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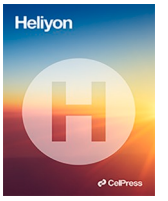

Research article

A retrospective study investigating semen parameter profiles among male patients attending a fertility center in the UAE: Insights from a nationality perspective

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ABSTRACT

Objectives: The current study assessed the epidemiological trends of semen phenotypes and their association with ethnicity among men seeking fertility treatment in the United Arab Emirates (UAE).

Methods: This retrospective study assessed the anthropometric information including age, body mass index (BMI), and nationality, along with semen parameters of men who visited a Fertility Center in Abu Dhabi, UAE between January 2011 and July 2022. To understand the epidemiological trend of semen parameters amongst UAE nationals, propensity score analysis and logistic regression were performed. Thus, the exposure variable of interest is ethnicity, categorized into UAE nationals (Emirati) and Others (minus UAE; Global). Statistical analysis was performed using SPSS, R packages and STATA.

Results: In this study, 32,664 samples were collected from 19,482 patients from 113 countries worldwide over a period of 11 years. Most participants made multiple visits, with around 40 % attending at least once. Following covariates adjustment, logistic regression indicated a non-significant increase (4 %) in the prevalence of asthenozoospermia among the UAE population compared to Global. Further modeling adjusted for propensity score and Emirati status suggested that Emiratis were 13 % less likely to have lower total sperm count (TSC) compared to Global ($p < 0.001$). Whereas approximately 58 % of UAE nationals' samples exhibited teratozoospermia compared to 56 % in other nationalities. After adjusting for confounders, analysis revealed a significantly higher prevalence (12 %) of teratozoospermia among Emiratis compared to other nationals.

Conclusion: Samples from UAE nationals displayed reduced sperm motility and normal morphology but increased TSC. While the underlying cause of these observed phenotypes was not investigated, it is worth noting that all the men including those from other nationalities resided in the UAE and were subjected to the same climate. Thus, other factors, such as ethnicity, may have primarily influenced the differences observed in these parameters, with genetic makeup also potentially contributing to these outcomes.

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1. Introduction

Conventional semen analysis is a pivotal tool and remains the gold standard for diagnosing and treating male infertility, with the added evaluation of medical records, hormonal analysis, physical examination, and other fundamental parameters. It is well documented that semen is heterogenous, and can be influenced by an array of diverse factors, including but not limited to, diet [1], stress [2], smoking [3], excessive exercise [4–6], exposure to endocrine disrupting chemicals [7,8], pesticides [9], heat [10], environmental factors [11,12] and several other factors [13]. The role of race, ethnicity, sociocultural background, seasonality and geographical region have also been reported [14–16].

For instance, it was reported that infertile men from the United States displayed lower sperm concentration, total sperm count (TSC), as well as reduced total and progressive motility when compared to counterparts from Iraq [17]. Jensen et al. reported a difference in sperm concentration between men from two separate settings (rural and urban) in Denmark. From their findings, it was unclear whether these variations were entirely geographically dependent or due to the sampling methods [18]. Additionally, a steep difference in sperm count was reported between semen samples from four European countries, including Finland, Denmark, France and Scotland [19]. While Auger et al. reported variations in semen parameters of men located in various geographical districts of France [20].

Coupled with semen parameters variation associated with geographical region, the frequency and prevalence of male infertility differ across regions and populations. The incidence of male infertility ranged from 4.5 to 6% in North America, 8–12 % in Europe, 8–9% in Australasia, and 9.4 % in the USA [21]. In Eastern Europe, infertility due to the male factor ranged from 40 to 60 % [22,23], 36.2 % in Sudan [24], 25.6 % in Mongolia [25], 13 % in Egypt [26], 25.3 % in Iran [27], 20 % in the French regions (including France) [28] and 42.4 % in South-eastern Nigeria [29].

In the Middle East, as well as in the broader Middle East and North Africa (MENA) region, studies have reported higher male infertility prevalence. The study of Mascarenhas et al. showed that infertility prevalence was highest in South Asia, Sub-Saharan Africa, North Africa and the Middle East, Central/Eastern Europe and Central Asia [30]. While another study reported that the incidence of primary infertility in the MENA region is estimated at 3.8 %, secondary infertility at 17.2 %, and demographic infertility is estimated at 22.6 % [31]. Similarly, higher male infertility rates were also observed in the Middle East (Turkey; 1.498 %) and North Africa (1.676 %) following analysis of global age-standardized prevalence of infertility [32].

While regions such as the Middle East and North Africa have been identified with higher infertility prevalence, current estimates predominantly rely on data collected from female partners of infertile couples, and studies dating back to 1988. One landmark study that reported the prevalence of male infertility in the Middle East used survey data consisting of interviews with female partners from infertile couples, and subsequent male infertility estimate were indexed on the women only [30]. Another study showed that the percentage of infertile couples, and the incidence of male infertility in the Middle East was unknown [33]. Nonetheless, the study reported that couples in which the male factor is one of the multiple causes of infertility was about 60–70 %. This estimation was based on the report of a study conducted in 1988 [34]. This shows that there is great paucity in data from the Middle East, and this could allow for over or under estimation of the prevalence and incidence of male infertility. Thus, there is need for epidemiological studies describing semen phenotypes of men from these regions. This will enhance future studies to appropriately incorporate and evaluate the prevalence of male infertility, and how this would impact the interpretation of global data. Therefore, the current study assessed the epidemiological trends of semen phenotypes and their association with geographic regions among men seeking fertility treatment in the UAE.

2. Methods

2.1. Data acquisition

In this retrospective study, upon receiving ethical approvals from the Mohammed Bin Rashid University of Medicine and Health Sciences (MBRU) Ethics Committee (MBRU-IRB-2021-12) and HealthPlus Research and Ethics Committee (REC/2022/P27), de-identified data were extracted from the fertility center's database and stored on password protected secured server.

2.2. Data collection

The anthropometric information including age, weight, height, body mass index (BMI), and nationality, along with semen parameters (semen volume, semen pH, sperm concentration, TSC, total motility, progressive motility, normal morphology, viability) of all men who attended a Fertility Center in Abu Dhabi, between January 2011 and July 2022 were assessed. Semen parameters were analysed based on the 5th edition of the World Health Organization (WHO) laboratory manual for the examination and processioning of human semen. During the 11 years of study period, 32664 samples were obtained from 19482 patients from 113 different nationalities across all regions of the world, most of whom visited more than once.

Based on nationality, data of patients were categorized into regions according to the World Bank classification of countries [35]. The regions include Sub-Saharan Africa, North Africa, North America, Central America, South America, Asia, Europe, Middle East, and Oceania.

2.3. Data filtering

To avoid data misrepresentation, misanalysis, and subsequent misinterpretation, de-identified data were filtered and vetted upon extraction. Data point having N/A for weight (kg) and height (cm) were deleted and the cell was left empty. Following appropriate filtering, vetting, and cleaning, data analysis commenced.

2.4. Unadjusted data analysis

Unadjusted descriptive statistical analysis, unpaired t-tests and chi-squared tests were employed for data description and comparison. To have a better understanding of the study cohort, further analyses were performed after categorizing data into regional subgroups, laying emphasis on the UAE, Middle East, and the MENA region.

