Check for updates

International Journal of Immunopathology & Pharmacology

Original Research Article

International Journal of Immunopathology and Pharmacology
Volume 36: 1–8
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/20587384211066718
journals.sagepub.com/home/iji
SAGE

Abnormal sperm morphology is associated with sensitization to inhaled allergens

Rafał Adamczak[1], Natalia Ukleja-Sokołowska[2], Magdalena Pasińska[3], Joanna Zielińska[4], Mateusz Leśny[4] and Mariusz Dubiel[1]

Abstract

Background: Allergy is associated with the loss of tolerance of environmental antigens, combined with a pathological immune response. There were no studies up to date that would show whether the quality of semen decreases in people with allergic diseases. Material and methods: The research included men who reported to the Gynecological Outpatient Clinic due to reproductive difficulties, defined as the lack of pregnancy after one year of regular intercourse. Semen quality was assessed according to the World Health Organization (WHO) standard. All patients underwent skin prick tests with the most important inhalation allergens (such as hazel, silver birch, mugwort, rye, dog, cat, *Dermatophagoides farinae, Dermatophagoides pteronyssinus*, alder, *Alternaria alternata, Cladosporium herbarum*, and grass mix). The data was statistically analyzed. Results: Results of 52 patients aged 25–52 years (34.62 ± 4.96) were analyzed. The mean BMI (Body mass index) was 28.25 (+ −3.77). It was found that 38 men (73%) had increased body weight, and 14 men (26.9%) were obese (BMI > = 30). 13 patients were smokers (25%), and 24 patients (46%) had skin tests positive for at least one inhaled allergen. Sperm tail defects were statistically more significant in patients allergic to birch, rye, cat, alder, and grass. In patients allergic to *Alternaria alternata*, head defects were statistically more significant ($p < .05$). No association was found between allergy to house dust mites, mugwort, hazel, and dogs and the deterioration of semen. Conclusion: Allergy due to inhalation allergens had an influence on the quality of male semen. Further research is necessary to establish the immunological bases of this phenomenon.

Keywords

reproduction, semen, allergy, fertility, allergens

Date received: 17 May 2021; accepted: 18 November 2021

Introduction

Over the past 50 years, the quality of semen in men of reproductive ages has declined sharply. The key to fertilization is when a spermatozoid can travel from the testicles to the fallopian tube. This process is controlled by extra and intracellular factors, which also play a key role in the regulation of sperm motility and during the process of chemotaxis.[1]

It is very important to analyze the causes of deterioration of male semen. Etiology of this process takes into account environmental pollution, smoking, age, and all the accompanying diseases. Obesity is also an increasing issue. It

[1]Department of Obstetrics, Gynecology and Oncology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland
[2]Department of Allergology, Clinical Immunology and Internal Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland
[3]Department of Clinical Genetics, Faculty of Medicine, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń, Poland
[4]Student Scientific Society, Department of Allergology, Clinical Immunology and Internal Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland

Corresponding author:
Natalia Ukleja-Sokołowska, Department of Allergology, Clinical Immunology and Internal Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Ujejskiego 75, Bydgoszcz 85-168, Poland.
Email: ukleja@10g.pl

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

is worth noting that in the last 50 years, there has been a dramatic increase in the incidence of allergic diseases in the population of developed countries. In fact, allergy is associated with the loss of tolerance of environmental antigens, associated with a pathological immune response.[2] There were no studies that would show whether the quality of semen decreases in people with allergic diseases.

The aim of this research is to compare the sperm parameters in patients with and without sensitization to common inhaled allergens. The data underwent statistical analysis to establish if there is an association between allergy and the quality of sperm.

Material and methods

The study included men who reported to the Gynecological Outpatient Clinic due to reproductive difficulties, defined as the lack of pregnancy in a relationship after one year of regular intercourse. All patients went through detailed medical interview and physical examination, including examination of the prostate and external genitalia.

Exclusion criteria were as follows:

1. Serious, chronic diseases and patients on medication that could impact the results of this study.
2. Past surgery concerning testicles in the medical interview.
3. Problems with sexual function in the interview (e.g., difficulty with ejaculation or small volumes of fluid ejaculated, erectile dysfunction).
4. Abnormalities in the examination of the testicle area (pain, swelling, or a lump in the area, varicocele).
5. Signs of a chromosomal or hormonal abnormality in physical examination (gynecomastia, decreased facial or body hair, or other).
6. Ongoing or completed allergen-specific immunotherapy.

