

## Routine assessment of occupational exposure and its relation to semen quality in infertile men: a cross-sectional study

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**Background/aim:** Concerns about the detrimental effects of occupational and environmental exposure on male reproductive function have been raised by reports of declining sperm quality over the last decades. The aim of this study was to investigate the association between altered semen parameters and exposure to occupational risk factors as assessed by questionnaire.

**Materials and methods:** We conducted a cross-sectional questionnaire-based study among a population of 2122 men who underwent andrological investigation for couple infertility. All participants were interviewed and their semen samples were analyzed. Information about medical history and occupational exposure was used to classify participants into exposed and unexposed groups.

**Results:** Exposure to pesticides was associated with a significantly higher risk of asthenozoospermia (adjusted odds ratio [OR] = 1.6; 95% CI, 1.0–2.4) and necrozoospermia (OR = 2.6; 95% CI, 1.4–4.7). Exposure to cement was found to be correlated with a higher risk of oligozoospermia (OR = 1.1; 95% CI, 0.9–1.4). There was no association between semen impairment and exposure to solvents, excess heat, or mechanical vibrations.

**Conclusion:** We found an association between self-reported occupational exposure and altered semen parameters. These results support the usefulness of questionnaires for routine assessment and management of occupational exposures in infertile men.

**Key words:** Male infertility, occupational exposure, questionnaire, semen quality

### 1. Introduction

It is estimated that one in six couples has problems conceiving a child. Despite its negative psychological and social impact, the financial burden of infertility is substantial. A male factor is responsible in about half of infertile couples (1). Furthermore, increasing evidence suggests a decline of semen quality in developed countries over the past decades (2–4). In a previous report (5), we found the same trend among a Tunisian infertile population with a decreased sperm count and morphology for over a decade. Several hypotheses have been advanced to explain these observations, such as exposure to occupational and environmental pollutants and rapid changes in lifestyles (6).

In the literature, risk factors are continuously added to a long list of specific occupational exposures that could alter male reproductive function. A number of reviews have pointed out that exposure to chemical agents such

as pesticides, solvents, and heavy metals could result in reduced semen quality and increased abortion rates (7,8). Excess heat, mechanical vibrations, ionizing radiations, and, recently, electromagnetic fields are classified as physical factors and reported to increase the risk of disrupted spermatogenesis and altered sperm parameters (7,9).

Assessing the effects of occupational exposures on fertility is difficult given the wide variety of epidemiologic methods used for this purpose. Experimental animal models provide interesting information about specific exposure targets and their mechanisms of toxicity. However, the results of these studies need to be interpreted with caution.

Despite its limitations (10), self-reported exposure was reported to have similar accuracy and reliability to other common methods of exposure assessment, such as quantitative exposure measurement (11) and job-exposure matrices (12).

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In the present study we aimed to investigate the association between semen quality and self-reported occupational exposures among infertile men. To accomplish this goal, we designed a questionnaire for use during routine consultation in couples attending our reproductive biology laboratory for infertility investigation.

## 2. Materials and methods

### 2.1. Study population

We conducted a retrospective cross-sectional study on 2122 men attending the Laboratory of Histology, Embryology and Reproductive Biology at the Faculty of Medicine of Sfax, Tunisia, for couple infertility. Study subjects were recruited between January 1996 and December 2012. Each one of them provided at least one semen sample for analysis as a part of the infertility investigation of the couple. Subjects with a known male infertility factor that was not linked to occupational exposure were excluded: varicocele, cryptorchidism, genetic or endocrine disorders, urogenital tract infection, and medication associated with male fertility impairment. We also excluded those aged under 20 or above 55 years.

### 2.2. Study design

All patients' data were extracted from a database built on the basis of a questionnaire that consisted of two sections. The first section includes questions about age, geographic origin, lifestyle, medical history, and risk factors for semen quality impairment. The second section focuses on occupational information, i.e. job title and duties and duration of occupational exposure. All questionnaires were completed by four trained interviewers during routine consultations.

We tried to keep the questionnaire short and focused by including only risk factors that were most related to male fertility impairment in the literature. Information about occupational exposure was used to classify subjects into exposed or unexposed groups. Those classified as

potentially exposed were divided into six categories as detailed in Table 1.

