The effect of ethnicity on semen analysis and hormones in the infertile patient

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Abstract

Introduction: We aimed to study the association of ethnicity on semen parameters and hormones in patients presenting with infertility.
Methods: Data from men presenting for infertility assessment were prospectively collected and retrospectively reviewed. Demographic and clinical history was self-reported. Semen analysis included volume, count, motility, morphology, and vitality. The 2010 World Health Organization cutoffs were used. Baseline total testosterone and follicle-stimulating hormone (FSH) levels were recorded. Ethnicity data was classified as Caucasian, African Canadian, Asian, Indo-Canadian, Native Canadian, Hispanic, and Middle Eastern. All patients with complete data were included and statistical analysis was performed.
Results: A total of 9079 patients were reviewed, of which 3956 patients had complete data. Of these, 839 (21.2%) were azoospermic. After adjusting for age, African Canadians (odds ratio [OR] 1.70; 95% confidence interval [CI] 1.28–2.25) and Asians (1.34; 95% CI 1.11–1.62) were more likely to be azoospermic compared to Caucasians. Similarly, African Canadians (OR 1.75; 95% CI 1.33–2.29) were more likely to be oligospermic and Asians (OR 0.82; 95% CI 0.70–0.97) less likely to be oligospermic. Low volume was found in African Canadian (OR 1.42; 95% CI 1.05–1.91), Asians (OR 1.23; 95% CI 1.01–1.51), and Indo-Canadians (OR 1.47; 95% CI 1.01–2.13). Furthermore, Asians (OR 0.73; 95% CI 0.57–0.93) and Hispanics (OR 0.58; 95% CI 034–0.99) were less likely to have asthenospermia. Asians (OR 0.73; 95% CI 0.57–0.94) and Indo-Canadians (OR 0.58; 95% CI 0.35–0.99) were less likely to have teratozospermia. No differences were seen for vitality. No differences were seen for FSH levels, however, Asians ($p<0.01$) and Indo-Canadians ($p<0.01$) were more likely to have lower testosterone.
Conclusions: Our study illustrates that variations in semen analyses and hormones exist in men with infertility. This may provide insight into the workup and management for infertile men from different ethnicities.

Introduction

Male factor infertility is identified in up to 50% of couples presenting with infertility.[1,2] The primary investigation for men with infertility is a semen analysis examining semen parameters, used to identify any abnormalities, as well as potential avenues for intervention and management.[3] Along with semen analyses, many patients often complete other investigations, including diagnostic imaging and hormonal profiles (serum levels of follicle stimulating hormone [FSH], luteinizing hormone [LH], and testosterone).[4]

Semen parameters reference ranges were based on the World Health Organization (WHO) standardized semen analysis, which were derived from the values of semen parameters from men with known fertility.[5]

The 2010 WHO edition was developed having examined semen quality from fertile men in the general population from a total of 15 countries on five continents, with the majority from Europe and North America: Australia (Sydney, Melbourne), Europe (Edinburgh, Manchester, Munster, Paris, Turku, Copenhagen, Oslo, Stockholm, Szeged, Bicetre, Bologna), North America (Los Angeles, Columbia, Davis, Seattle), South America (Santiago), and Asia (Singapore, Beijing, Nanjing, Chengdu).[5] These ranges do not account for potential inherent ethnic and racial influences based on the limited heterogeneity of the reference value population from the WHO 2010 edition, nor the consideration of genetic, environmental, or behavioral factors that may vary based on ethnicity. Little is known regarding racial and ethnic disparities for semen parameters and hormones, and has only been examined by very few studies.[6] These studies have shown some altered concentration, count, and volume parameter differences between White and Asian and White and Black men.

The goal of our study was to retrospectively review a large database of semen parameters and hormone levels to identify any trends or associations by ethnicity. Our study population is fairly heterogenous in Ontario, Canada, and is, therefore, useful in studying various ethnicities. This may aid in the initial workup of these patients with infertility.

Methods

Data from Canadian men from 2008–2017 presenting for an infertility assessment at a single, high-volume referral institution was prospectively collected and retrospectively reviewed. All patients were included who had complete data available for ethnicity, semen analysis, and hormonal data. Ethics approval was obtained from the research ethics board at the University of Toronto.