This cross-sectional study took place between August 2018 and December 2019. The size of the study population was established prior to conducting the study and was based on previous studies concerning allergen profile of patients allergic to canine and inhaled allergy, as well as different causes of deteriorated semen parameters. Another factor taken into account when establishing the size of population was the financial support received for the research.[3,4]

Patients who met the criteria were qualified for the study so as to report to the Clinic. Detailed medical history and environmental history were gathered, and all the patients underwent a physical examination. Their heights and weights were measured. The semen quality was assessed in the participants' partners according to the WHO standard of seminology assessment, using the computer-assisted semen analysis (CASA). Biological materials were submitted for analysis immediately after its receipt by masturbation. Moreover, skin prick tests with inhalation allergens were also performed in all the patients using the HAL kit (including positive control, negative control, hazel, silver birch, mugwort, rye, dog, cat, *Dermatophagoides farinae, Dermatophagoides pteronyssinus*, alder, *Alternaria alternata, Cladosporium herbarum*, and grass mix). Skin prick tests were considered to be positive if the mean diameter of the resulting blister was 3 mm, with normal skin reactivity (histamine > = 3 mm, negative control negative), which is the most commonly used method.[5,6]

A permission was obtained from the Committee of Bioethics no. KB 432/2018 to carry out the study. The study was funded by the Statuary Activity of the L. Rydygier Collegium Medicum, Nicolaus Copernicus University, WL-121. The authors declare no conflict of interests in regards to this research.

All patients submitted their written informed consents on the participation in the study.

Statistical analysis was performed with the help of Microsoft Excel 365 and R software, version 4.0.3. Comparison of values of quantitative variables between two groups was performed using the Mann–Whitney U test. Correlations between quantitative variables were analyzed using the Spearman's correlation coefficient. A significance level of 0.05 was adopted in the analysis. Thus, all p values below .05 were interpreted as showing significant relationships.

Results

Results of 52 patients aged 25–52 years (34.62 ± 4.96) were analyzed. The mean BMI was 28.25 (+3.77). It was found that 38 men (73%) had increased body weight, and 14 men (26.9%) were obese (BMI> = 30). 13 patients were smokers (25%). The patients donated 0.5–9 ml of semen for the study. The evaluation of semen parameters is presented in Table 1.

It was found that in the studied population, age correlated significantly ($p < .05$) and positively ($r > 0$) with the semen leukocyte count and with the presence of immobile and abnormal spermatozoids. Moreover, age correlated significantly ($p < .05$) and negatively ($r < 0$) with parameters such as progressive movement and normal spermatozoids. In general, the older the age, the worse were the semen parameters in the study population. Results of the analysis are presented in Table 2.

No correlation was demonstrated between male body weight, BMI, and semen quality ($p > .05$).

Smoking had a statistically significant ($p < .05$) effect on the Teratozoospermia index (Figure 1). No statistically significant influence was found on the remaining semen parameters.

In the study population, 24 patients (46%) had positive skin tests for at least one inhaled allergen. The number of patients with positive skin tests for individual allergens is shown in Figure 2.

Table 1. Semiogram of patients, with the analysis of abnormalities.

Assessed parameter	Mean	SD	Median	Min	Max	Q1	Q3
No. of round cells (M/mL)	1.83	1.22	1.5	0.2	5.9	1	2.2
Leukocyte count (M/mL)	0.24	0.2	0.2	0	0.9	0.1	0.3
Concentration (M/mL)	73.47	91.25	43.9	1	389.9	9.45	92.1
Total count in ejaculate (M)	260.35	328.76	152.25	1	1370.6	40.75	329.83
Viability (%)	56.84	15.78	56.5	21	87	46.25	67.5
Progressive movement (%)	30.57	17.54	28	1	70	15	45.5
Non-progressive movement (%)	9.33	3.69	9	0	19	7	10.75
Immobile (%)	60.26	17.61	63	24	92	46.5	73
Normal spermatozoids	7.2	4	6.5	0	18	5	10
Abnormal spermatozoids	92.98	3.86	94	82	100	90	95
Defects of the head	88.8	5.15	89	78	99	86	92
Defects of the midpiece	28.37	11.27	27	9	52	19	35
Defects of the tail	8.93	11.82	5	0	62	2	11
Cytoplasm drops	0.38	0.88	0	0	5	0	0.75
Teratozoospermia index	1.37	0.16	1.3	1.1	1.7	1.3	1.5

Table 2. Relationship between age and semen condition.

