Hindawi
Andrologia
Volume 2023, Article ID 4917056, 7 pages
https://doi.org/10.1155/2023/4917056

Research Article

Geographical Differences in Male Infertility between the United States and Canada: Insights from the Andrology Research Consortium

Kian Asanad,[1] **Keith Jarvi**,[2] **Katherine Lajkosz**,[2] **James F. Smith**,[3] **Susan Lau**,[2] **Kirk Lo**,[2] **Ethan Grober**,[2] **and Mary K. Samplaski**[1]

[1]*Institute of Urology, University of Southern California, 1441 Eastlake Avenue, Suite 7416, Los Angeles, CA 90033, USA*
[2]*Division of Urology, Mount Sinai Hospital, University of Toronto, 600 University Avenue, Toronto, Ontario, Canada*
[3]*Department of Urology, University of California, San Francisco, 400 Parnassus Ave Sixth Floor, Suite A610, San Francisco, CA 94143, USA*

Correspondence should be addressed to Kian Asanad; kian.asanad@med.usc.edu

Received 21 October 2022; Revised 21 March 2023; Accepted 24 March 2023; Published 13 April 2023

Academic Editor: R. Henkel

We sought to compare the demographics and fertility characteristics of men presenting to reproductive urologists (RU) for evaluation in the United States (US) and Canada using data from the Andrology Research Consortium. A standardized patient questionnaire was used to prospectively evaluate men across fifteen North American male infertility practices between 2015 and 2018. Patient demographics, fertility histories, including female partner infertility testing and treatment, and referral data were assessed. Univariate analysis was used to determine geographical differences between the various patient characteristics and the geographical region. We sampled 6,462 men with a mean age of 36.6 ± 7.5 years. The average duration of infertility was significantly higher in US men (4.5 ± 7.2 years) compared to Canadian men (3.6 ± 4 years) ($p = 0.007$). Significantly more men in the US were obese (63% vs. 26%, $p < 0.001$) compared to Canada. Intrauterine insemination use among female partners was more common in Canada (13% vs. 7%, $p < 0.001$) while in vitro fertilization was less common (6% vs. 9%, $p = 0.01$) when compared to the US. Finasteride (3% vs. 0%) and testosterone usage (4% vs. 1) were more common among US men versus Canadians, respectively. In conclusion, geographical differences exist between North American males undergoing fertility evaluation. American men are older and more obese and have a longer average duration of infertility. Potentially reversible factors contributing to male infertility are more prevalent in the US.

1. Introduction

Infertility affects approximately 15% of couples globally, of which a male factor is solely responsible in nearly 20% of cases and contributory in 50% of cases [1, 2]. Complete diagnostic evaluation of the male partner of an infertile couple should be performed by a urologist or male reproduction specialist when the initial screening demonstrates abnormal semen parameters, abnormal male reproductive history, or couples with unexplained infertility [3]. Reproductive urologist (RU) evaluation is important to improve a couple's baseline natural fertility potential [4, 5], improve assisted reproductive technology (ART) outcomes [6], and detect underlying pathology that may contribute to the male's long-term health [7].

Despite these guidelines, almost 15% of couples undergo ART even before a standard-of-care male factor investigation [8]. Of the men who are referred to a RU for an infertility evaluation, nearly 60% of these referrals are from reproductive endocrinologists (REI), demonstrating that REIs are the gatekeepers for male infertility evaluation in North America.

While the demographics and referral data of men presenting for male infertility evaluation in North America has been well characterized, there are no studies comparing and contrasting these characteristics between the US and

Canada. This is despite known differences in healthcare systems, which may impact how couples seek care, particularly for infertility which is largely cash-based in the US.

Previous studies have evaluated the importance of geographical differences in semen parameters of infertile men. Specifically, Palani et al. found that men in the US had lower sperm concentration, total count, and motility compared to men in Iraq, demonstrating the impact of geographical location on semen quality such as lifestyle habits, ethnicity, and other possible global confounding factors such as temperature variations [9]. This finding was similarly seen in Middle Eastern and North African men who were found to have lower semen quality compared to men outside of these regions [10]. Within the US, different states have also found to have variations in semen quality [11]. These studies highlight the importance of geographical location on fertility and fecundity.