Firstly, data was categorized into MENA and non-MENA countries. Thereafter, we conducted a comparative analysis of semen parameters between patients from the Middle Eastern nations and those from other parts of the world. Additionally, semen parameters of patients from the UAE were also compared to those from other Middle Eastern nations, other MENA, and finally to Global data. To mitigate potential biases resulting from skewed data distributions, we further analysed semen parameters based on the WHO reference values for each parameter across various regions [36]. We assessed semen parameters characteristics according to age and BMI. Qualitative and quantitative measurements were summarised using frequency with percentage, mean ± SD, median and interquartile ranges (IQR). Descriptive statistics summarised the demographic and characteristics of the patients for each region. For all analyses, a $p < 0.05$ was considered statistically significant. SPSS (IBM SPSS, v28.0, USA) and GraphPad Prism™ (GraphPad™ Software, Version 9.0, San Diego, CA, USA) were employed for this analysis.

2.5. Adjusted data analysis

Skewness in data distribution is observed in the current study, potentially limiting the extent of outcome interpretation. Among the 32,664 samples collected from 19,612 patients representing 113 different countries, 21,649 samples originated from UAE nationals, leading to an uneven distribution of data. However, to address this bias, models such as logistic regression and propensity score analysis were employed, accounting for variables such as nationality, age, BMI, height, and weight.

In the adjusted analysis, ethnicity was the exposure variable of interest. Thus, data was categorized into UAE nationals (Emirati) and others (comprising of individuals other than UAE nationals to represent the global population; Global). The outcome variables are morphology (<4 %; teratozoospermia), progressive motility (<32 %; asthenozoospermia), total motility (<40 %; asthenozoospermia), sperm concentration (<15 M/ml; oligozoospermia) and TSC (<39 x 10^6/ejaculate; oligozoospermia). The covariates are age, height, and weight of the subjects. To balance the above covariates between the two races, as in the randomized controlled trials, covariates adjustment was done using Propensity Score Analyses (PSA). The probability of a patient being an UAE national given the set of above covariates was computed using logistic regression analyses [37]. This method has widely been used in observational studies to balance the covariates or adjust the covariates between the exposures [38,39]. As PSA, we have used the following methods: Propensity Score (PS) Matching with 1:2 ratio, Inverse Probability Weighting and Regression modelling with ethnicity and PS as covariates. Odds ratio, and 95 % CI were estimated using the above methods. These statistics were used to construct forest plot. The adjusted analyses were performed using R packages (version 4, The R Foundation for Statistical Computing Platform) and STATA software (version 18, StataCorp, USA).

3. Results

The results section of the current study presents findings from both unadjusted and adjusted analyses. The adjusted analysis

Table 1
Descriptive statistics for entire study cohort.

Parameters	Mean	Standard Deviation	Median	Percentile 25	Percentile 75	n
Age at Test (years)	37.40	8.00	37.00	32.00	42.00	32664
Weight (kg)	88.18	17.54	86.00	76.05	97.50	29044
Height (cm)	173.30	7.00	173.00	169.00	178.00	30275
BMI	29.33	5.61	28.41	25.66	32.15	28919
Semen pH	7.70	0.38	7.50	7.50	8.00	29961
Liquefaction time (mins.)	30.60	21.78	30.00	21.00	33.00	30400
Volume (ml)	2.59	1.47	2.30	1.50	3.00	31585
Sperm Concentration (M/ml)	63.01	55.97	51.00	20.00	90.50	29206
Total sperm count (x10^6)	160.99	173.61	110.50	38.00	225.00	29173
Progressive Motility AB (%)	39.78	19.53	40.00	26.00	54.00	28732
Non-Progressive Motility C (%)	8.54	7.14	7.00	4.00	11.00	28693
Immotile D (%)	51.62	19.77	50.50	37.00	65.00	28708
Total Motility (%)	48.35	19.77	49.20	35.00	62.50	28707
Normal Morphology (%)	7.80	10.70	3.00	2.00	6.00	24613
Vitality (%)	15.30	22.40	4.50	0.00	24.50	72

primarily examines the comparison of semen phenotypes (observable characteristics of semen, including parameters such as sperm concentration, motility, and morphology) between UAE nationals and individuals from other regions of the world.

3.1. Findings from unadjusted analysis

3.1.1. Anthropometric parameters

In the current study, 32664 samples were obtained from 19482 patients from 113 different countries across all regions of the world over a period of 11 years. Most of the study participants made multiple visits, with approximately 40 % visiting at least once. The median number of visits was 2, while the highest recorded number of visits reached 32 (Supplementary Tables 1A–D). The study cohort's mean age at test was 37.40 ± 8 years, with an average weight of 88.18 ± 17.54 kg and a mean BMI of 29.33 ± 5.61 (Table 1).

Subsequently, samples were grouped into regions, allowing for a descriptive analysis of individual anthropometric parameters such as age, weight, height, and BMI based on region (Supplementary Tables 2A–D). In the present study cohort, the mean age at test was highest among Sub-Saharan African nationals (41.7 ± 7.7 years) and lowest among South Americans (32.9 ± 7.2 years). Regarding BMI, the highest values were observed in patients from North Africa (29.68 ± 5.28) and the Middle East (29.49 ± 5.73), while patients from Central America exhibited the lowest mean BMI (25.93 ± 0.90).

3.1.2. Semen parameters

For semen macroscopic parameters, the study cohort exhibited a mean semen volume of 2.59 ± 1.47 ml, with an average liquefaction time of 30.60 ± 21.78 min. Regarding microscopic semen parameters, the mean sperm concentration was 63.01 ± 55.97 million per milliliter (M/ml), with progressive motility averaging 39.78 ± 19.53 % and total motility averaging 48.35 ± 19.77 %. The mean percentage of spermatozoa with normal morphology was 7.8 ± 10.7 %, with a median of 3 %. Viability was conducted only when no motile sperm were present in the ejaculate. Therefore, viability was assessed in only 72 samples over the 11-year period. Among these samples, the mean percentage of viable cells was 15.3 ± 22.4 %, with a median of 4.5 % Table 1.

After categorizing samples based on regions, there was no difference in liquefaction time across the regions (Supplementary Table 2E). Patients from Central America had the lowest mean semen volume at test (1.50 ± 0.51 ml), while patients from South America have the highest mean semen volume (3.15 ± 1.41 ml) (Supplementary Table 2F).

Due to data distribution skewness, microscopic semen parameters will be reported as median and IQR. The mean values are shown in the representative tables. As shown in Supplementary Table 2G, the median sperm concentration across different population ranged from 31.5 to 68 M/ml, with TSC ranging from 95.25 million to 172.50 million per ejaculate (Supplementary Table 2H). The median progressive motility ranged from 35.50 to 46 % across different regions, with Sub-Saharan Africa having the lowest (35.50 %; 22–50 %) and Central America (46 %; 42–48 %) exhibiting the highest (Supplementary Table 2I). Similar trend was observed in total motility, as it ranged from 45.50 to 57 % across different regions (Supplementary Table 2J). Interestingly, the median percentage of morphological normal spermatozoa was below the WHO lower limit reference value (≥4 %) in all regions except for Central America (Supplementary Table 2K), while the 25th and 75th percentile are 2 and 6 % respectively.

We further assessed the correlation between semen parameters and age (Table 2), and BMI (Table 3). Findings showed that sperm progressive motility decreases with advancing age, and similar findings were observed with total motility. While sperm concentration increases with increase in age, reaching its peak at 60 years, and thereafter starts to decline (Table 2). Moreover, TSC increases with advancing age until 45years and thereafter starts declining.