	Age
Semiogram	Spearman correlation coefficient
No. of round cells (M/mL)	r = 0.166. p = .274
Leukocyte count (M/mL)	r = 0.352. p = .012*
Concentration (M/mL)	r = 0. p = .998
Total count in ejaculate (M)	r = 0.02. p = .89
Viability (%)	r = −0.033. p = .836
Progressive movement (%)	r = −0.369. p = .011*
Non-progressive movement (%)	r = −0.028. p = .853
Immobile (%)	r = 0.354. p = .015*
Normal spermatozoids	r = −0.312. p = .035*
Abnormal spermatozoids	r = 0.301. p = .045*
Defects of the head	r = 0.155. p = .335
Defects of the midpiece	r = 0.043. p = .788
Defects of the tail	r = 0.161. p = .315
Cytoplasm drops	r = 0.015. p = .923
Teratozoospermia index	r = 0.113. p = .487

The effect of the presence of allergy to at least one inhaled allergen on semen quality was analyzed and no relationship was found. The situation was slightly different in the case of the analysis of allergy to individual allergens. It turned out that sperm tail defects were statistically more significant in patients allergic to birch, rye, cat, alder, and grass ($p < .05$)—Figure 3. In patients allergic to *Alternaria alternata*, head defects were statistically more significant ($p < .05$). However, no association was found between allergy to house dust mites, mugwort, hazel, and dogs and the deterioration of semen.

Discussion

In developed countries, 14% of couples have difficulties related to pregnancy.[7] Male infertility occurs in approximately 40% of the cases.[8]

A number of causes are considered to contribute in the deterioration of the semen quality. The influence of environmental pollution, sedentary lifestyle, the influence of mobile phones, obesity, smoking, and many other factors are taken into account.[9–11]

Overweight and obesity are a growing problem in the general population. According to the epidemiological study

completed in 2013, these complications affect about 36.9% of men. This is a significant increase since 1980, when BMI> 25 was found to be 28.8%.[12] Shayeb AG et al. found that obese men had a lower volume of semen, but the semen parameters were normal.[13] In the study by Belloc S. et al., conducted from 2010 to 2011 on a large population of 10,665 men, it was found that increased BMI had an impact on reduced sperm quality, volume, concentration, and mobility. It had no effect on the number of normal spermatozoids.[14] In 2010 and 2013, two meta-analyses were published, the conclusions of which were contradictory. Sermondade et al. found that obesity increased the risk of abnormal sperm count.[15] However, in a study by MacDonald et al., no relationship was found between BMI and semen quality.[16] Our research did not confirm the existence of a relationship between being overweight and obese and semen quality. At the same time, there were a significant percentage of overweight and obese men in the study population.

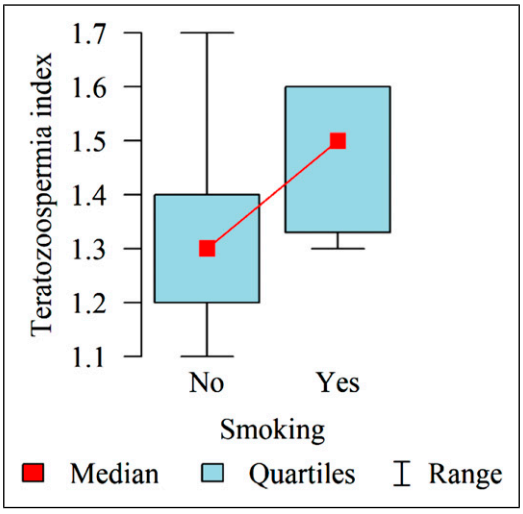

Figure 1. Smoking and tetratozoospermia index.

Smoking is a recognized factor deteriorating semen quality. The meta-analysis published in 2016, based on the analysis of 5865 cases of men, indicated that smoking reduced the number of spermatozoids and their viability.[17] Asare-Anane H. came to similar conclusions, indicating a significantly lower semen volume, spermatozoid concentration, motility, and total count.[18] In our study, smoking had a statistically significant ($p < .05$) effect only on the Teratozoospermia index.