Demographic and clinical history, including past medical history, surgical history, medications, and infertility history, was obtained from a self-reported patient questionnaire. Ethnicities were self-classified as Caucasian, African Canadian, Asian, Indo-Canadian (from Indian subcontinent), Native Canadian, Hispanic, and Middle Eastern. Secondary infertility was classified based on participants reporting any child with either their current or previous partner; the remainder were considered to have primary infertility. Duration of infertility was categorized based on patient-reported duration of unprotected intercourse (per month). Patients were excluded if they did not report their ethnicity or did not a recorded semen analysis.

Semen analysis data was obtained directly from the Department of Pathology and Laboratory Medicine at our institution using an identical protocol throughout the period of the study. Semen parameters recorded included volume, count, motility, morphology, and vitality. Blood work was completed at various laboratories and included FSH and testosterone. Cutoff values were adopted from the 2010 WHO documented reference ranges for semen parameters to define azoospermia (concentration 0 million/ml), oligospermia (concentration <15 million/ml), asthenospermia (motility <40%), teratozospermia (normal morphology <4%), low vitality (<58%), and low volume (<1.5ml).[5] To limit the influence of previous treatments, only first-time semen analysis and hormone levels were used after presentation to the infertility clinic.

Data was analyzed descriptively. Linear regression was used to compare hormonal profile differences between ethnicities. Multivariate logistic regression evaluated the association between ethnicity and with various semen parameters. Models were adjusted for age. Odds ratios (OR) were presented with 95% confidence intervals (CI), with significance tested using a two-sided p-value <0.05. Statistical analysis was completed using Stata version 14.1.

Results

A total of 9079 patients were reviewed, of which 3956 patients had documented semen analysis, as well as ethnicity data. Patients without these were excluded from the analysis. Table 1 illustrates demographic data for the included patients. Overall, median age was 36 years (interquartile range [IQR] 32–40). The vast majority (3325, 84%) were non-smokers, and almost half (1745, 44%) did not consume any alcohol.

About half of the patients were Caucasian (2226, 56%) with Asians representing the second largest group (843, 21%). Further breakdown of patients by ethnicity is seen in Table 1, which also highlights significant inter-group differences for both demographic and infertility factors. Smoking rates were highest among Hispanics and lowest in Asians and African Canadians. Alcohol consumption was most prevalent in Caucasians and lowest in Asians and Middle Eastern individuals. Native Canadians, African Canadians, and Hispanics were found to have the lowest rates of primary infertility. Intercourse frequency was generally ranged between 7–10 times per month across various ethnicities. Duration of infertility was fairly similar, with a median of 24–36 years in all groups.

Semen parameters

Table 2 illustrates the frequency distribution of patients with abnormal semen parameters according to WHO 2010

Table 1. Demographic characteristics based on ethnicity (n=3956)

	African Canadian (n=276, 7.0%)	Asian (n=843, 21.3%)	Indo-Canadian (n=167, 4.2%)	Caucasian (n=2226, 56.3%)	Native Canadian (n=29, 0.7%)	Hispanic (n=117, 3.0%)	Middle Eastern (n=298, 7.5%)
Demographics	Ipsum						
Age (mean, range)‡	37 (32–43)	36 (33–41)	35 (33–39)	36 (32–41)	36 (33–42)	38 (34–42)	37 (33–43)
Smoking (n, %)*	39 (14.1%)	114 (13.5%)	31 (18.6%)	388 (15.2%)	8 (27.6%)	53 (45.3%)	52 (17.4%)
Alcohol (n, %)*	114 (41.3%)	276 (32.7%)	100 (60.0%)	1556 (69.9%)	19 (65.5%)	53 (45.3%)	92 (30.9%)
Infertility							
Primary infertility (%)*	201 (72.8%)	782 (92.8%)	152 (91.0%)	1744 (78.3%)	14 (48.3%)	85 (72.6%)	261 (87.6%)
Secondary infertility (%)*	75 (27.2%)	61 (7.2%)	15 (9.0%)	482 (21.7%)	15 (51.7%)	32 (27.4%)	37 (12.4%)
Intercourse frequency (per month) (mean, range)‡	9 (0–90)	7 (0–40)	7 (0–30)	8 (0–90)	10 (0–30)	9 (0–31)	8 (0–45)
Duration of infertility (months) (median, IQR) (mean)‡	36 (24–60) 52	24 (18–60) 44	24 (18–48) 41	24 (12–48) 40	36 (18–96) 67	24 (12–60) 48	24 (12–48) 42

‡ANOVA p<0.05. *Chi² p <0.05. IQR: interquartile range.