During the data collection process, we considered occupational activities undertaken in the 3 to 6 months before semen analysis. One semen analysis was considered for each subject. A shorter period between filling out questionnaire date and semen analysis date was the main selection criterion if there was more than one semen analysis.

Ethical approval for the study was obtained from the Research Ethics Committee of the Faculty of Medicine of Sfax, Tunisia.

### 2.3. Semen analysis

Semen samples were collected in the laboratory by masturbation after 2–5 days of abstinence. After liquefaction, semen analysis was performed by two trained technicians according to prevailing guidelines of the World Health Organization (WHO) at the time of analysis (13–15). This test evaluates ejaculate volume, sperm count, motility, vitality, and morphology. The modified David classification was used to assess sperm morphology (14).

In the present study, semen anomalies were defined according to the WHO 5th edition criteria as follows (15): hypospermia (semen volume <1.5 mL), oligozoospermia (sperm count <15 × 10<sup>6</sup>/mL), asthenozoospermia (sperm progressive motility <32% or sperm total motility <40%), and necrozoospermia (sperm vitality <58%). Teratozoospermia was defined by a percentage of normal forms less than 30%, according to the fourth edition of the WHO manual (14) for sperm morphology assessment using David's classification.

### 2.4. Statistical analysis

Statistical analysis was carried out using SPSS version 13.0 (IBM Corp., Armonk, NY, USA) in order to compare age, duration of infertility, and semen parameters between unexposed and exposed groups (chi-square test). Logistic regression models adjusted for age and abstinence period were performed to evaluate the odds of semen abnormalities as a function of exposure risk factor.

**Table 1.** Occupational exposure groups considered by the questionnaire.

Occupational exposure group		Occupational activities
Unexposed group		Teacher, professor, lawyer, physician, trader
Exposed group	Pesticides	Farmer, gardener
	Solvents	Painter, printer, carpenter, shoe and leather worker, rubber and plastic product maker
	Cement	Bricklayer, cement industry worker
	Mechanical vibrations	Truck and fork-lift driver, pneumatic drill worker
	Excess heat	Baker, cook, blacksmith, welder

### 3. Results

Overall, the median age was  $36 \pm 6$  years, and two out of three men (65%) were aged between 30 and 40 years. Of the 2122 men included, 1804 (85%) lived in urban areas and 318 (15%) were rural inhabitants. Most of the participants (86%) were from the city of Sfax and surroundings. The mean infertility duration was  $3.7 \pm 3$  years.

Based on questionnaire information, we classified 847 (40%) men as unexposed and 1275 (60%) men as exposed to occupational risk factors. There was no significant difference with regard to age between exposed and unexposed groups (35.8 vs. 36.2 years). Mean duration of infertility was significantly longer in the exposed group (3.6 vs. 4.4 years,  $P = 0.01$ ).

The most common risk factor identified in our exposed population was cement (35.3%), followed by solvents (31.4%) and pesticides (11%). Exposure to mechanical vibrations and excess heat concerned only 16.4% and 6% of exposed men, respectively.

A comparison of semen parameters between the exposed and unexposed categories is shown in Table 2. Semen parameters were comparable between the unexposed and total exposed groups. However, there was a significant decrease in semen volume, motility, and vitality in men exposed to pesticides.

Considering WHO thresholds, the total exposed group was at a higher risk of oligozoospermia (adjusted odds ratio [OR] = 1.1; 95% confidence interval [CI], 0.9–1.4;  $P = 0.04$ ) (Table 3).

Exposure to pesticides was associated with a significantly higher risk of asthenozoospermia (OR= 1.6; 95% CI, 1.0–2.4;  $P = 0.02$ ) and necrozoospermia (OR = 2.6; 95% CI, 1.4–4.7;  $P = 0.001$ ). Exposure to cement was found to be correlated to a higher risk of oligozoospermia (OR = 1.1; 95% CI, 0.9–1.4;  $P = 0.05$ ).

Finally, there was no evidence of significant association between semen parameters and exposure to solvents, excess heat, or mechanical vibrations.

### 4. Discussion

This is, to the best of our knowledge, the first epidemiological study that investigates the hazardous effects of occupational exposure on male fertility in Tunisia and North Africa.