With this in mind, we sought to evaluate for geographical differences in demographics and fertility histories of men presenting for male infertility evaluation between the US and Canada.

2. Materials and Methods

2.1. Study Cohort. We used data from the Andrology Research Consortium (ARC). The ARC is comprised of 15 male infertility centers between the US and Canada. At participating centers, a single-page deidentified questionnaire is completed by patients and providers at the time of their initial clinic evaluation, seen in Supplementary Figure 1. There were no exclusion criteria to receiving a patient questionnaire.

No incentive was provided to patients for completing the questionnaire. Institutional Review Board (IRB) approval (IRB #00000971) was obtained for all participating centers. The questionnaires were uploaded via data capturing software at the University of California at San Francisco. The data repository is held at the University of Toronto.

2.2. Study Variables. From the ARC data, we compared differences between US and Canadian men presenting for fertility evaluation. The specific variables evaluated included patient age, race (White, Black/African American, Hispanic, Asian, American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, and "other race"), ethnicity (Hispanic/Latino or Non-Hispanic/Latino), partner age, height, weight, fertility history, previous semen analysis, previous fertility therapies, vasectomy status, recreational substance use (tobacco, alcohol, marijuana, and cocaine), and use of testosterone, finasteride (i.e., Propecia), or steroids. Semen analysis obtained was a standard semen analysis that includes the variables of volume, morphology, motility, sperm count, motility, and vitality as illustrated by the World Health Organization. Referral data was categorized as self-referred, primary care doctor referral, REI referral, and other. Men with abnormal semen parameters seen on semen analysis and clinical history of infertility were then defined as infertile. Duration of infertility was calculated as mean and median number of years. Female partners undergoing assisted reproductive technology was classified as intrauterine insemination (IUI) and in vitro fertilization (IVF). The mean and mean number of IUI and IVF cycles were reported. Responses to medication and drug use were defined as "yes" or "no" responses. The female partner's prior number of pregnancies and number of offspring were calculated as a mean.

2.3. Statistical Analysis. Univariate analyses were conducted to evaluate for geographical differences between the US and Canada with patient demographic variables, including age, partner age, race and ethnicity, body mass index (BMI), referral source, fertility history (vasectomy status, previous semen analysis), and lifestyle and medication factors (smoking, alcohol, testosterone, and finasteride use) using Mann–Whitney U tests and Pearson chi-square tests. p values < 0.05 were considered statistically significant, and missing data was not imputed. Statistical analyses were conducted using R version 3.6.2.

3. Results

We identified 6,647 men presenting for male infertility evaluation between 2014 and 2020 in the ARC database. We excluded 121 men missing race data and 64 men missing institution data. The final cohort consisted of 6,462 men. This totaled 684 (10.6%) and 5778 (89.4%) men from the US and Canada, respectively. The majority (84%) of the data was obtained from the Toronto site. The patient demographics stratified by the US and Canada are summarized in Table 1. The mean age of the men and their female partners in the entire cohort was 36.6 ± 7.5 years and 33.1 ± 5.0 years, respectively. We found significant differences in age, race, ethnicity, and BMI between US and Canadian males. Men in the US were older (37.5 ± 7.4 years vs. 36.4 ± 7.5 years), had older female partners (34.5 ± 5.1 years vs. 32.8 ± 5.0 years), and were more commonly White (74% vs. 49%) or Hispanic (13% vs. 3%) when compared to Canadians, all $p < 0.001$. On the other hand, Canada had a higher percentage of men presenting for infertility evaluation who were Asian (21% vs. 13%) when compared to the US, $p < 0.001$.

The average BMI was 33.3 kg/m^2 and 27.9 kg/m^2 in the US and Canada, respectively ($p < 0.001$). When BMI was categorized as normal (18-24.9), overweight (25-29.9), and obese (≥30), a significantly larger proportion of men in Canada had a normal BMI when compared to the US (29% vs. 12%, $p < 0.001$). More than half of men in the US were obese when compared to Canada (63% vs. 26%, $p < 0.001$). When obesity was trichotomized into three groups of BMI, we observed that 26%, 21%, and 17% of men in the US had a BMI of 30-34.9, 35-39.9, and ≥40, respectively.