Another important parameter taken into account in our analysis was the age of the patients. It was found that with age, semen parameters deteriorated, including an increase in the presence of immobile and abnormal spermatozoids, as well as a decrease in the progressive movement and the count of normal spermatozoids. During the research of Li WN. et al. in 2019, which included an analysis of 71,623 infertile men who were diagnosed at the Reproductive and Genetic Hospital in Hunan, China between 2011 and 2017, it was found that various semen parameters decreased with the age of patients, and that the concentration and motility of spermatozoids were the best predictor of fertility.[19] In a 2018 study from Hong Kong, it was found that age > = 40 years is negatively correlated with the volume of semen and the progressive movement of spermatozoids.[20]

It is interesting to analyze the influence of atopic diseases on semen quality. The incidence of these diseases is increasing in Poland. There are many reports of the development of post-coital symptoms in women with atopic diseases. Hypersensitivity to semen, manifested by symptoms developing after sexual intercourse, was already described in the 1970s.[21] Symptoms of semen hypersensitivity in women may take the form of local reactions as

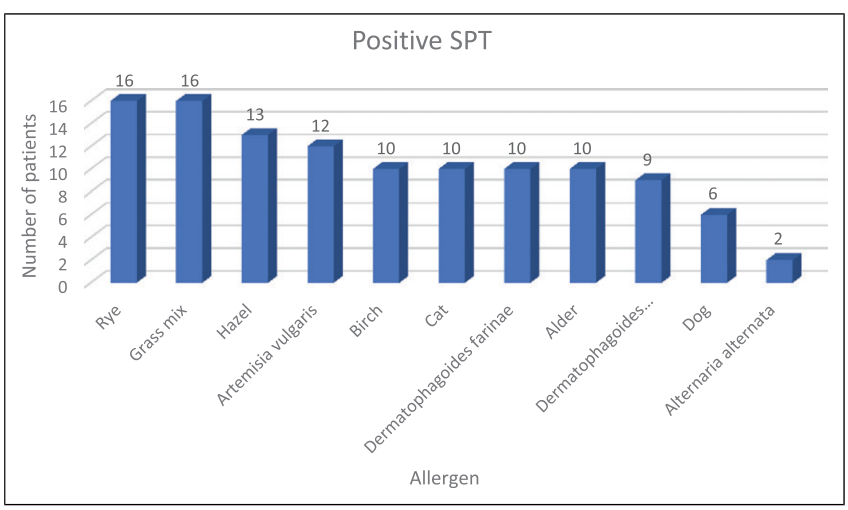

Figure 2. Distribution of positive skin tests for individual allergens in the studied population.