Total motility and progressive motility decrease with increase in BMI, while the effect of BMI on semen volume showed a bell-shaped characteristic. That is, semen volume was low in underweight patients, highest in normal weight individuals, and lowest in

Table 2
Association between age and other anthropometric and semen parameters.

Parameters	Age at Test (years)[a]										
	≤20	21–25	26–30	31–35	36–40	41–45	46–50	51–55	56–60	61–65	66+
	Mean	Mean	Mean	Mean	Mean	Mean	Mean	Mean	Mean	Mean	Mean
Weight (kg)	76.73	83.08	87.15	88.51	88.81	89.57	89.08	86.35	83.87	84.06	81.84
Height (cm)	174.30	173.10	173.30	173.90	173.70	173.10	172.90	171.40	170.60	168.80	168.30
BMI	25.15	27.69	29.01	29.23	29.43	29.86	29.79	29.42	28.71	29.53	28.82
Semen pH	7.80	7.69	7.70	7.71	7.70	7.70	7.70	7.72	7.72	7.76	7.74
Liquefaction time (mins.)	28.35	29.74	31.04	30.60	30.23	30.18	30.61	33.33	31.61	33.62	32.46
Volume (ml)	2.18	2.64	2.71	2.71	2.62	2.52	2.34	2.28	1.95	1.83	1.33
Sperm Concentration (M/ml)	31.59	52.31	58.85	60.67	62.60	67.37	70.78	72.66	72.85	55.25	60.15
Total sperm count (x106)	60.84	137.89	160.80	161.96	163.61	167.32	162.18	156.20	131.33	112.91	102.66
Progressive Motility AB (%)	43.25	43.13	41.68	41.16	40.10	39.43	36.45	32.07	30.96	28.31	17.80
Non-Progressive Motility C (%)	11.27	9.28	9.09	8.86	8.47	8.16	7.75	7.74	7.72	8.77	5.99
Immotile D (%)	45.47	47.53	49.12	49.92	51.35	52.39	55.78	60.20	61.33	62.89	76.26
Total Motility (%)	54.53	52.49	50.85	50.05	48.62	47.59	44.21	39.82	38.66	37.08	23.73
Normal Morphology (%)	5.70	9.20	9.40	8.40	7.30	7.00	6.70	6.50	6.80	7.00	4.70
Vitality (%)	.	46.00	14.50	19.40	6.30	17.10	11.40	22.00	10.00	0.00	0.00

[a] Classification was based on the entire cohort samples.

Table 3
Association between BMI and other anthropometric and semen parameters.

Parameters	BMI[a]									
	Low - 18.5 Under Weight		18.6–24.9 Normal		25–29.9 Overweight		30–39.9 Obese		40+ Morbid Obese	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age at Test (years)	32.6	8.4	35.4	7.8	37.4	7.8	37.8	7.6	36.4	7.4
Weight (kg)	51.24	6.56	69.35	7.36	82.75	7.58	100.32	11.16	130.92	16.39
Height (cm)	172.4	6.9	173.6	6.9	173.6	6.8	173.2	6.8	171.1	8.7
BMI	17.21	1.54	22.97	1.56	27.43	1.36	33.37	2.55	44.82	6.33
Semen pH	7.75	0.37	7.71	0.37	7.71	0.37	7.70	0.37	7.67	0.42
Liquefaction time (mins.)	28.40	9.82	30.33	24.38	30.37	20.21	30.35	22.67	31.09	16.80
Volume (ml)	2.54	1.42	2.65	1.48	2.60	1.45	2.55	1.44	2.41	1.45
Sperm Concentration (M/ml)	63.28	43.73	66.37	56.87	64.36	55.43	62.01	56.06	46.64	49.58
Total sperm count (x106)	159.07	144.51	170.81	178.10	165.02	173.90	156.70	170.14	110.16	128.63
Progressive Motility AB (%)	41.72	19.19	39.72	19.24	39.86	19.34	39.85	19.62	38.35	20.68
Non-Progressive Motility C (%)	8.88	8.34	8.42	7.01	8.36	6.93	8.49	7.09	9.04	8.13
Immotile D (%)	49.40	19.71	51.80	19.39	51.68	19.59	51.61	19.88	52.60	21.05
Total Motility (%)	50.60	19.71	48.20	19.41	48.29	19.57	48.37	19.89	47.42	20.99
Normal Morphology (%)	9.2	11.4	7.1	9.9	7.2	9.9	8.0	10.8	9.3	11.6
Vitality (%)	.	.	18.5	25.5	16.1	22.1	11.5	22.4	17.0	20.3

[a] Classification was based on the entire cohort samples.

overweight, obese, and morbid obese individuals (Table 3). Additionally, TSC was highest in patients with normal BMI and decreases with increase in BMI, as such, TSC was lowest in the morbid obese (>40 BMI) patients.

3.1.3. Comparison between regions

To have a clearer picture of the study cohort, further analyses were performed after categorizing data into subregions, laying emphasis on the UAE, Middle East, and the MENA region.

Data were classified into MENA and non-MENA countries. Semen parameters remained within the normal WHO reference values in the two categories (Table 4). However, there was a significant reduction in semen volume in the MENA region compared to non-MENA region (2.58 ± 1.48 versus 2.62 ± 1.38 ml; $p < 0.00001$). This was also true for sperm concentration between MENA and non-MENA (62.70 ± 55.47 versus 64.99 ± 59.01 M/ml; $p = 0.017$). However, there was a significant increase in progressive motility in the MENA region (40.03 ± 19.72 %) compared to the non-MENA (38.18 ± 18.19 %; $p < 0.00001$).

Furthermore, a comparative analysis was performed to assess potential differences between samples from the Middle East and the rest of the world. Findings showed comparable mean age at test between the two subgroups (Table 5). Semen parameters were also comparable between patients from the Middle East and the rest of the world (Table 5).

Seeing that most of the study cohort are from the Middle East, we compared semen parameters of patients from the UAE to patients from other Middle Eastern countries. While semen parameters remained within normal WHO reference values, there was a reduction in the percentage of progressively motile spermatozoa in participants from other Middle Eastern countries compared to the UAE (Table 6).

Thereafter, samples from UAE nationals were compared to those from other MENA countries. Although samples remained within normal WHO reference values, other MENA countries displayed reduced sperm concentration, TSC and motility when compared to the UAE samples (Table 7). However, there was a significant reduction in the mean semen volume and percentage of spermatozoa with

Table 4
Comparison analysis between MENA and Non-MENA countries.

Parameters	MENA			Non-MENA			
	Mean	SD	n	Mean	SD	n	P value
Age at Test (years)	37.1	8.1	28348	39.0	7.1	4316	0.000
Weight (kg)	88.24	17.79	25357	87.72	15.71	3687	0.089
Height (cm)	172.9	6.7	26473	176.5	7.5	3802	0.000
BMI	29.50	5.71	25255	28.15	4.64	3664	0.000
Semen pH	7.69	0.37	25941	7.77	0.39	4020	0.000
Liquefaction time (mins.)	30.42	20.76	26343	31.79	27.47	4057	0.000
Volume (ml)	2.58	1.48	27387	2.62	1.38	4198	0.000
Sperm Concentration (M/ml)	62.70	55.47	25245	64.99	59.01	3961	0.017
Total sperm count (x106)	160.16	174.21	25214	166.28	169.66	3959	0.000
Progressive Motility AB (%)	40.03	19.72	24862	38.18	18.19	3870	0.000
Non-Progressive Motility C (%)	8.35	7.01	24826	9.77	7.86	3867	0.000
Immotile D (%)	51.54	19.97	24833	52.15	18.47	3875	0.065
Total Motility (%)	48.43	19.96	24830	47.85	18.49	3877	0.074
Normal Morphology (%)	8.1	11.0	21147	5.9	8.2	3466	0.074

Table 5
Comparison statistics for Middle East and Global (excluding Middle East).