The fertility histories and previous infertility treatments of men stratified by Canada and the US are shown in Table 2. The mean duration of infertility was 3.7 years across the two groups with an average of 4.5 years in the US compared to 3.6 years in Canada, $p = 0.007$. While more men in Canada had a prior semen analysis at the time of RU presentation (88% vs. 80%, $p = 0.002$), only 69% of men in Canada

Table 1: Patient demographics of men presenting for infertility investigation stratified by Canada and the US.

Covariate	Full sample ($n = 6462$)	Canada ($n = 5778$)	US ($n = 684$)	p value
Race				**<0.001**
American Indian or Alaska Native	67 (1%)	65 (1%)	2 (0%)	
Asian	1302 (20%)	1210 (21%)	92 (13%)	
Black or African American	392 (6%)	347 (6%)	45 (7%)	
Native Hawaiian or other Pacific Islander	8 (0%)	1 (0%)	7 (1%)	
White	3320 (51%)	2812 (49%)	508 (74%)	
Other race	1373 (21%)	1343 (23%)	30 (4%)	
Patient age (years)				**<0.001**
Mean (SD)	36.6 (7.5%)	36.4 (7.5%)	37.5 (7.4%)	
Missing	1541	1528	13	
Age group (years)				
<20	38 (1%)	34 (1%)	4 (1%)	**<0.001**
20-25	135 (3%)	122 (3%)	13 (2%)	
26-30	730 (15%)	669 (16%)	61 (9%)	
31-35	1565 (32%)	1351 (32%)	214 (32%)	
36-40	1224 (25%)	1027 (24%)	197 (29%)	
41-45	690 (14%)	585 (14%)	105 (16%)	
46-50	307 (6%)	263 (6%)	44 (7%)	
51-55	137 (3%)	118 (3%)	19 (3%)	
56-60	57 (1%)	51 (1%)	6 (1%)	
60+	38 (1%)	30 (1%)	8 (1%)	
Missing	1541	1528	13	
Partner age (years)				
Mean (SD)	33.1 (5)	32.8 (5)	34.5 (5.1)	**<0.001**
Median (range)	33 (18-63)	33 (18-63)	34 (18-55)	
Missing	2056	2025	31	
Ethnicity				
Latino/Hispanic	170 (3%)	142 (3%)	28 (13%)	**<0.001**
Non-Latino/Hispanic	5527 (97%)	5332 (97%)	195 (87%)	
Missing	765	304	461	
Body mass index				
Mean (SD)	28.4 (6)	27.9 (5.4)	33.3 (8)	**<0.001**
Median (range)	27.2 (13.3-64.4)	26.9 (13.3-61.6)	32.2 (15.9-64.4)	
Underweight (<18.5)	46 (1%)	43 (1%)	3 (0)	**<0.001**
Normal (18.5-24.9)	1688 (27%)	1617 (29%)	71 (12%)	
Overweight (25.0-29.9)	2621 (42%)	2472 (44%)	149 (25%)	
Obese (30+)	1837 (30%)	1455 (26%)	382 (63%)	
Missing	270	191	79	

Bold values represent statistically significant p-values.

had knowledge of their semen analysis results compared to 80% of men in the US, $p = 0.002$. It is important to note that almost 85% of semen analyses were missing from the dataset.

Rates of ART usage was also significantly different between American and Canadian males. Female partners undergoing IUI were more common in Canadian males (13% vs. 7%, $p < 0.001$) while IVF was less common (6% vs. 9%, $p = 0.01$) when compared to the US. Canadians also had fewer prior pregnancies (12% vs. 28%, $p < 0.001$) and prior children (7% vs. 29%, $p < 0.001$).

Lifestyle factors and medication use that would affect fertility stratified by Canada and the US are summarized in Table 3. We found significant differences in smoking history (17% vs. 10%, $p < 0.0001$), alcohol use (79% vs. 88%, $p = 0.018$), and marijuana use (18% vs. 9%, $p < 0.001$), among men in Canada and the US, respectively. Finasteride (3% vs. 0%), steroids (5% vs. 0%), and testosterone usage (4%

Table 2: Fertility histories and previous infertility treatments of men stratified by Canada and the US.