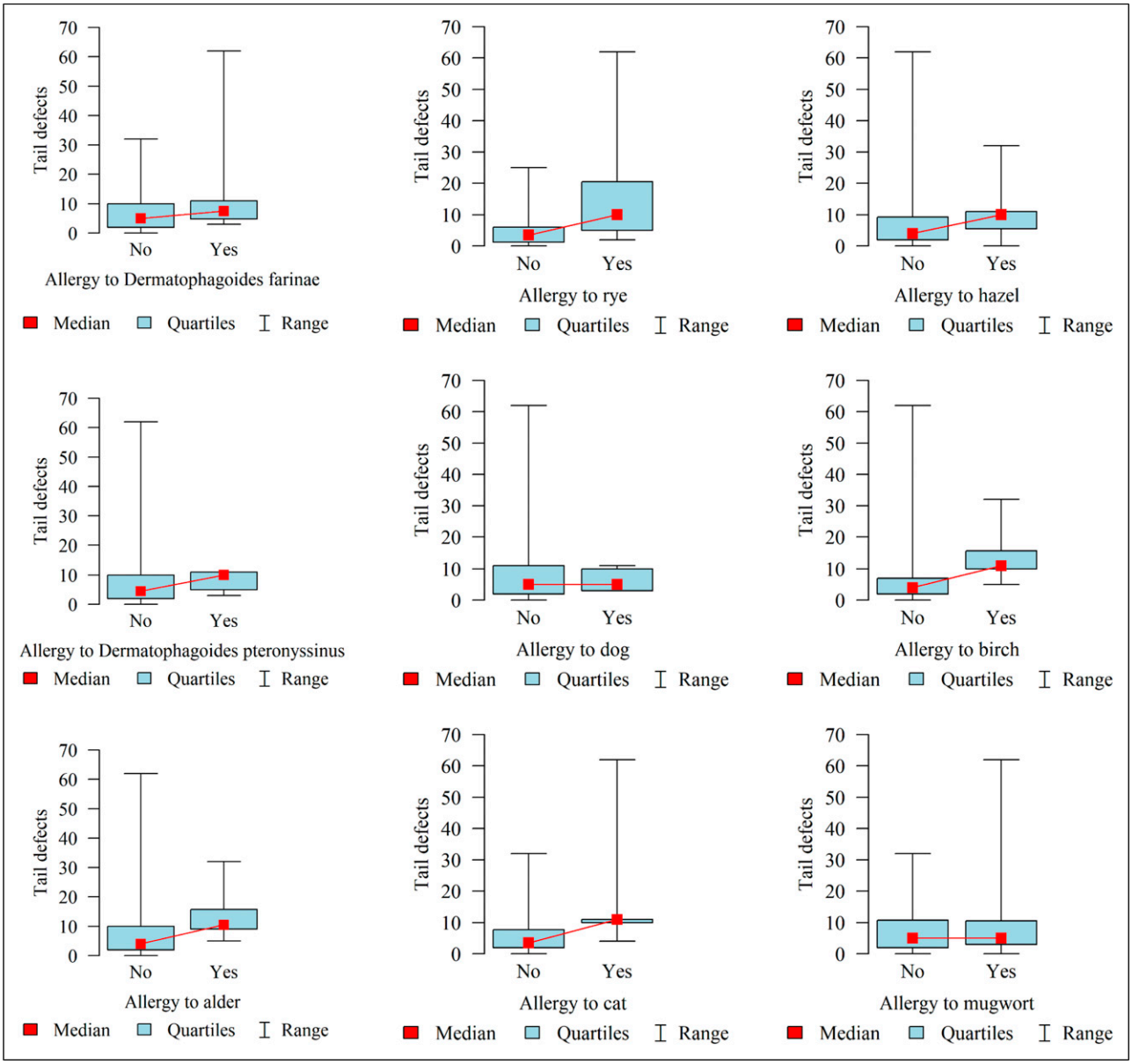

Figure 3. Occurrence of sperm tail defects in patients allergic to individual allergens.

well as severe generalized reactions (*human seminal plasma anaphylaxis*—HSPA).[22,23] An interesting issue is the reported cross-allergy, which occurs in patients who are allergic to dogs. Can f 5, a prostate kallikrein, which is structurally related to human prostate-specific antigen (PSA), is the major allergen among canine antigens that are potentially sensitizing in women.[24,25] Esfandiari et al. found that the prevalence of allergy among female patients seeking infertility treatment is high compared to the general population (54,7% vs 10–30%). However, allergy was not found to be associated with in vitro fertilization (IVF) cycle outcomes.[26]

The way atopic diseases influence infertility may have different etiopathogenesis. It might be gathered with low grade systemic inflammation, influence of medication used to treat allergies, hypersensitivity to fertility treatment, and possibly other factors as well.[27]

There are studies showing it is likely that systemic inflammation found in asthma patients also affects the uterine mucosal layer and impairs effective implantation of the embryo. Inflammatory cells play an important role in reproductive health during pregnancy. However, controlled asthma may be associated with a reduced risk of infertility, even if the exact mechanism remains unclear.[28,29] An interesting case report was published on two women, who were able to conceive naturally after starting mepolizumab treatment for severe eosinophilic asthma. Although in

general, mepolizumab is contraindicated in pregnancy due to lack of safety data, it is possible that unexplained infertility in people with severe eosinophilic asthma may be corrected by mepolizumab treatment, or effective asthma treatment in general.[30]

One interesting subject is the use of medication on male fertility. Histamine receptors (HRH1, HRH2, and HRH4) have been described in Leydig cells of different species, including human. Furthermore, HRH1 and HRH2 receptors are present in peritubular and germ cells, and HRH2 antagonists have been found to negatively affect peritubular cells and reduce sperm viability. Testicular mast cells are the major source of locally produced histamine. It should then be considered that anti-histamines may affect testicular homeostasis by increasing or decreasing steroid production.[31] Anti-histamines are widely used in most allergic diseases and are available OTC in many countries. Additional data on a large population are required to show the real-life influence of long-term anti-histamine treatment on sperm parameters.

In dermatology, the negative effect of treatment of common conditions on male fertility is well recognized. Administration of methotrexate and finasteride has resulted in severe oligospermia and reversible infertility. Ketoconazole has had negative effects on sperm motility and testosterone production. There are also some limited data on negative effects of tetracyclines, erythromycin, chloroquine, glucocorticoids, spironolactone, and antihistamines on fertility.[32]

The association of fertility with other atopic diseases is less recognized. In 2020, Napolitano et al. published an interesting systematic review of the influence of treatment on fertility in atopic dermatitis (AD) patients.[28] The JAK/STAT pathway has been shown to be involved in cell adhesion and cell polarity. Baricitinib in a dose high above registered for humans has shown to reduce fertility, have a teratogenic effect, reduce bone growth and fetal weight in the uterus, and increase embryolethality in a murine model.[33] The impact of new systemic, biological medications (Dupilumab, Lebrikizumab, and Fezakinumab) for AD on future fertility is largely unknown. In most cases, animal models have shown no negative effect, but it does not exclude an adverse impact on human gametes or reproduction.[28]