	Middle East and Global							
	Middle East				Global (minus Middle East)			
	Mean	Standard Deviation	Median	n	Mean	Standard Deviation	Median	n
Age at Test (years)	37.0	8.2	36.0	26910	38.8	7.0	38.0	5754
Weight (kg)	88.03	17.79	85.70	24081	88.89	16.30	87.00	4963
Height (cm)	172.7	6.7	173.0	25153	176.4	7.3	176.0	5122
BMI	29.49	5.73	28.69	23986	28.55	4.86	27.78	4933
Semen pH	7.69	0.37	7.50	24596	7.77	0.39	7.90	5365
Liquefaction time (mins.)	30.39	20.99	30.00	24992	31.59	25.08	30.00	5408
Volume (ml)	2.56	1.48	2.20	25981	2.69	1.41	2.50	5604
Sperm Concentration (M/ml)	62.88	55.71	51.00	23976	63.60	57.14	52.00	5230
Total sperm count (x106)	159.75	173.57	108.90	23946	166.67	173.69	120.00	5227
Progressive Motility AB (%)	40.05	19.74	40.00	23619	38.53	18.49	39.00	5113
Non-Progressive Motility C (%)	8.29	6.97	7.00	23586	9.74	7.81	8.00	5107
Immotile D (%)	51.59	19.99	50.50	23591	51.80	18.74	51.00	5117
Total Motility (%)	48.39	19.98	49.50	23588	48.19	18.75	49.00	5119
Normal Morphology (%)	8.1	11.0	3.0	20112	6.4	8.9	3.0	4501
Vitality (%)	16.5	23.4	5.0	63	6.9	10.2	1.0	9

Table 6
Comparison statistics between UAE and Other Middle East Countries.

Parameters	UAE and Other ME Countries							
	UAE				Other Middle East			
	Mean	Standard Deviation	Median	n	Mean	Standard Deviation	Median	n
Age at Test (years)	36.8	8.4	36.0	21649	38.1	7.0	37.0	5261
Weight (kg)	87.24	17.73	85.00	19438	91.34	17.65	89.00	4643
Height (cm)	172.3	6.5	172.0	20319	174.5	7.2	175.0	4834
BMI	29.38	5.82	28.41	19364	29.96	5.34	29.06	4622
Semen pH	7.69	0.37	7.50	19846	7.71	0.40	7.50	4750
Liquefaction time (mins.)	30.42	21.73	30.00	20174	30.23	17.56	30.00	4818
Volume (ml)	2.53	1.49	2.00	20966	2.70	1.46	2.50	5015
Sperm Concentration (M/ml)	65.07	56.33	54.00	19426	53.55	51.94	41.00	4550
Total sperm count (x106)	163.93	176.57	112.50	19401	141.88	158.91	92.25	4545
Progressive Motility AB (%)	40.38	19.69	40.00	19175	38.64	19.88	39.00	4444
Non-Progressive Motility C (%)	8.06	6.66	6.50	19149	9.28	8.08	7.00	4437
Immotile D (%)	51.50	19.93	50.50	19151	51.97	20.26	50.50	4440
Total Motility (%)	48.49	19.92	49.50	19148	47.95	20.24	49.50	4440
Normal Morphology (%)	8.1	11.0	3.0	16425	8.2	11.1	3.0	3687
Vitality (%)	16.3	25.9	2.5	44	16.9	16.9	12.0	19

Table 7
Descriptive statistics by UAE and Other MENA countries.

Parameters	UAE and Other MENA						
	UAE			Other MENA			P Value
	Mean	SD	n	Mean	SD	n	
Age at Test (years)	36.8	8.4	21649	38.1	7.0	5261	0.000
Weight (kg)	87.24	17.73	19438	91.34	17.65	4643	0.000
Height (cm)	172.3	6.5	20319	174.5	7.2	4834	0.000
BMI	29.38	5.82	19364	29.96	5.34	4622	0.000
Semen pH	7.69	0.37	19846	7.71	0.40	4750	0.000
Liquefaction time (mins.)	30.42	21.73	20174	30.23	17.56	4818	0.522
Volume (ml)	2.53	1.49	20966	2.70	1.46	5015	0.000
Sperm Concentration (M/ml)	65.07	56.33	19426	53.55	51.94	4550	0.000
Total sperm count (x106)	163.93	176.57	19401	141.88	158.91	4545	0.000
Progressive Motility AB (%)	40.38	19.69	19175	38.64	19.88	4444	0.000
Non-Progressive Motility C (%)	8.06	6.66	19149	9.28	8.08	4437	0.000
Immotile D (%)	51.50	19.93	19151	51.97	20.26	4440	0.151
Total Motility (%)	48.49	19.92	19148	47.95	20.24	4440	0.103
Normal Morphology (%)	8.1	11.0	16425	8.2	11.1	3687	0.002

normal morphology in the UAE (8.1 ± 11 %) compared to other MENA countries (8.2 ± 11.1 %) (p = 0.002).

To investigate the semen phenotypes of UAE nationals in comparison to the global population, particular attention was given to these two subgroups. Samples were classified into those originating from the UAE versus those from other regions worldwide, referred to as "Global".

The mean age of patients from the UAE (n = 21649) at test was 36.8 years, while that of patients from other parts of the world (n = 11015) was 38.5 years (Table 8). While the mean of all semen parameters remained within the WHO reference limit values in both categories, there was a reduction in progressive motility of participants from other part of the world compared to the UAE (38.58 ± 19 versus 40.38 ± 19.69 %) respectively. Similar trend was observed in the mean percentage of morphologically normal spermatozoa. However, the median percentage of morphologically normal spermatozoa remained below the WHO lower reference limit values in both groups (Table 8).

Moreover, semen parameters were further analysed based on WHO lower reference limit values for each parameter across the different regions. As shown in Table 9, 33 % of samples from the Middle East are asthenozospermic (total motility <40 %), while patients from the Sub-Saharan Africa (39.3 %) have the highest percentage of asthenozospermia (Table 9). Of note, 58.4 % of the participants from the Middle East displayed teratozoospermia, while more than 60 % of the participants from Sub-Saharan Africa and South America have teratozoospermia (Table 9). Moreover, 20.3 % of the participants from the Middle East displayed oligozoospermia, and 29.6 % of patients from South America displayed oligozoospermia, representing the highest in our study cohort (Table 9).

3.2. Findings from adjusted analysis

Seeing that data distribution is very skewed after classifying patients into the different regions, we opted for logistic regression and propensity score analysis to reduce bias and allow for correctness in data interpretation. This also allows for having a clearer picture of the semen phenotypes of UAE nationals compared to the rest of the world (Global), especially since most of the study cohort are from the UAE, which gives more power to the statistical robustness for study outcome. Thus, for the adjusted analysis, the study cohort were divided into UAE nationals and other parts of the world.