Covariate	Full sample ($n = 6462$)	Canada ($n = 5778$)	USA ($n = 684$)	p value
Referral				**<0.001**
Self-referred	154 (3%)	41 (1%)	113 (17%)	
Primary care physician/family doctor	781 (16%)	674 (16%)	107 (16%)	
Gynecologist/reproductive endocrinologist/women's fertility specialist	3163 (66%)	2812 (68%)	351 (54%)	
Other	713 (15%)	628 (15%)	85 (13%)	
Missing	1651	1623	28	
Infertility duration, years				**0.0066**
Mean (SD)	3.7 (4.4)	3.6 (4)	4.5 (7.2)	
Median (range)	2 (0-67)	2 (0-45)	2 (0-67)	
Missing	837	758	79	
Vasectomy				**<0.001**
No	6091 (94%)	5469 (95%)	622 (91%)	
Yes	371 (6%)	309 (5%)	62 (9%)	
Semen analysis				**0.0019**
No	172 (17%)	41 (12%)	131 (20%)	
Yes	815 (83%)	294 (88%)	521 (80%)	
Missing	5475	5443	32	
Semen analysis results				**0.0021**
No	105 (13%)	47 (17%)	58 (11%)	
Unknown	84 (11%)	40 (14%)	44 (9%)	
Yes	602 (76%)	193 (69%)	409 (80%)	
Missing	5671	5498	173	
Intrauterine insemination				**<0.001**
No	5665 (88%)	5028 (87%)	637 (93%)	
Yes	797 (12%)	750 (13%)	47 (7%)	
Intrauterine insemination cycles				0.32
Mean (SD)	1.6 (1.0)	1.6 (1.0)	1.9 (1.3)	
Median (range)	1 (1-8)	1 (1-8)	1 (1-5)	
In vitro fertilization				**0.014**
No	6034 (93%)	5411 (94%)	623 (91%)	
Yes	428 (7%)	367 (6%)	61 (9%)	
In vitro fertilization cycles				0.40
Mean (SD)	1.4 (0.8)	1.4 (0.9)	1.3 (0.6)	
Median (range)	1 (1-8)	1 (1-8)	1 (1-3)	
Number of pregnancies				**<0.001**
0	2339 (85%)	2132 (88%)	207 (66%)	
1+	405 (15%)	296 (12%)	109 (34%)	
Missing	3718	3350	368	
Number of babies				**<0.001**
0	2441 (91%)	2262 (93%)	179 (71%)	
1+	237 (9%)	164 (7%)	73 (29%)	
Missing	3784	3352	432	
Number of pregnancy losses				1
0	269 (69%)	122 (69%)	147 (69%)	
1+	122 (31%)	55 (31%)	67 (31%)	
Missing	6071	5601	470	

Bold values represent statistically significant p-values.

Table 3: Lifestyle factors and medication use potentially effective male fertility stratified by Canada and the US.

Covariate	Full sample ($n = 6462$)	Canada ($n = 5778$)	USA ($n = 684$)	p value
Smoking	1029 (16%)	958 (17%)	71 (10%)	**<0.001**
Alcohol	5084 (79%)	4551 (79%)	533 (83%)	**0.018**
Missing	*52*	*11*	*41*	
Marijuana	1075 (17%)	1016 (18%)	59 (9%)	**<0.001**
Cocaine	98 (2%)	94 (2%)	4 (1%)	0.058
Missing	*97*	*37*	*60*	
Propecia	30 (0%)	9 (0%)	21 (3%)	**<0.001**
Steroids	61 (1%)	28 (0%)	33 (5%)	**<0.001**
Testosterone	61 (1%)	33 (1%)	28 (4%)	**<0.001**

Bold values represent statistically significant p-values.

vs. 1%) were more common among US men versus Canadians, respectively, all $p < 0.001$.

4. Discussion

In the present study, we provide the first analysis of the geographical differences in demographics and fertility histories of men presenting for male infertility evaluation using a multicenter North American male fertility database. We found that domiciliary differences exist between North American males undergoing RU fertility evaluation. Our study has several important findings.