Table 2. Semen parameters and hormones by ethnicity (n=3956)

	African Canadian (n=276, 7.0%)	Asian (n=843, 21.3%)	Indo-Canadian (n=167, 4.2%)	Caucasian (n=2226, 56.3%)	Native Canadian (n=29, 0.7%)	Hispanic (n=117, 3.0%)	Middle Eastern (n=298, 7.5%)
Semen parameters	Ipsum						
Concentration (million/ml) (median, IQR)	5.3 (0.0–24.8)	13.4 (0.1–13.4)	11.2 (0.4–51.9)	9.5 (0.5–35.7)	17.6 (0.0–38.2)	19.4 (0.4–63.5)	8.15 (0.3–25.1)
Motility (%) (median, IQR)	19.2 (9.6–29.0)	25.1 (13.6–34.2)	24.4 (14.0–34.3)	24.1 (14.3–32.9)	15.5 (12.5–26.7)	29.8 (16.7–38.1)	21.5 (11.7–31.6)
Volume (ml) (median, IQR)	2.0 (1.5–3.0)	2.5 (1.5–3.5)	2.0 (1.5–3.0)	2.5 (1.5–3.5)	2.5 (1.5–3.5)	2.5 (1.5–3.5)	2.5 (2.0–4.0)
Morphology (%) (median, IQR)	10 (5–15)	10 (5–20)	10 (5–20)	10 (5–15)	5 (0–15)	10 (5–20)	5 (5–15)
Vitality (%) (median, IQR)	70 (50–70)	70 (55–75)	65 (55–75)	70 (60–80)	75 (65–85)	70 (55–75)	70 (60–80)
Semen parameters (per WHO)							
Azoospermia (n=839) (n, %)	78 (28.3%)	203 (24.1%)	33 (19.8%)	428 (19.2%)	8 (27.6%)	24 (20.5%)	65 (21.8%)
Oligospermia (n=2239) (n, %)	190 (68.8%)	437 (51.8%)	90 (53.9%)	1269 (57.0%)	14 (48.3%)	57 (48.7%)	182 (61.1)
Asthenospermia (n=2658) (n, %)	180 (65.2%)	530 (62.9%)	109 (65.3%)	1549 (69.6%)	19 (65.5%)	74 (63.2%)	197 (66.1%)
Teratozoospermia (n=581) (n, %)	39 (14.1%)	99 (11.7%)	17 (10.2%)	353 (15.9%)	8 (27.6%)	13 (11.1%)	52 (17.4%)
Low-volume (n=748) (n,%)	67 (24.3%)	176 (20.9%)	39 (23.4%)	386 (17.3%)	7 (24.1%)	27 (23.1%)	49 (16.4%)
Poor vitality (n=654) (n, %)	51 (18.5%)	147 (17.4%)	30 (18.0%)	353 (15.9%)	5 (17.2%)	13 (11.1%)	55 (18.5%)
Hormones							
FSH (median, IQR)	5.9 (3.6–10)	5.5 (3.5–10)	4.8 (3.3–8.3)	5.5 (3.5–10)	6.0 (4.3–12)	5.6 (3.8–8.8)	5.1 (3.1–9.0)
Testosterone (median, IQR)	13 (11–17)	11 (8.4–16)	9.9 (8.4–14)	13 (9.6–17)	13 (11–16)	13 (8.7–16.5)	12 (9.4–16)

FSH: follicle-stimulating hormone; IQR: interquartile range.

criteria. The most common abnormalities seen among all ethnicities were asthenospermia (n=2658, 67%) and oligospermia (n=2239, 57%); the least common were teratozospermia (n=581, 15%) and low vitality (n=654, 17%). African Canadians had the lowest median sperm concentration, with Native Canadians and Hispanics having the highest median sperm concentrations.

Multivariate analysis was completed and is illustrated in Table 3. After adjusting for age, we found that African Canadians (OR 1.70; 95% CI 1.28–2.25) and Asians (OR 1.34; 95% CI 1.11–1.62) were more likely to be azoospermic compared to Caucasians. African Canadians (OR 1.75; 95% CI 1.33–2.29) were more likely to be oligospermic and Asians (OR 0.82; 95% CI 0.70–0.97) less likely to be oligospermic. Low-volume ejaculate was more commonly found in African Canadians (OR 1.42; 95% CI 1.05–1.91), Asians (OR 1.23; 95% CI 1.01–1.51), and Indo-Canadians (OR 1.47; 95% CI 1.01–2.13). Furthermore, Asians (OR 0.73; 95% CI 0.57–0.93) and Hispanics (OR 0.58; 95% CI 0.34–0.99) were less likely to have asthenospermia. Asians (OR 0.73; 95% CI 0.57–0.94) and Indo-Canadians (OR 0.58; 95% CI 0.35–0.99) were less likely to have teratozospermia. No differences were seen for vitality.