Upon categorizing into two groups, microscopic semen parameters (total motility, progressive motility, sperm concentration, TSC and morphology) were classified based on the WHO reference limit values. That is, progressive motility was sub-grouped in <32 % or ≥32 %; total motility as <40 % or ≥40 %; sperm concentration as <15M/ml or ≥15M/ml; TSC as $<39 \times 10^6$ or $\geq 39 \times 10^6$/ejaculate; and for morphology <4 % or ≥4 %.

3.2.1. Motility

After classifying based on the WHO guidelines, of the 19148 samples from the UAE, 3893 have progressive motility <32 %, making a total of 20.3 % (Fig. 1A). While out of the 9559 samples from the rest of the world, 20 % (1912) had progressive motility <32 %. Subsequently, propensity scores were computed for all data points, and four distinct statistical models were employed. These models comprised a crude analysis, logistic regression, propensity score adjustment accounting for Nationality, propensity score matching (1:2 ratio), and inverse probability weighting.

After adjusting for covariates, all the different models showed no significant difference in the progressive motility between the two subgroups. However, logistics regression models indicated that there was a non-significant increase (4 %) in the percentage of patients with progressive motility <32 % (asthenozoospermia) in the UAE population compared to the rest of the world (Fig. 1B). Additionally, the crude prevalence of total motility (<40 %), that is, asthenozoospermia in UAE nationals was 33 % which is about 1 % higher as compared to other national. Nevertheless, the difference is not statistically significant (Fig. 1C). However, after adjusting for

Table 8
Comparison analysis between UAE and Global (excluding UAE).

Parameters	UAE and Global Minus UAE							
	UAE				Global minus UAE			
	Mean	Standard Deviation	Median	n	Mean	Standard Deviation	Median	n
Age at Test (years)	36.8	8.4	36.0	21649	38.5	7.0	38.0	11015
Weight (kg)	87.24	17.73	85.00	19438	90.07	17.01	88.00	9606
Height (cm)	172.3	6.5	172.0	20319	175.5	7.3	175.0	9956
BMI	29.38	5.82	28.41	19364	29.23	5.15	28.45	9555
Semen pH	7.69	0.37	7.50	19846	7.74	0.40	7.50	10115
Liquefaction time (mins.)	30.42	21.73	30.00	20174	30.95	21.87	30.00	10226
Volume (ml)	2.53	1.49	2.00	20966	2.70	1.43	2.50	10619
Sperm Concentration (M/ml)	65.07	56.33	54.00	19426	58.92	55.01	47.50	9780
Total sperm count (x106)	163.93	176.57	112.50	19401	155.14	167.43	106.00	9772
Progressive Motility AB (%)	40.38	19.69	40.00	19175	38.58	19.15	39.00	9557
Non-Progressive Motility C (%)	8.06	6.66	6.50	19149	9.52	7.94	7.50	9544
Immotile D (%)	51.50	19.93	50.50	19151	51.88	19.46	51.00	9557
Total Motility (%)	48.49	19.92	49.50	19148	48.08	19.46	49.00	9559
Normal Morphology (%)	8.1	11.0	3.0	16425	7.2	10.0	3.0	8188
Vitality (%)	16.3	25.9	2.5	44	13.7	15.6	8.5	28

Table 9
Distribution of semen parameters by region according to the WHO lower reference limit values.

Parameters	Regions								
	Sub-Saharan Africa	North Africa	North America	Central America	South America	Asia	Europe	Middle East	Oceania
Total Motility									
<40 % (Count)	359	379	45	0	6	468	272	7789	77
N (%)	39.30	30.50	32.10	0.00	23.10	31.70	26.50	33.00	26.70
≥ 40 % (Count)	554	863	95	9	20	1007	754	15799	211
N (%)	60.70	69.50	67.90	100.00	76.90	68.30	73.50	67.00	73.30
Progressive Motility									
<32 % (Count)	225	229	26	0	4	278	157	4848	38
N (%)	24.60	18.40	18.60	0.00	15.40	18.80	15.30	20.60	13.20
≥32 % (Count)	688	1013	114	9	22	1197	869	18740	250
N (%)	75.40	81.60	81.40	100.00	84.60	81.20	84.70	79.40	86.80
Morphology									
<4 % (Count)	443	535	75	4	17	744	492	11745	132
N (%)	60.50	51.70	59.10	44.40	68.00	54.70	50.80	58.40	54.10
≥4 % (Count)	289	500	52	5	8	617	476	8367	112
N (%)	39.50	48.30	40.90	55.60	32.00	45.30	49.20	41.60	45.90
Sperm Concentration									
<15 million/ml (count)	183	256	27	0	8	235	219	4863	63
N (%)	19.70	20.20	18.80	0.00	29.60	15.60	20.80	20.30	21.40
≥ 15 million/ml (Count)	747	1013	117	9	19	1270	832	19113	232
N (%)	80.30	79.80	81.30	100.00	70.40	84.40	79.20	79.70	78.60
Total Sperm Count									
<39 million (Count)	256	298	34	1	8	274	253	6146	78
N (%)	27.60	23.50	23.60	11.10	29.60	18.20	24.10	25.70	26.40
≥ 39 million (Count)	673	970	110	8	19	1231	797	17800	217
N (%)	72.40	76.50	76.40	88.90	70.40	81.80	75.90	74.30	73.60

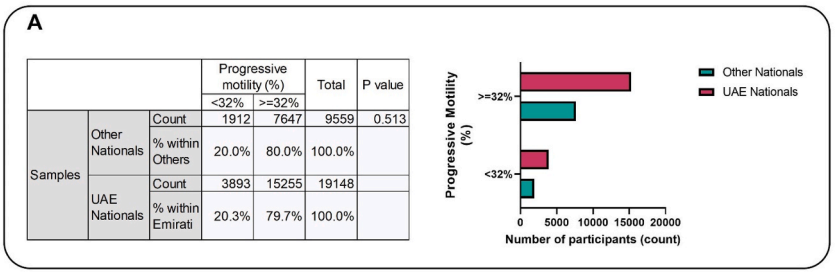

Fig. 1A. The association between progressive motility and nationality. The figure showed that 20.3 % of the Emirati population exhibited progressive motility <32 %, whereas 20 % of individuals from other nationalities displayed a comparable level of progressive motility, and this difference reached statistical significance.

confounders, the percentage of patients with asthenozoospermia (<40 % total motility) within the UAE national was non-significantly higher (4 %) than the other regions (Fig. 1D).

3.2.2. Sperm concentration and total sperm count

The mean sperm concentration was significantly higher in UAE nationals as compared to others ($p < 0.001$). The association analysis showed that the prevalence of oligozoospermia was significantly higher in other nationals (22.4 %) compared to the UAE (18.9 %) (Fig. 2A). While the crude analysis suggested that odds risk for Emiratis to display oligozoospermia is 19 % less when compared to others Additional methods, such as logistic regression showed that there is 24 % less risk for Emiratis to display oligozoospermia when compared to others (Fig. 2B).