First, American men are older with older female partners when they present for fertility evaluation, compared to males in Canada. Several factors may explain this dissimilarity such as various attitudes towards pregnancy; disparities in access, costs, and insurance coverage of fertility care; later or second marriages; and increased life expectancy. Over the past half-century in the United States, men over the age of 35 at the time of birth have increased from 4% to 10% [12, 13]. While there is no clear definition for advanced paternal age, some studies use 40 years and above as the age limit. Advanced paternal age has been associated with various genetic abnormalities and nonchromosomal birth defects [14]. A plethora of studies have documented an association between advanced paternal age and various psychiatric and neurocognitive disorders such as schizophrenia, autism, and obsessive-compulsive disorder [15–20]. While these are risks that all RU should be aware of, it is potentially something that should be highlighted more in American men, given their slightly more advanced age at the time of fertility evaluation. It is important to note that we found a statistical difference in age between the US and Canada; however, this may not be clinically different (37.5 years in the US vs. 36.4 years in Canada). Additionally, the implication of age on male infertility is not a new finding. Nonetheless, this is a novel finding determined between these two geographic locations.

Second, American men are significantly more obese compared to Canadian men. Obesity in the US is a public health crisis with the prevalence of obesity increasing from 30.5% from 1999 to 2000 to 42.4% in 2017-2018 [21]. This is consistent with significant differences in prevalence of obesity estimates between the US and Canada. Obesity in Canada was approximately 24% in 2007-2009, compared to 34% in the US [22]. With the increase in obesity, there has been a parallel decrease in male fertility. Not surprisingly, we found a significantly higher proportion of men in the US presenting for male infertility evaluation were obese (63%) compared to men in Canada (26%), with 17% of men in the US categorized as severe obesity (BMI > 40 kg/m^2). The inverse association between obesity and poor sperm quality has been well studied with obese men being at an increased risk of oligozoospermia and azoospermia compared to normal-weight men [23]. This data suggests that American men who are more commonly obese may be more likely to ultimately require medical and surgical treatment by male infertility specialists compared to Canadian men. Thus, these men may benefit from earlier RU referral and evaluation.

Third, American men have a longer average duration of infertility compared to men in Canada. In our study, we found that the mean duration of infertility was 4.5 years in the US compared to 3.6 years in Canada. This may be related to differences in health insurance coverages between the US and Canada. In the US, there is limited inclusion of coverage for infertility evaluation and/or treatment, resulting in high out-of-pocket expenses. In a patient questionnaire of men undergoing infertility evaluation and treatment, these out-of-pocket costs have been reported to be approximately $15,000 in 64% of men and up to $50,000 in 16% of men [24]. Of these, 46% had treatment options limited by these costs. As a result, this may be a critical deterring factor in couples seeking male infertility evaluation and treatment in the US, and thus, these men may present with a longer average duration of infertility.

Fourth, we demonstrate that potentially reversible lifestyle factors contributing to male infertility such as smoking, alcohol, marijuana, and steroid use are significantly different between the US and Canada. Tobacco and marijuana use were more commonly seen in Canadian men, while alcohol use was more commonly seen in American men. Differences in marijuana usage may be attributed to recent changes in cannabis legalization laws in Canada as well as certain states of the US. This finding is consistent with data prior to the implementation of Canada's Cannabis Act in 2018, which legalized and regulated nonmedical cannabis use at the

federal level. However, recent national data suggests a higher prevalence of use in "legal" states of the US compared to Canada. It is important to note that the ARC database spans 2014-2020 with a large proportion of data reflecting usage prior to 2018.

Additionally, we found that 4% of men were using exogenous testosterone and 5% of men were using other steroids, compared to <1% of men in Canada. It is unclear why these findings are more common in the US compared to Canada outside of environmental factors inherent in the country itself; however, RU in the US should pay increasing attention to the patient's medication history as these potentially reversible causes of male infertility appear to be more frequently seen. This also highlights the importance of referring men seeking reproductive health care to a RU for a standard-of-care male reproductive evaluation, previously demonstrated by the initial ARC data publication [8].

Finally, we found significant differences in ART usage between the US and Canada. IUI was more common in female partners of Canadian males, while IVF was significantly more common in the US. This may in part be explained by the vastly different healthcare systems between the US and Canada. With the passing of the Assisted Human Reproduction Act in 2004 providing federal oversight to fertility care in Canada, ART is regulated very differently in Canada and the US. While fertility care coverage represents a financial barrier to both countries, there are four provinces within Canada where treatment coverage exists. For instance, Ontario provides funding to cover the first round of IVF, Manitoba provides a tax credit, and New Brunswick has a grant to partially cover costs. Conversely, the lack of federal oversight, lack of mandated fertility insurance coverage, and high out-of-pocket costs in the US provide an increasing financial incentive and thus speeding couples into IVF.