Hormonal profiles

Table 2 illustrates the distribution of FSH and total testosterone by ethnicity. African Canadians had both the highest FSH, as well as highest total testosterone. Indo-Canadians had the lowest total testosterone, and Middle Eastern individuals had the lowest FSH.

Linear regression for hormones is displayed in Table 4. When adjusted for age, no differences were seen for FSH levels; however, Asians ($p<0.01$) and Indo-Canadians ($p<0.01$) were more likely to have lower total testosterone levels.

Discussion

Male factor infertility is a significant contributor in the work-up of couples for infertility, and includes semen analysis and

Table 3. Multivariate analysis semen parameters by ethnicity (adjusted by age)

	Azoospermia (n=839)	Oligospermia (n=2239)	Asthenospermia (n=2658)	Teratozoospermia (n=581)	Low-volume (n=748)	Poor vitality (n=654)
Caucasian	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**
African Canadian	1.70 (1.28–2.25)	1.75 (1.33–2.29)	1.50 (0.90–2.48)	1.08 (0.74–1.57)	1.42 (1.05–1.91)	1.27 (0.89–1.82)
Asian	1.34 (1.11–1.62)	0.82 (0.70–0.97)	0.73 (0.57–0.93)	0.73 (0.57–0.94)	1.23 (1.01–1.51)	1.17 (0.94–1.47)
Indo-Canadian	1.03 (0.69–1.53)	0.87 (0.64–1.20)	0.72 (0.46–1.14)	0.58 (0.35–0.99)	1.47 (1.01–2.13)	1.38 (0.89–2.15)
Native Canadian	1.60 (0.70–3.63)	0.70 (0.34–1.46)	1.49 (0.34–6.44)	2.45 (0.99–6.04)	1.37 (0.59–3.19)	1.14 (0.41–3.21)
Hispanic	1.10 (0.70–1.75)	0.74 (0.51–1.08)	0.58 (0.34–0.99)	0.66 (0.36–1.21)	1.37 (0.88–2.14)	0.59 (0.32–1.09)
Middle Eastern	1.19 (0.89–1.60)	1.22 (0.95–1.56)	0.84 (0.57–1.23)	1.19 (0.85–1.66)	0.83 (0.60–1.16)	1.20 (0.85–1.68)

serum hormones. Current reference standards are based on the 2010 WHO criteria, which has limited accountability for variations in ethnicity. Our study explored the impact of ethnicity on both semen parameters and gonadotropin levels, and illustrates differences do exist between ethnicities, which may be useful in the workup and management of these individuals.

Published, online demographic statistics of the province of Ontario, Canada in 2016 indicate that approximately one-third of the population (29.3%) are visible minorities, where our study had 43.7% in minority groups.[7] More than half of our study population was Caucasian, followed by Asians, Middle Eastern individuals, and African Canadians (Table 1). In comparison to the provincial racial distribution, the largest visible minority groups are South Asian (29.6%), Chinese (19.4%), Black (16.2%), Filipino (8.0%), and Middle Eastern (5.4%).[7] Overall, this indicates reasonable applicability of our data to the province and the representativeness of our patient population.

Few studies have examined ethnicity correlated to semen parameters.[6] One study by Redmon et al, which originally looked at geographic variation in the U.S., showed poorer semen quality in rural populations, but also looked at Hispanic/Latino, White, and Black individuals in further analysis. They studied 557 White men and 57 Black men and found that Blacks had statistically significant lower semen volumes (p=0.0001), concentration (p=0.009), and total sperm counts (p=0.0001).[6] A more recent study by Khandwala et al has looked at differences between White and Asian populations in a large cohort of 1230 White men and 701 Asian men, and illustrated that differences in concentration (p<0.001), count (p=0.002), and volume (p<0.0001) are present.[8] Glazer et al also demonstrated that Asians had the highest sperm concentrations and Blacks the lowest, similar to our data.[9] Furthermore, additional studies have looked at Chinese populations but lack a comparator group,[10] and Japanese populations with limited sample size of only 324 men.[11]