Furthermore, the mean TSC was significantly higher in Emirati nationals as compared to Global ($p < 0.001$). Following analysis of the categorical data of TSC by Emirati and others, 26.3 % of other nationalities had significantly lower TSC (<39 million) as compared to 24.6 % in the Emirati groups ($p < 0.001$) (Fig. 2C). This suggests that the Emirati population has significantly higher TSC as compared to other nationals. Crude analysis suggested that the Emirati population were 9 % less likely to have a lower TSC as compared to Global. While all other methods have suggested the same, the modelling (adjusted for propensity score and Emirati) suggested that the Emirati's were 13 % less likely to have lower TSC as compared to others ($p < 0.001$). The PS matching method suggested that the Emirati men attending the fertility center were 11 % less likely to have lower TSC as compared to others. The IPW

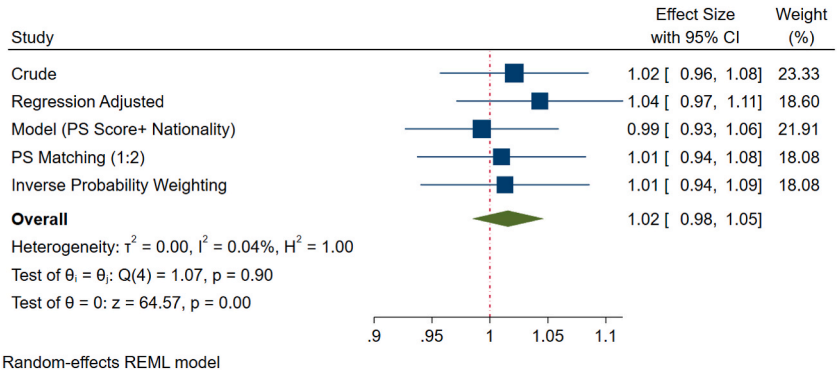

Fig. 1B. Forest plot of progressive motility of various methods of propensity score adjustment analysis. The crude analysis revealed a 2 % elevation in progressive motility <32 % (asthenozoospermia) among Emirati nationals in comparison to individuals from other nationalities, with logistic regression indicating a potential 4 % variance. However, this observed difference did not attain statistical significance.

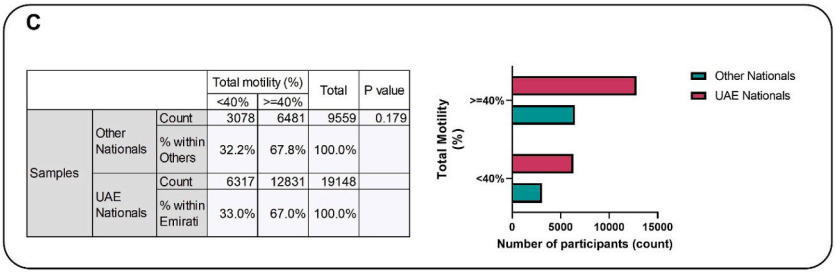

Fig. 1C. The association between total motility and nationality. The prevalence of total motility (<40 %), that is, asthenozoospermia in Emirati nationals was 33 % which is about 1 % higher as compared to other nationalities. However, the difference is not statistically significant.

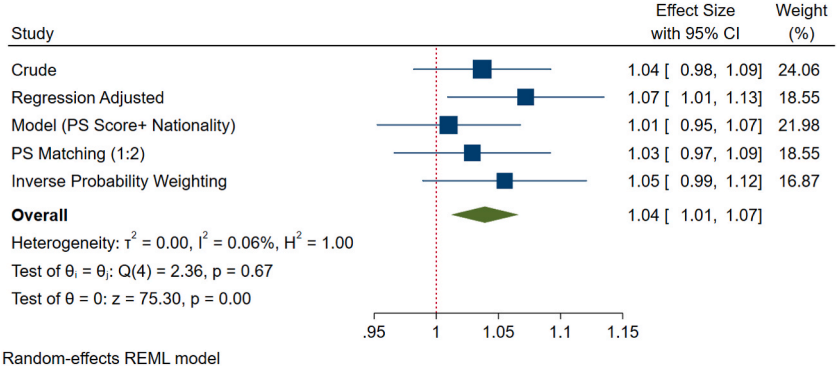

Fig. 1D. Forest plot of total motility of various methods of PS adjustment analysis. After adjusting for confounders, the percentage of patients with asthenozoospermia (<40 % total motility) within the Emirati national was 4 % higher than the other nationalities on the average. However, the difference is not statistically significant. However, regression logistics model showed a 7 % increase in the prevalence of asthenozoospermia among samples collected from the UAE nationals compared to other nationalities.

method suggested that this is 14 % ($p < 0.001$) (Fig. 2D).

3.2.3. Sperm morphology

About 58 % of the Emiratis had normal morphology <4 % (teratozoospermia), while this was 56 % in the other nationals. The difference of 2 % is statistically significant (Fig. 3A). After adjusting for co-founders, analyses revealed that UAE nationals had significantly higher prevalence (12 %) of teratozoospermia compared to other nationals, which on the long run may be as low as 9 % or as high as 16 % (Fig. 3B).

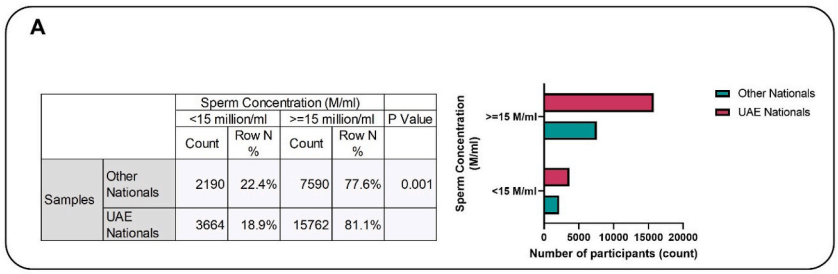

Fig. 2A. The association between sperm concentration and nationality. Before adjustment for disparity between the two subgroups (UAE versus Others) baselines characteristics, UAE nationals had significantly lower (18.9 %) percentage of patients with oligogozoospermia compared to others (22.4 %) ($p < 0.001$).

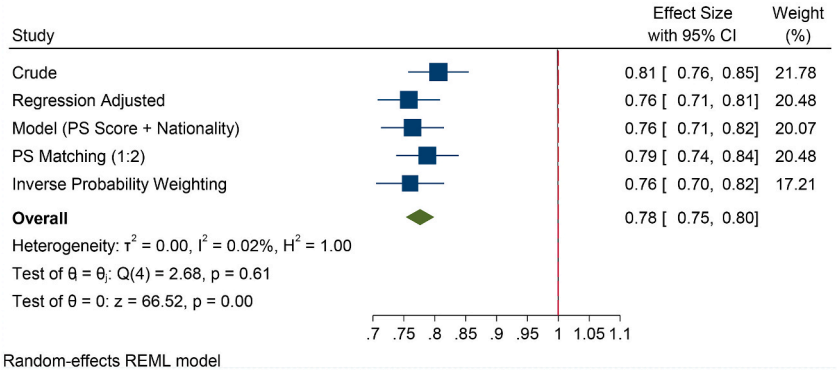

Fig. 2B. Forest plot of sperm concentration of various methods of PS adjustment analysis. The crude (unadjusted) analysis suggested that there is a 19 % less odds risk for Emiratis to display oligozoospermia when compared to others. However, the other methods such as logistic regression suggested that there is 24 % less risk for Emiratis to display oligozoospermia when compared to others.

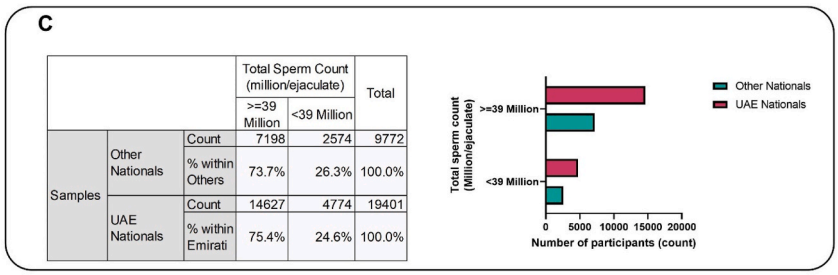

Fig. 2C. The association between total sperm count and nationality. This figure shows that 26.3 % of other nationalities had significantly lower total sperm count (<39 million) as compared to 24.6 % in the Emirati groups ($p < 0.001$).

