable tool for patient communication regarding potential workplace risks.

This study stands as the first in Turkey to establish a link between self-reported occupational exposures and SDF Index (DFI). Consequently, our findings can inform health policymakers about the impact of occupational exposure on the reproductive health of the labor force in Turkey. Additionally, men grappling

with infertility should carefully scrutinize their work history, considering that exposure to specific agents may contribute to, if not trigger, infertility.

Finally, our research provides clinicians with valuable insights into occupational hazards, enabling the development of more effective infertility treatment strategies tailored to address specific risk factors. Future research and public health interventions are imperative to gain a more comprehensive understanding of occupational exposures and their implications.

Acknowledgments

The authors extend their heartfelt gratitude to Prof. Ates Kadioglu, from the Department of Surgical Sciences, Division of Urology at Istanbul University, for providing invaluable assistance with clinical data.

References

1. Esteves SC, Sánchez-Martín F, Sánchez-Martín P, Schneider DT, Gosálvez J. Comparison of reproductive outcome in oligozoospermic men with high sperm DNA fragmentation undergoing intracytoplasmic sperm injection with ejaculated and testicular sperm. Fertil Steril. 2015;104:1398–405. doi: 10.1016/j.fertnstert.2015.08.028.
2. Panner Selvam MK, Ambar RF, Agarwal A, Henkel R. Etiologies of sperm DNA damage and its impact on male infertility. Andrologia. 2020;00:e13706. doi: 10.1111/and.13706.
3. Bonde JPE. Occupational causes of male infertility. Curr Opin Endocrinol Diabetes Obes. 2013;20:234–9. doi: 10.1097/MED.0b013e32835f3d4b.
4. Kumar S. Occupational exposure associated with reproductive dysfunction. J Occup Health. 2004;46:1-19. doi: 10.1539/joh.46.1.
5. Figa-Talamanca I, Traina ME, Urbani E. Occupational exposures to metals, solvents and pesticides: Recent evidence on male reproductive effects and biological markers. Occup Med. 2001;51:174–88. doi: 10.1093/occmed/51.3.174.
6. Martenies SE, Perry MJ. Environmental and occupational pesticide exposure and human sperm parameters: a systematic review. Toxicology. 2013;307:66-73. doi: 10.1016/j.tox.2013.02.005.
7. Sharma R, Biedenharn KR, Fedor JM, Agarwal A. Lifestyle factors and reproductive health: taking control of your fertility. Reprod Biol Endocrinol. 2013;11:66. doi: 10.1186/1477-7827-11-66.
8. Evenson DP, Wixon R. Environmental toxicants cause sperm DNA fragmentation as detected by the Sperm Chromatin Structure Assay (SCSA). Toxicol Appl Pharmacol. 2005;207(2):532-7. doi: 10.1016/j.taap.2005.03.021.
9. Tielemans E, Heederik D, Burdorf A, Vermeulen R, Veulemans H, Kromhout H, et al. Assessment of occupational exposures in a general population: comparison of different methods. Occup Environ Med. 1999;56:145-51. doi: 10.1136/oem.56.3.145.
10. Caliskan Z, Kucukgergin C, Aktan G, Kadioglu A, Ozdemirler G. Evaluation of sperm DNA fragmentation in male infertility. Andrologia. 2022;54(11):e14587. doi: 10.1111/and.14587.
11. De Fleurian G, Perrin J, Ecochard R, Dantony E, Lanteaume A, Achard V, et al. Occupational exposures obtained by questionnaire in clinical practice and their association with semen quality. J Androl. 2009;30:566. doi: 10.2164/jandrol.108.005918.
12. Ianos O, Sari-Minodier I, Villes V, Lehucher-Michel MP, Loundou A, Perrin J. Meta-Analysis Reveals the Association Between Male Occupational Exposure to Solvents and Impairment of Semen Parameters. J Occup Environ Med. 2018;60(10):e533-e542. doi: 10.1097/JOM.0000000000001422.
13. Marchetti F, Eskenazi B, Weldon RH, Li G, Zhang L, Rappaport SM, et al. Occupational exposure to benzene and chromosomal structural aberrations in the sperm of Chinese men. Environ Health Perspect. 2012;120(2):229-34. doi: 10.1289/ehp.1103921.