In Tunisia, uncontrolled use of pesticides for several decades has led to a worrying situation. Despite being banned since the early 1980s, highly toxic pesticides such as polychlorinated biphenyls (PCB), organochlorine (OC), and dichlorodiphenyltrichloroethane (DDT) are suspected to have persistent environmental and health effects on the Tunisian population (16,17). There are also concerns about old stocks of obsolete pesticides scattered throughout the country and causing disposal problems (18).

In our study, we found that semen volume, motility, and vitality were decreased in men exposed to pesticides. These findings suggest that some pesticides could affect posttesticular sperm maturation, in which epididymis, prostate, and seminal vesicles are particularly involved. Likewise, Yurca et al. (19) noted reduced seminal volume, percentage of motility, percentage of normally shaped sperm, and seminal zinc concentration (a marker of prostatic secretory function), and increased seminal pH among Peruvian pesticide sprayers. They pointed out a disruptive role of pesticides on sex hormones activities, which could lead to secretory dysfunction of male accessory glands (19). Sperm motility decrease was also reported in cases of specific pesticide exposure such as pyrethroids (20), organochlorines (21,22), and organophosphates (23,24), as well as multiple pesticide exposure (25). In a synthesis review of four cross-sectional studies of the INUENDO project assessing the impact of persistent organic pollutants (POPs) on human fertility (26), PCB congener CB-153 blood levels were inversely related to sperm motility and to neutral  $\alpha$ -glucosidase activity, a marker of epididymal function. Hence, it is thought that a posttesticular effect of POPs, occurring during epididymal sperm transit, could affect the acquisition of progressive motility (26).

**Table 2.** Comparison of the average of semen parameters between exposed (n = 1275) and unexposed subjects (n = 847).

	N (%), Total = 2122	Volume (mL) Mean (SD)	Count ( $\times 10^6$ /mL) Mean (SD)	Motility (%) Mean (SD)	Vitality (%) Mean (SD)	Normal morphology (%) Mean (SD)
Unexposed	847 (40)	3.3 (1.6)	61.1 (75.6)	40.6 (15.2)	64.2 (18.6)	16.9 (15.1)
Total exposed	1275 (60)	3.3 (1.7)	60.6 (75.8)	39.3 (15)	64.8 (18.5)	16.0 (15.1)
Pesticides	140 (6.6)	2.9 (1.8)*	62.7 (74.3)	35 (16.3)*	55.4 (23.7)*	17 (14.3)
Solvents	400 (18.8)	3.2 (1.7)	57.8 (70)	39.5 (14.7)	64 (18.2)	15.4 (14.2)
Cement	450 (21.2)	3.2 (1.6)	62.5 (84.7)	39.5 (14.5)	65.2 (17.3)	15 (15.1)
Mechanical vibrations	209 (9.8)	3.6 (1.6)	57.7 (72.5)	39.7 (15.7)	66.6 (18.3)	18.2 (17.4)
Excess heat	76 (3.6)	3.5 (1.6)	62.2 (69.1)	42.7 (14.6)	66.9 (18.6)	17.9 (16.1)

\* $P < 0.05$

**Table 3.** Comparison of semen abnormalities between exposed (n = 1275) and unexposed subjects (n = 847).

	Hypospermia			Oligozoospermia			Asthenozoospermia			Necrozoospermia			Teratozoospermia		
	%	OR* (95% IC)	P	%	OR (95% IC)	P	%	OR (95% IC)	P	%	OR (95% IC)	P	%	OR (95% IC)	P
Unexposed	17			33			47			19			43		
Total exposed	20	1.4 (0.9–1.8)	0.09	37	1.1 (0.9–1.4)	0.04	49	1.1 (0.9–2.2)	0.5	17	0.9 (0.7–1.4)	0.6	47	0.9 (0.7–1.1)	0.4
Pesticides	27	1.2 (0.9–1.4)	0.07	38	1.3 (0.9–1.9)	0.1	59	1.6 (1.0–2.4)	0.02	37	2.6 (1.4–4.7)	0.001	52	0.7 (0.3–1.4)	0.3
Solvents	22	1.0 (0.8–1.3)	0.8	36	1.1 (0.87–1.47)	0.32	48	1.9 (0.9–3.5)	0.8	19	1.1 (0.6–1.7)	0.9	46	0.7 (0.5–1.1)	0.2
Cement	20	1.2 (0.7–2.05)	0.4	38	1.2 (1.6–1.9)	0.05	48	1.4 (0.7–2.2)	0.9	14	1.3 (0.7–2.5)	0.4	50	1.06 (0.7–1.5)	0.7
Mechanical vibrations	16	0.4 (0.2–0.97)	0.1	38	1.3 (0.97–1.8)	0.07	49	0.9 (0.5–1.4)	0.7	17	2.2 (0.5–6.4)	0.6	42	0.8 (0.5–1.2)	0.3
Excess heat	21	2 (1.3–3.2)	0.6	36	1.2 (0.7–2.05)	0.37	43	2.5 (0.95–6.5)	0.6	13	1.4 (0.7–2.0)	0.8	46	1.05 (0.6–1.8)	0.1