It is worth noting that basic semen parameters, sperm functions, and DNA integrity may be affected by chronic inflammation of the male genital tract. Adequate management of affected patients appears mandatory, but low-dose corticosteroids, used also in allergic disorders, can be considered as one of the therapeutic options.[34]

As per our knowledge, the current study is the first in trying to answer the question whether the presence of atopic diseases has an impact on the quality of semen. In 2009, Allam JP analyzed the influence of mast cells—key cells in the development of allergic reaction symptoms—on sperm quality. The researchers found no correlation between a higher concentration of mast cells and significant semen parameters.[35]

In the group of patients we studied, sperm tail defects were more common in patients allergic to birch, rye, cat, alder, and grass. Head defects were found to be significantly more frequent in patients allergic to *Alternaria alternata*. This observation certainly requires further research. It can be hypothetically assumed that a chronic inflammation associated with an allergic disease affects semen quality. It is known that the semen of healthy men contains numerous interleukins, including cytokines responsible for the Th2 response, such as IL 10 and IL 13.[36] The response dependent on pro-inflammatory cytokines (IL-17, IL-6, IL-18, and IL-12) and related to corresponding Th (IFN-γ, IL-4, IL-10, and IL-13) underlies atopic diseases.[37]

Risk factors for allergic diseases and fertility problems may be similar to some extent. Environmental pollution is a frequently described etiological factor for atopic diseases.[38] Environmental contamination is also one of the factors that can potentially reduce the quality of semen.[39,40] Unfortunately, the qualitative and quantitative differentiation of particles that create environmental pollution make it difficult to compare reports published so far and draw final conclusions.[41]

Limitations of this study include relatively small patients' population. An interesting approach would be to widen allergy diagnosis, for instance, using molecular in vitro methods to find an association between specific allergen components sensitization and sperm parameters. Some defects could be gathered with direct influence of specific IgE or IgG due to cross-reactivity. There is scarce data on this subject, although were reports on antigenic cross-reactivity between the venom allergen (antigen 5) and mammalian testis proteins, which did not possess a high risk to develop autoantibodies, leading to infertility.[42] Another limitation of the study is the lack of detailed examination of other causes of male infertility, including hormonal and immunological profile, and karyotype assessment. Exclusion criteria were based on the interview and medical history, followed by careful physical examination (which included genital area assessment). Further in-depth studies are required to examine other possible patomechanisms behind the observed sperm defects, on a large population of patients.

Conclusion

There is no doubt that the development of civilization has brought about some changes in our living environment, diet, and lifestyle of far-reaching consequences. Amongst them, there is certainly an increase in the frequency of

atopic diseases and the growing problem of infertility. Finding associations among the factors causing the above-mentioned abnormalities may help to understand better the natural course of these diseases.[27]

In our research, we found an association between sperm tail defects and allergy to birch, rye, cat, alder, and grass. Head defects were found to be significantly more frequent in patients allergic to *Alternaria alternata.* Those results, however interesting, require further analyses. Studies, based on a larger population, are needed to confirm the relationship between atopic diseases and semen quality.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics approval

Ethical approval for this study was obtained from Collegium Medicum in Bydgoszcz, NCUCommittee of Bioethics KB 432/2018.

Informed consent

Written informed consent was obtained from all subjects before the study.