4. Discussion

The impact of seasonality, race, ethnicity and geographical location on semen parameters and overall male fertility potential is becoming widely investigated [40,41]. Resulting evidence have associated variation in semen parameters characteristics with geographical region, and that the frequency of male infertility differs across regions and population [33]. Although the Middle East and the MENA region at large have been reported to have higher male infertility prevalence, these estimates predominantly rely on data collected from female partners of infertile couples, while data from the UAE is very scarce [31]. The recognition of this gap in epidemiological data regarding semen parameter characteristics among UAE nationals and those from other Middle Eastern and North African countries has spurred the current study to investigate the epidemiological patterns/trends of semen phenotypes and their association with geographic regions among men seeking fertility treatment in the UAE.

In the current study, it was observed that individuals from Sub-Saharan Africa had the highest mean age at test, whereas those from South America had the lowest. Individuals from the Middle East and North Africa region fell between these two extremes. Prior studies that collected data from female partners of infertile couples has indicated that patients from the MENA region tend to seek fertility

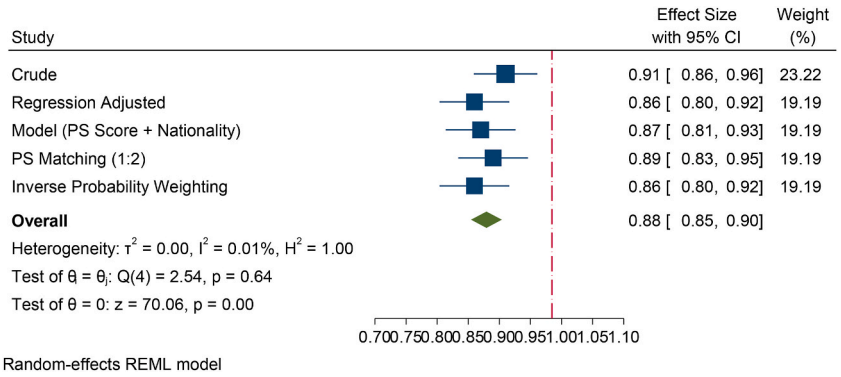

Fig. 2D. Forest plot of total sperm count of various methods of PS adjustment analysis. The crude analyses suggested that the Emirati population had 9 % less likely to have lower total sperm count as compared to other population. While all other methods have suggested the same, the modelling (adjusted for propensity score and Emirati) suggested that the Emirati's were 13 % less likely to have lower total sperm count as compared to others ($p < 0.001$). The PS matching method suggested that the Emirati were 11 % less likely to have lower total sperm count as compared to others. The Inverse Probability Weighting method suggested that this is 14 % ($p < 0.001$).

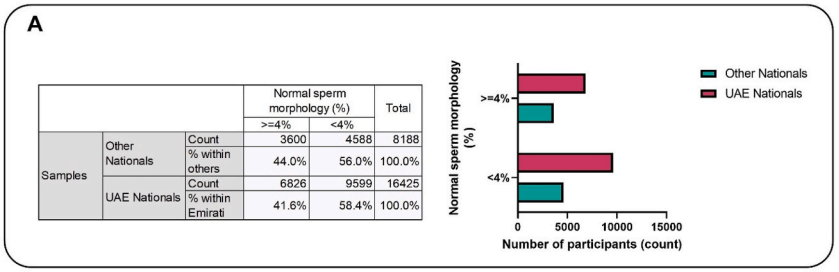

Fig. 3A. The association between sperm morphology and nationality. About 58 % of the Emiratis had normal morphology <4 % (teratozoospermic), while this was 56 % in the other nationals. The difference of 2 % is statistically significant.

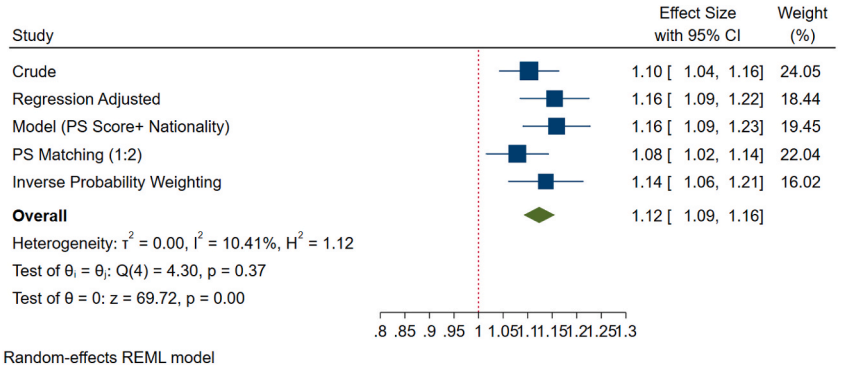

Fig. 3B. Forest plot of sperm morphology of various methods of PS adjustment analysis. In summary, UAE nationals had 12 % higher odds of having teratozoospermia as compared to other nationals. This higher odd was statistically significant. In the long run, these higher odds will be as low as 9 % or as high as 16 %.

treatment at a younger age compared to those from other regions [41,42]. Additionally, Elbardisi et al. found that men from the MENA region were notably younger at the time of testing compared to their counterparts from non-MENA regions [15].

While it has been documented that female partners of infertile couples from the MENA region tend to have higher BMI compared to their European counterparts [41], similar observations have not been reported for MENA men. In the current study, men from North Africa and the Middle East had the highest BMI, while those from Central America had the lowest BMI. While there is limited information available regarding the weight-to-height index of MENA men seeking treatment at fertility centres, it is well-established that the MENA region, particularly high-income countries such as those within the Gulf Cooperation Council (GCC) [43–45], experiences a high prevalence of obesity among adults. Several factors have been proposed to contribute to the elevated BMI in the MENA region,

including sedentary behaviour such as prolonged computer use time associated with childhood obesity [46], socio-economic status [47], parental obesity [48] and sleep deprivation [49].

After correlating age with semen parameters, sperm progressive motility and total motility decreases with increase in age, while sperm concentration increases with increase in age, reaching its peak at 60 years and thereafter starts declining. Prior studies have reported decline in sperm motility and semen volume with increase in age, but sperm concentration tend to remain the same [50]. However, the concept of unchanging sperm concentration over time is not generally agreed upon, as one study reported a significant decrease in both motility and sperm count per year [51]. Although sperm count was reduced in Israeli men over time (10 years), the reason for the change was not investigated [51]. Nevertheless, the study alluded to the potential influence of lifestyle and environmental factors, along with the emotional and psychological stress experienced by many Israelis due to continuous violence and political instability. Nonetheless, the precise mechanisms by which these factors might have impacted sperm parameters were not thoroughly elucidated. All findings taken together, it is evident that sperm motility declines with advancement in age. However, there is possibility that sperm concentration increases with advancement in age until the age of 60 years, and thereafter starts declining.