Our study is not without its limitations. Our data is limited by nonresponse bias inherent to a cross-sectional questionnaire-based study, as well as recall bias inherent in a patient-completed questionnaire. We additionally do not have a sense of how many men of those that present for male infertility evaluation actually complete the questionnaire to determine an exact response rate. We sampled over 6000 men, representing a robust sample size, albeit this may not be representative of all men presenting for a male factor infertility evaluation. Furthermore, several of our findings are statistically significant; however, they may not be clinically significant. Given our robust sample size, statistical differences should be weighed in terms of clinical significance. The data may also be skewed towards Canadian men given almost 90% of the sample were provided from Canadian participating centers. However, we argue that despite the data being skewed, we observed significant differences weighted heavily towards American men, which demonstrates the strength of the data. Finally, the use of ART without completely knowing the factor of infertility (sole male or sole female or both) is a source of bias in this study. Despite these limitations, there are several strengths of our study. This is a multicenter, broad, North American study encompassing 15 participating centers. The survey provides granular data points in regard to demographic characteristics, infertility histories, prior evaluation, and referral data.

5. Conclusions

This is the first study evaluating geographical differences in fertility histories and demographics for males undergoing a male infertility evaluation between American and Canadian males. We found that key differences exist between North American males undergoing RU fertility evaluation. American men are more likely to suffer from potentially reversible lifestyle factors contributing to male infertility such as obesity, drug use, and exogenous testosterone supplementation. Significant differences in ART usage also exists between the US and Canada. Understanding these differences will enable RU to provide more geographically tailored counseling and awareness to particular risks more commonly seen in American men compared to Canadian men presenting for male factor infertility investigation.

Data Availability

The questionnaires were uploaded via data capturing software at the University of California at San Francisco. The data repository is held at the University of Toronto.

Conflicts of Interest

The authors have no conflicts of interest to report.

Acknowledgments

The authors acknowledge that this manuscript was originally presented as an abstract as a podium presentation in the 2021 American Society of Reproductive Medicine Scientific Congress & Expo.

Supplementary Materials

Supplementary Figure 1: copy of the Andrology Research Consortium fertility patient questionnaire integrating patient demographics, fertility history, and lifestyle factors. *(Supplementary Materials)*

References

[1] P. Thonneau, S. Marchand, A. Tallec et al., "Incidence and main causes of infertility in a resident population (1 850 000) of three French regions (1988–1989)*," *Human Reproduction*, vol. 6, no. 6, pp. 811–816, 1991.

[2] A. Agarwal, A. Mulgund, A. Hamada, and M. R. Chyatte, "A unique view on male infertility around the globe," *Reproductive Biology and Endocrinology*, vol. 13, no. 1, p. 37, 2015.

[3] P. N. Schlegel, M. Sigman, B. Collura et al., "Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I," *Fertility and Sterility*, vol. 115, no. 1, pp. 54–61, 2021.

[4] V. S. Talaulikar and S. Arulkumaran, "Maternal, perinatal and long-term outcomes after assisted reproductive techniques (ART): implications for clinical practice," *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, vol. 170, no. 1, pp. 13–19, 2013.

[5] H. Ghanem, O. Shaeer, and A. El-Segini, "Combination clomiphene citrate and antioxidant therapy for idiopathic male infertility: a randomized controlled trial," *Fertility and Sterility*, vol. 93, no. 7, pp. 2232–2235, 2010.

[6] L. A. Lazaros, G. A. Vartholomatos, E. G. Hatzi et al., "Assessment of sperm chromatin condensation and ploidy status using flow cytometry correlates to fertilization, embryo quality and pregnancy following in vitro fertilization," *Journal of Assisted Reproduction and Genetics*, vol. 28, no. 10, pp. 885–891, 2011.

[7] F. Del Giudice, A. M. Kasman, M. Ferro et al., "Clinical correlation among male infertility and overall male health: a systematic review of the literature," *Investigative and Clinical Urology*, vol. 61, no. 4, pp. 355–371, 2020.