Table 4. Linear regression for hormone profiles by ethnicity (adjusted by age)

	FSH	Testosterone
Caucasian	Ref	Ref
African Canadian	0.49 (-0.68–1.66)	0.55 (-0.22–1.32)
Asian	-0.07 (-0.85–0.70)	-1.26 (-1.77-(-0.76))
Indo-Canadian	-1.38 (-2.82–0.04)	-1.92 (-2.85-(-0.99))
Native Canadian	1.65 (-1.37–4.67)	-1.43 (-3.38–0.52)
Hispanic	0.23 (-1.79–2.24)	-0.47 (-1.78–0.84)
Middle Eastern	-0.78 (-1.94–0.38)	-0.59 (-1.35–0.17)

FSH: follicle-stimulating hormone.

Our analysis, similar to the data in the study by Redmon et al, even after adjusting for age, showed that African Canadians were most likely to have more abnormal semen parameters, including azoospermia, oligospermia, or low volume. Asians, who had been previously reported by Khandwala et al to have higher rates of azoospermia and higher sperm concentrations, in our study were similarly more likely to be azoospermic, but also have improved motility and morphology and less likely to be simply oligospermic. Indo-Canadians, on adjusted analysis, were still shown to have decreased rates of teratozospermia. No significant differences in semen parameters or hormones were shown for Middle Eastern individuals, Native Canadians, and Hispanics, but small differences may not have been identified with the relatively small sample sizes of these groups in our study.

In our study, we found that Asians and Indo-Canadians were more likely to have lower testosterone levels and no differences were seen for FSH in our adjusted analysis. Many studies in the literature investigating hormonal profiles between patients have been completed in the prostate cancer subpopulation or in adolescents.[12,13] One study in adolescents showed Mexican Americans to have the highest testosterone compared to non-Hispanic Whites, and non-Hispanic Blacks,[12] and another showed that Blacks had a higher level of testosterone only in the age category 20–39.[14] While some studies have shown no difference,[15] a recent meta-analysis compared sex steroid hormone concentration in Black and White men and found that Black men had a slightly significant higher level of free testosterone.[16]

Identified racial differences in semen parameters and hormones may be genetic or due to sociodemographic factors; however, some differences may be due to cultural and/or environmental/dietary variations.[17,18] Explanations may include

less time before seeking fertility treatments, which may dilute the population with more normal parameters, or in certain cultures, not presenting for fertility evaluations at all out of fear, shame, or religious concerns. The under-representation of certain minority groups may also be due to financial burdens, given the cost of many assisted reproductive technologies.[19] Recent work has also highlighted semen quality differences based on various sociodemographic factors, including race, education, and geographic location, in the U.S.[9] However, in a Canadian healthcare system, there is likely less resource accessibility and financial barriers than one would expect in a private system.[20] With respect to hormonal differences, some theories may relate to variable genetics of hormone metabolism or lifestyle factors that differ by ethnicity.[16,21]

The clinical implications of this are important, as they may alter patient management; for example, in deciding which patients would be more likely to benefit from hormonal manipulation.

Limitations of our study include the retrospective nature and self-reported patient questionnaire for demographic data, which may lead to misclassification and recall bias. Data related to immigration and other socioeconomic variables not included in the questionnaire were not available. There is also variation of serum hormone levels, as results were obtained from numerous laboratories. However, the sample size is large, and includes all patients seen for infertility at a specialized center. The semen analysis data is robust in that it uses a single lab, increasing reliability and comparability. Only first-time semen analyses were included to reduce bias from any treatments or intervention. Finally, all patients were included from the same geographic region to reduce any environmental bias and minimize variation.

Conclusions

Currently global thresholds for male infertility are based on the 2010 WHO standards, however, racial and ethnic differences may exist. Our study illustrates that among Canadian men who present for male infertility and who represent a diverse population, differences in semen analysis and hormones are present. An understanding of this variation may aid in the counselling and workup of these patients. Further validation and assessment of current references is required in large and varying populations to help understand the potential genetic, environmental, behavioral, and cultural patters that may explain these differences.

Competing interests: Dr. Jarvi has been a consultant for and received honoraria from Ferring and Pharmascience Center US; and was the principal investigator in a clinical trial supported by Allergan looking at the use of Botox to treat scrotal pain. Dr. Lau was a research coordinator for a clinical trial supported by Allergan looking at the use of Botox to treat scrotal pain. The remaining authors report no competing personal or financial interests related to this work.

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