\*OR: odds ratio; IC: confidence interval;

Exposure to cement was the most common occupational factor identified in our study population. In fact, according to the Tunisian National Statistics Institute (INST), it is estimated that over 22% of the male active population of Sfax are employed in building and public works and the construction materials sectors (27). Workers may be exposed to cement dust at two levels: either in the cement production industry or during building and construction activities. We found that cement exposure was correlated to a higher risk of oligospermia. There are almost no data in the literature about the relationship between cement exposure and semen quality, except for the study by De Fleurian et al. (28). In their questionnaire-based study conducted in 402 infertile French men, cement exposure was found to be correlated to impaired sperm motility and morphology.

Cement composition is a complex mixture of limestone, clay, gypsum, and many metals such as chromium, thallium, selenium, nickel, and arsenic (29,30). Workers exposed to cement are reported to be at higher risk of respiratory and dermal irritation by the route of inhalation and skin contact (31,32). Nevertheless, other adverse health effects might be underestimated given the finding of elevated tissues and blood metal and metalloid levels among cement-exposed workers (33–35). Moreover, there is growing evidence of detrimental effects of environmental and occupational exposure to metals on semen quality (36,37). Many mechanisms for metal-induced exposure are involved in the alteration of reproductive function, including spermatogenesis disorders, oxidative stress, and endocrine disruption (36). Nevertheless, the influence of associated metal exposure, being the most frequent situation in practice, is still unclear. In future work, we intend to investigate cement exposure effects on male fertility, taking into account the

complexity of this exposure and the possible contribution of confounders.

Although the use of solvents is widespread in the region of Sfax, especially in the shoe and leather industry (38), semen quality was not affected in the solvent-exposed group. Duration and intensity of solvent exposure, which are determining for their impact on reproductive function, were not assessed in our study. Moreover, despite the large number of studies focusing on solvent exposure, there is a lack of evidence about their specific effects on male fertility (39). This is mainly due to substantial heterogeneity between these studies with regard to exposure characterization, the study population, and the choice of the measurement of fertility.

The lack of statistical association between exposure to physical factors and semen quality does not exclude such a relationship. One possible explanation for our result is the relatively small number of exposed participants, for whom information about the extent of exposure is not specified.

In this study, we tried to respect literature recommendations regarding optimization of exposure estimation methods. The use of an objective and measurable endpoint (sperm parameters), questionnaire formulation on the basis of the literature and of expert opinion, and the use of a simple and familiar vocabulary for better understanding of the questions are highly recommended (10).

Another strong point of this survey is that questionnaire was designed for routine consultation, allowing us to considerably enlarge our study population. Moreover, semen quality was used as a direct and objective measurement of male reproductive capacity (40), and all semen samples were analyzed by the same technicians with respect to standardized procedures. In order to minimize differential misclassification, the questionnaire

was filled out in the same conditions by a limited number of interviewers, regardless of the result of semen analysis.

However, there were a number of limitations in this study. Although the assignment of subjects to single (group of) agents is widely applied in retrospective occupational studies, there is usually a lack of evidence about the effect of possible combined exposure. In fact, exposure to a single occupational factor is rare, and there may be a wide variability in the duration and the intensity of exposure. In addition, nonoccupational risk factors that can affect male fertility, such as smoking and alcohol consumption, were not analyzed in this study.

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