ORCID iD

Natalia Ukleja-Sokołowska https://orcid.org/0000-0001-5957-8382

References

1. Luconi M, Forti G and Baldi E (2006) Pathophysiology of sperm motility. *Frontiers in Bioscience* 11: 1433–1447. DOI: 10.2741/1894.
2. Sicherer SH and Sampson HA (2018) Food allergy: a review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *Journal of Allergy and Clinical Immunology* 141(1): 41–58. DOI: 10.1016/j.jaci.2017.11.003.
3. Ukleja-Sokołowska N, Gawrońska-Ukleja E, Żbikowska-Gotz M et al. (2016). Analysis of feline and canine allergen components in patients sensitized to pets. *Allergy, Asthma & Clinical Immunology* 12(1): 61. DOI: 10.1186/s13223-016-0167-4.
4. Silva GP, Grangeiro VPX and Carneiro FP (2018) Semen quality and ferritin and transferrin seminal levels. *Folia Medica* 60(4): 632–636. DOI: 10.2478/folmed-2018-0044.
5. Van der Valk JP, Gerth Van Wijk R, Hoorn E, et al. (2016). Measurement and interpretation of skin prick test results. *Clinical and Translational Allergy* 6:8. DOI: 10.1186/s13601-016-0092-0.
6. Heinzerling L, Mari A, Bergmann K, et al. (2013) The skin prick test – European standards. *Clinical and Translational Allergy* 3(1): 3. DOI: 10.1186/2045-7022-3-3.
7. Wilkes S, Chinn D, Murdoch A, et al. (2009) Epidemiology and management of infertility: a population-based study in UK primary care. *Family Practice* 26: 269–274.
8. Fleming S, Green S and Hall J (1995) Analysis and alleviation of male infertility. *Microscopy Anal* 35: 37–39.
9. Adams JA, Galloway TS, Mondal D, et al. (2014) Effect of mobile telephones on sperm quality: a systematic review and meta-analysis. *Environment International* 70: 106–112. DOI: 10.1016/j.envint.2014.04.015.
10. Carré J, Gatimel N, Moreau J, et al. (2017) Does air pollution play a role in infertility? a systematic review. *Environmental Health* 16(1): 82. DOI: 10.1186/s12940-017-0291-8.
11. Guo D, Wu W, Tang Q, et al. (2017) The impact of BMI on sperm parameters and the metabolite changes of seminal plasma concomitantly. *Oncotarget* 8(30): 48619–48634. DOI: 10.18632/oncotarget.14950.
12. Ng M, Fleming T, Robinson M, et al. (2014) Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the global burden of disease study 2013. *Lancet* 384(9945): 766–781. DOI: 10.1016/S0140-6736(14)60460-8.
13. Shayeb AG, Harrild K, Mathers E, et al. (2011) An exploration of the association between male body mass index and semen quality. *Reproductive BioMedicine Online* 23(6): 717–723. DOI: 10.1016/j.rbmo.2011.07.018.
14. Belloc S, Cohen-Bacrie M, Amar E, et al. (2014) High body mass index has a deleterious effect on semen parameters except morphology: results from a large cohort study. *Fertility and Sterility* 102(5): 1268–1273. DOI: 10.1016/j.fertnstert.2014.07.1212.
15. Sermondade N, Faure C, Fezeu L, et al. (2013) BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. *Human Reproduction Update* 19(3): 221–231. DOI: 10.1093/humupd/dms050.
16. MacDonald AA, Herbison GP, Showell M, et al. (2010) The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis. *Human Reproduction Update* 16(3): 293–311. DOI: 10.1093/humupd/dmp047.
17. Sharma R, Harlev A, Agarwal A, et al. (2016) Cigarette smoking and semen quality: a new meta-analysis examining the effect of the 2010 world health organization laboratory methods for the examination of human semen. *European Urology* 70(4): 635–645.
18. Asare-Anane H, Bannison SB, Ofori EK, et al. (2016) Tobacco smoking is associated with decreased semen quality. *Reproductive Health* 13(1): 90. DOI: 10.1186/s12978-016-0207-z.