[8] M. K. Samplaski, J. F. Smith, K. C. Lo et al., "Reproductive endocrinologists are the gatekeepers for male infertility care in North America: results of a North American survey on the referral patterns and characteristics of men presenting to male infertility specialists for infertility investigations," *Fertility and Sterility*, vol. 112, no. 4, pp. 657–662, 2019.

[9] A. Palani, P. Sengupta, A. Agarwal, and R. Henkel, "Geographical differences in semen characteristics: comparing semen parameters of infertile men of the United States and Iraq," *Andrologia*, vol. 52, no. 3, article e13519, 2020.

[10] H. Elbardisi, A. Majzoub, S. Al Said et al., "Geographical differences in semen characteristics of 13 892 infertile men," *Arab Journal of Urology*, vol. 16, no. 1, pp. 3–9, 2018.

[11] S. H. Swan, C. Brazil, E. Z. Drobnis et al., "Geographic differences in semen quality of fertile U.S. males," *Environmental Health Perspectives*, vol. 111, no. 4, pp. 414–420, 2003.

[12] Y. S. Khandwala, V. L. Baker, G. M. Shaw, D. K. Stevenson, Y. Lu, and M. L. Eisenberg, "Association of paternal age with perinatal outcomes between 2007 and 2016 in the United States: population based cohort study," *BMJ*, vol. 363, p. k4372, 2018.

[13] Y. S. Khandwala, C. A. Zhang, Y. Lu, and M. L. Eisenberg, "The age of fathers in the USA is rising: an analysis of 168 867 480 births from 1972 to 2015," *Human Reproduction*, vol. 32, no. 10, pp. 2110–2116, 2017.

[14] S. Harlap, O. Paltiel, L. Deutsch et al., "Paternal age and preeclampsia," *Epidemic*, vol. 13, no. 6, pp. 660–667, 2002.

[15] R. Sharma, A. Agarwal, V. K. Rohra, M. Assidi, M. Abu-Elmagd, and R. F. Turki, "Effects of increased paternal age on sperm quality, reproductive outcome and associated epigenetic risks to offspring," *Reproductive Biology and Endocrinology*, vol. 13, no. 1, p. 35, 2015.

[16] D. Malaspina, S. Harlap, S. Fennig et al., "Advancing paternal age and the risk of schizophrenia," *Archives of General Psychiatry*, vol. 58, no. 4, p. 361, 2001.

[17] J. S. Brandt, M. A. Cruz Ithier, T. Rosen, and E. Ashkinadze, "Advanced paternal age, infertility, and reproductive risks: a review of the literature," *Prenatal Diagnosis*, vol. 39, no. 2, pp. 81–87, 2019.

[18] C. M. Hultman, S. Sandin, S. Z. Levine, P. Lichtenstein, and A. Reichenberg, "Advancing paternal age and risk of autism: new evidence from a population- based study and a meta-analysis of epidemiological studies," *Molecular Psychiatry*, vol. 16, no. 12, pp. 1203–1212, 2011.

[19] S. L. Conti and M. L. Eisenberg, "Paternal aging and increased risk of congenital disease, psychiatric disorders, and cancer," in *Paternal Influences on Human Reproductive Success*, pp. 93–102, Cambridge University Press, Cambridge, 2010.

[20] M. Ek, S. Wicks, A. C. Svensson, S. Idring, and C. Dalman, "Advancing paternal age and schizophrenia: the impact of delayed fatherhood," *Schizophrenia Bulletin*, vol. 41, no. 3, pp. 708–714, 2015.

[21] https://www.cdc.gov/obesity/data/adult.html.

[22] https://www.cdc.gov/nchs/products/databriefs/db56.htm.

[23] N. Sermondade, C. Faure, L. Fezeu, R. Lévy, S. Czernichow, and Obesity-Fertility Collaborative Group AT, "Obesity and increased risk for oligozoospermia and azoospermia," *Archives of Internal Medicine*, vol. 172, no. 5, pp. 440–442, 2012.

[24] P. A. Elliott, J. Hoffman, M. Abad-Santos, C. Herndon, P. P. Katz, and J. F. Smith, "Out-of-pocket costs for men undergoing infertility care and associated financial strain," *Urology Practice*, vol. 3, no. 4, pp. 256–261, 2016.