14. Irnandi DF, Hinting A, Yudiwati R. DNA fragmentation of sperm in automobile painters. Toxicol Ind Health. 2021;37(4):182-8. doi: 10.1177/0748233721989892.
15. Migliore L, Naccarati A, Zanello A, Scarpato R, Bramanti L, Mariani M. Assessment of sperm DNA integrity in workers exposed to styrene. Hum Reprod. 2002;17(11): 2912–8. doi: 10.1093/humrep/17.11.2912.
16. Jeng HA, Pan CH, Chao MR, Chiu CC, Zhou G, Chou CK, et al. Sperm quality and DNA integrity of coke oven workers exposed to polycyclic aromatic hydrocarbons. Int J Occup Med Environ Health. 2016;29(6):915-26. doi: 10.13075/ijomeh.1896.00598.
17. Jurewicz J, Radwan M, Sobala W, Radwan P, Bochenek M, Hanke W. Effects of occupational exposure - is there a link between exposure based on an occupational questionnaire and semen quality? Syst Biol Reprod Med. 2014;60(4): 227–33. doi: 10.3109/19396368.2014.907837.
18. Jamalan M, Ghaffari MA, Hoseinzadeh P, Hashemitabar M, Zeinali M. Human sperm quality and metal toxicants: protective effects of some flavonoids on male reproductive function. Int J Fertil Steril. 2016;10(2):215–23. doi: 10.22074/ijfs.2016.4912.
19. Zhou Y, Fu XM, He DL, Zou XM, Wu CQ, Guo WZ, et al. Evaluation of urinary metal concentrations and sperm DNA damage in infertile men from an infertility clinic. Environ Toxicol Pharmacol. 2016;45:68-73. doi: 10.1016/j.etap.2016.05.020.
20. Quintanilla-Vega B, Hoover D, Bal W, Silbergeld EK, Waalkes MP, Anderson LD. Lead effects on protamine-DNA binding. Am J Ind Med. 2000;38:324–9. doi: 10.1002/1097-0274(200009)38:3.
21. Jeng HA, Sikdar S, Huang YL, Pan CH. Mixture analysis of associations between exposure to low levels of multiple metals and semen quality and sperm DNA integrity. J Environ Sci Health - Part A, Toxic/Hazard. 2022;57(4):318–26. doi: 10.1080/10934529.2022.2061256.
22. Perry MJ. Effects of environmental and occupational pesticide exposure on human sperm: a systematic review. Hum Reprod Update. 2008;14:233-42. doi: 10.1093/humupd/dmm039.
23. Mehrpour O, Karrari P, Zamani N, Tsatsakis AM, Abdollahi M. Occupational exposure to pesticides and consequences on male semen and fertility: a review. Toxicol Lett. 2014;230:146-56. doi: 10.1016/j.toxlet.2014.01.029.
24. Bian Q, Xu LC, Wang SL, Xia YK, Tan LF, Chen JF, et al. Study on the relation between occupational fenvalerate exposure and spermatozoa DNA damage of pesticide factory workers. Occup Environ Med. 2004;61:999–1005. doi: 10.1136/oem.2004.014597.
25. Xia Y, Cheng S, Bian Q, Xu L, Collins MD, Chang HC, et al. Genotoxic effects on spermatozoa of carbaryl-exposed workers. Toxicol Sci. 2005;85:615–23. doi: 10.1093/toxsci/kfi066.
26. Gill K, Jakubik J, Kups M, Rosiak-Gill A, Kurzawa R, Kurpisz M, et al. The impact of sedentary work on sperm nuclear DNA integrity. Folia Histochem Cytobiol. 2019;57:15–22. doi: 10.5603/FHC.a2019.0002.
27. Durairajanayagam D, Sharma RK, du Plessis SS, Agarwal A. Testicular Heat Stress and Sperm Quality. In: du Plessis S, Agarwal A, Sabanegh Jr E, eds. Male Infertility. New York: Springer; 2017. Pp. 105-25. doi: 10.1007/978-1-4939-1040-3_8.
28. Bujan L, Daudin M, Charlet JP, Thonneau P, Mieusset R. Increase in scrotal temperature in car drivers. Hum Reprod. 2000;15(6):1355–7. doi: 10.1093/humrep/15.6.1355.
29. Eisenberg ML, Chen Z, Ye A, Buck Louis GM. Relationship between physical occupational exposures and health on semen quality: data from the Longitudinal Investigation of Fertility and the Environment (LIFE) Study. Fertil Steril. 2015;103:1271–7. doi: 10.1016/j.fertnstert.2015.02.010.
30. Daoud S, Sellami A, Bouassida M, Kebaili S, Ammar Keskes L, Rebai T, et al. Routine assessment of occupational exposure and its relation to semen quality in infertile men: a cross-sectional study. Turk J Med Sci. 2017;47(3):902–7. doi: 10.3906/sag-1605-47.