19. Li WN, Jia MM, Peng YQ, et al. (2019) Semen quality pattern and age threshold: a retrospective cross-sectional study of 71,623 infertile men in China, between 2011 and 2017. *Reproductive Biology and Endocrinology* 17(1): 107. DOI: 10.1186/s12958-019-0551-2.
20. Lai SF, Li RH, Yeung WS, et al. (2018) Effect of paternal age on semen parameters and live birth rate of in-vitro fertilisation treatment: a retrospective analysis. *Hong Kong medical journal = Xianggang yi xue za zhi* 24(5): 444–450. DOI: 10.12809/hkmj177111.
21. Frankland AW and Parish WE (1974) Anaphylactic sensitivity to human seminal fluid. *Clinical Experimental Allergy* 4(3): 249–253. DOI: 10.1111/j.1365-2222.1974.tb01382.x.
22. Ebo DG, Stevens WJ, Bridts CH, et al. (1995) Human seminal plasma anaphylaxis (HSPA): case report and literature review. *Allergy* 50(9): 747–750. DOI: 10.1111/j.1398-9995.1995.tb01218.x.
23. Sublett JW and Bernstein JA (2011) Characterization of patients with suspected seminal plasma hypersensitivity. *Allergy and Asthma Proceedings* 32(6): 467–471. DOI: 10.2500/aap.2011.32.3495.
24. Tanaka M, Nakagawa Y, Kotobuki Y, et al. (2019) A case of human seminal plasma allergy sensitized with dog prostatic kallikrein, Can f 5. *Allergology International* 68(2): 259–260. DOI: 10.1016/j.alit.2018.08.003.
25. Mattsson L, Lundgren T, Everberg H, et al. (2009) Prostatic kallikrein: a new major dog allergen. *Journal of Allergy and Clinical Immunology* 123(2): 362–368. DOI: 10.1016/j.jaci.2008.11.021.
26. Esfandiari N, Nesbit C, Litzky J, et al. (2020) High prevalence of allergy in patients undergoing in vitro fertilization and embryo transfer. *Journal of Assisted Reproduction and Genetics* 37(2): 311–320. DOI: 10.1007/s10815-020-01691-z.
27. Adamczak R, Ukleja-Sokołowska N and Bartuzi Z (2019) Fertility and allergy: is there a correlation? *Advances in Hygiene & Experimental Medicine/Postepy Higieny i Medycyny Doswiadczalnej* 73: 440–446.
28. Napolitano M, Ruggiero A, Fontanella G, et al. (2021) New emergent therapies for atopic dermatitis: a review of safety profile with respect to female fertility, pregnancy, and breastfeeding. *Dermatologic Therapy* 34(1): e14475. DOI: 10.1111/dth.14475.
29. Venter C, Greenhawt M, Meyer RW, et al. (2020) EAACI position paper on diet diversity in pregnancy, infancy and childhood: ovel concepts and implications for studies in allergy and asthma. *Allergy* 75(3): 497–523. DOI: 10.1111/all.14051.
30. Ozden G and Pınar Deniz P (2021) May mepolizumab used in asthma correct subfertility? *Annals of Medicine* 53(1): 456–458. DOI: 10.1080/07853890.2021.1900591.
31. Mondillo C, Varela ML, Abiuso AMB, et al. (2018) Potential negative effects of anti-histamines on male reproductive function. *Reproduction* 155(5): R221–R227. DOI: 10.1530/REP-17-0685.
32. Millsop JW, Heller MM, Eliason MJ, et al. (2013) Dermatological medication effects on male fertility. *Dermatologic Therapy* 26(4): 337–346. DOI: 10.1111/dth.12069.
33. Baricitinib O (2018) *EU Summary of Product Characteristics: Olumiant*. Utrecht, Netherlands: Eli Lilly Nederland B.V.
34. Haidl G, Haidl F, Allam JP, et al. (2019) Therapeutic options in male genital tract inflammation. *Andrologia* 51(3): e13207. DOI: 10.1111/and.13207.
35. Allam JP, Langer M, Fathy A, et al. (2009) Mast cells in the seminal plasma of infertile men as detected by flow cytometry. *Andrologia* 41(1): 1–6. DOI: 10.1111/j.1439-0272.2008.00879.x.
36. Politch JA, Tucker L, Bowman FP, et al. (2007) Concentrations and significance of cytokines and other immunologic factors in semen of healthy fertile men. *Human Reproduction* 22(11): 2928–2935. DOI: 10.1093/humrep/dem281.
37. Wong CK, Ho CY, Ko FW, et al. (2001) Proinflammatory cytokines (IL-17, IL-6, IL-18 and IL-12) and Th cytokines (IFN-gamma, IL-4, IL-10 and IL-13) in patients with allergic asthma. *Clinical and Experimental Immunology* 125(2): 177–183. DOI: 10.1046/j.1365-2249.2001.01602.x.
38. Hassoun Y, James C and Bernstein DI (2019) The effects of air pollution on the development of atopic disease. *Clinical Reviews in Allergy & Immunology* 57(3): 403–414. DOI: 10.1007/s12016-019-08730-3.
39. Radwan M, Jurewicz J, Polańska K, et al. (2016) Exposure to ambient air pollution–does it affect semen quality and the level of reproductive hormones? *Annals of Human Biology* 43(1): 50–56. DOI: 10.3109/03014460.2015.1013986.
40. Wdowiak A, Wdowiak E, Bień A, et al. (2019) Air pollution and semen parameters in men seeking fertility treatment for the first time. *International Journal of Occupational and Environmental Health* 32(3): 387–399. DOI: 10.13075/ijomeh.1896.01355.
41. Jurewicz J, Dziewirska E, Radwan M, et al. (2018) Air pollution from natural and anthropic sources and male fertility. *Reproductive Biology Endocrinology* 16(1): 109. DOI: 10.1186/s12958-018-0430-2.
42. Müller L, Vogel M, Stadler M, et al. (2008) Sensitization to wasp venom does not induce autoantibodies leading to infertility. *Molecular Immunology* 45(14): 3775–3785. DOI: 10.1016/j.molimm.2008.05.024.