Furthermore, semen parameters were correlated with BMI in the present study. It was found that total motility and progressive motility decreases with increase in BMI, whereas the effect of BMI on semen volume showed a bell-shaped characteristic. That is, semen volume was low in underweight patients, highest in normal weight individuals, and lowest in overweight, obese and morbid obese individuals. Likewise, TSC was highest in patients with normal BMI and decreases with increase in BMI, as such, TSC was lowest in the morbid obese (>40 BMI) patients.

The decrease in TSC observed in overweight and obese patients in this study aligns with the reports of Sermondade et al., who conducted a meta-analysis on BMI-related studies and showed an increased prevalence of oligozoospermia and azoospermia among overweight and obese individuals [4]. Similarly, findings from the current study is consistent with the reports of a study that examined the relationship between BMI, waist circumference, and semen quality [52], in that TSC decreases with increase BMI. Likewise, another study reported a significant association between lower semen volume, total motile spermatozoa, and both underweight and overweight [53], which parallels the results of our study. Contributing factors may include alterations in the hypothalamic-pituitary-gonadal (HPG) axis and elevated scrotal temperature due to accumulation of lower abdominal fat [54,55].

Prior studies have reported an increase in semen abnormalities in MENA men compared to other regions [15,30,31,33,45,56], most of which were conducted outside the MENA region itself [30,33]. Findings from unadjusted analysis of the current study indicated that samples from MENA men exhibited lower semen volume, and decreased sperm concentration. However, samples of MENA men showed increase in progressive motility. This is in-part similar to the findings of Elbardisi et al. who reported that MENA men displayed lower TSC. It however differs in that MENA men in their cohort displayed reduced motility and lesser spermatozoa with normal morphology [15]. The difference in findings may be because of the variation in composition of participants from the MENA region. For the current study, most of the population representing the MENA region are UAE nationals, while that of Elbardisi et al. are unknown, but the study took place in Doha, Qatar. Additionally, semen parameters of men from the Middle East were compared to the rest of the world. Findings showed that semen parameters were comparable between patients from the Middle East and the rest of the world.

As this study represents the first study characterizing the semen parameters of UAE nationals seeking assistance at a fertility centre, we ensured that a robust analysis was performed. Both unadjusted and adjusted statistical analyses were conducted, employing propensity score analysis to mitigate potential biases in data interpretation. This approach allows for a thorough statistical examination of semen parameters phenotype among UAE nationals and facilitates reliable comparisons with global counterparts.

Firstly, semen samples from UAE nationals were compared to those from other Middle Eastern countries. While semen parameters fell within the normal WHO reference values in both groups, participants from other Middle Eastern countries exhibited a lower percentage of progressively motile spermatozoa compared to those from the UAE. Subsequently, samples from UAE nationals were compared with that of other MENA nationals. While semen parameters remained within the normal WHO reference values, notable differences were observed. UAE nationals exhibited a significant reduction in semen volume, sperm concentration, and the percentage of spermatozoa with normal morphology compared to other MENA countries. However, samples of UAE nationals showed an increase in progressive motility compared to their MENA counterparts. Finally, the samples were categorized into UAE nationals versus those from the rest of the world. An increase in progressive motility was observed in UAE nationals compared to participants from other parts of the world. However, it is noteworthy that the median percentage of morphologically normal spermatozoa remained below the lower reference limit values set by the WHO in both groups. Thus, the summary of the findings of unadjusted analysis between UAE nationals versus other Middle Eastern, versus other MENA, and versus the rest of the world is that UAE nationals exhibited a significant reduction in semen volume, sperm concentration, and normal morphology. However, samples of UAE nationals showed an increase in progressive motility. Since the three independent comparisons have similar outcomes, the next phase of analysis was performed on one grouping, that is UAE nationals versus the rest of the world (Global).

A huge variation was observed between the means and medians of these semen parameters, thus showcasing the skewness in data distribution. Out of the 32664 samples obtained from 19,612 patients who are from 113 different countries, 21649 samples are from UAE nationals. As such, models such as logistic regression, propensity score adjustment accounting for Nationality, propensity score matching (1:2 ratio), and inverse probability weighting were applied to mitigate this bias.

After adjusting for covariates, all models indicated no significant difference in progressive motility and total motility between UAE nationals and the Global cohort. This suggests that the skewed distribution of data may have influenced the findings observed in the unadjusted analysis. Furthermore, upon stratifying based on the WHO lower reference limit criteria (progressive motility <32 % or ≥32 %; total motility <40 % or ≥40 %), logistic regression analysis revealed a non-significant increase (4 %) in the percentage of patients with asthenozoospermia among UAE nationals compared to those from other parts of the world. Similarly, UAE nationals exhibited a significantly higher prevalence (12 %) of teratozoospermia compared to the Global counterparts, which on the long run

may be as low as 9 % or as high as 16 %. However, all employed models consistently indicated that the Emirati population has a significantly higher TSC compared to Global cohort. In summary, the samples from UAE nationals in this study displayed reduced sperm quality (in terms of motility and morphology) but increased sperm quantity (TSC). While the underlying cause of these observed phenotypes was not investigated, it is worth noting that the UAE is situated in a hot climate region. Studies have shown that seasonality variation can impact semen parameters, and high temperatures are known to be detrimental to spermatogenesis processes. In line with this, is the reports of Ozelci et al. who showed that spermatozoa with normal morphology was significantly higher in the spring samples compared to summer [16], indicating that hot weather have a negative effect on sperm morphology. It was further added that both normozoospermic and oligozoospermic semen samples had better quality in spring and winter compared to summer. Although the concept of the effect of seasonality on semen parameters is true, it is less applicable to the participants of the current study since all of them are residents and were also exposed to the climate. Nonetheless, there might be genetical variation in play, which requires further investigations.

As the existing literature reveals a significant paucity of data on male reproductive health and fertility in the UAE and the wider Middle East, leveraging its substantial sample size and statistical robustness, this study provides evidence aimed at bridging this gap, thereby offering valuable insights for the interpretation of global data on reproductive health.

5. Conclusion

The Middle East and the MENA region at large have been reported to have higher male infertility prevalence based on estimates that predominantly rely on data collected from female partners of infertile couples. Whereas data from the UAE is very scarce. In the current study, samples from UAE nationals displayed reduced sperm quality (in terms of motility and morphology) but increased sperm quantity (TSC). While the underlying cause of these observed phenotypes was not investigated, other factors such as genetic makeup may have contributed to these outcomes. Overall, these findings underscore the influence of geographical and environmental variations on semen parameters and further iterate the impact of ethnicity on semen characteristics.

CRediT authorship contribution statement

Temidayo S. Omolaoye: Writing – review & editing, Writing – original draft, Project administration, Methodology, Formal analysis. **Jeyaseelan Lakshmanan:** Writing – review & editing, Formal analysis. **Irfan Aslam:** Writing – review & editing, Data curation. **Stefan S. Du Plessis:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

Ethical approval statement

Ethical approvals were obtained from Mohammed Bin Rashid University of Medicine and Health Sciences (MBRU) Ethics Committee (MBRU-IRB-2021-12; approved 21-04-2021) and HealthPlus Research and Ethics Committee (REC/2022/P27; received on 23-03-2022). Informed consent was not obtained from the study participants, as the approval covered the waiver, and **only** deidentified data were extracted, and extraction was performed by the IT department of the fertility center. Thus, researchers had no knowledge of any identifiable parameters.

Data availability statement

De-identified raw data can be shared upon request to the corresponding author, Professor Stefan Du Plessis. Howbeit, analysed data are available in this manuscript and in the supplementary materials.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e40288.

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