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ORIGINAL RESEARCH

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Temporal decline of semen quality amongst Saudi population in first two decades of 21st century

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Abstract

Background: Significant decline in the quality of semen has been reported in men living in Western countries. There is scarce evidence in middle eastern population and limited data from these countries was used in revised reference range values in the sixth edition of World Health Organization (WHO) manual for semen analysis. The objective of this study was to determine if semen quality has changed over time in Saudi Population in past 18 years (2004–2021). **Methods**: In this retrospective cohort, 9935 semen analysis reports were reviewed and temporal changes in semen parameters over 18 years were reported. Men who attended assisted reproductive technology Lab, King Faisal Specialist Hospital and Research Centre Jeddah, Kingdom of Saudi Arabia for semen analysis from 2004 to 2021 were included in this study. **Results**: Total sperm count (yearly slope = −3.63, 95% confidence interval (CI): −5.85 to −1.4, $p = 0.003$), motility (yearly slope −0.67, 95% CI: −0.86 to −0.47, $p < 0.0001$), morphology (yearly slope −0.51, 95% CI: −0.68 to −0.34, $p < 0.0001$), and semen volume (yearly slope −0.02, 95% CI: −0.036 to −0.009, $p = 0.002$) declined significantly from 2004 to 2021. The percentage of population with abnormal semen parameters, single/multiple sperm abnormalities including azoospermia (yearly slope 0.6, 95% CI: 0.16 to 1.0, $p = 0.01$), hypospermia (yearly slope 0.5, 95% CI: 0.23 to 0.78, $p = 0.001$), oligospermia (yearly slope 1.0, 95% CI: 0.67 to 1.46, $p < 0.0001$), asthenospermia (yearly slope 1.2, 95% CI: 0.92 to 1.55, $p < 0.0001$), teratospermia (yearly slope 3.1, 95% CI: 2.2 to 4.0, $p < 0.0001$) and oligoasthenoteratospermia (OAT) (yearly slope 1.4, 95% CI: 1.0 to 1.77, $p < 0.0001$) was significantly increased from 2004 to 2021. **Conclusions**: Significant decline in the semen parameters over the 18 years of study period suggest strong temporal relationship with quality of semen. The potential causes for such a significant regression in the semen characteristics were not explored in this study and warrant further research.

Keywords

Sperm; Decline; Temporal; Infertility; Semen

1. Introduction

Male factor contributes up to 50% in couples' infertility [1, 2]. This assessment is usually based on the results of a basic semen analysis which is cornerstone test in male infertility screening. Conventional semen analysis is largely standardised globally. Andrology laboratories use cut off values defined by the World Health Organisation (WHO) to report semen parameters as normal or abnormal and these values have been periodically revised since 1980 [3]. In the latest edition (WHO 6th) these reference values have been significantly lowered compared to when they were first introduced. Since 1992 when the first major study by Carlsen *et al.* [1] showed a significant decline in semen quality over time, there has been an ongoing controversy over temporal decline in semen quality [4]. Subsequent to Carlson's study [1] similar declining trend in semen quality was reported in some more recent studies [5, 6]. Contrary to this, others have reported mild increase in the sperm count in Danish men [7]. Interestingly, the same group reported no change in sperm count in a study published 6 years later [8].

The association between temporal decline in semen quality and periodic lowering in WHO reference values is not quite established but the evidence to link environmental factors, endocrine disrupting chemicals, lifestyle and nutrition to male infertility is well reported in the recent literature [9–12]. In current study we aimed to investigate the temporal changes in semen quality in Kingdom of Saudi Arabia (KSA) which has more than 36 million people. Due to geographic location and year-round weather conditions most, if not all, activities are indoor and there is heavy trend of weekly fast food consumption as high as in 88% of the population [13]. In the 5th edition of WHO Laboratory Manual for the Examination and Processing of Human Semen, reference values were calculated from data of 1800 individuals from North Europe, America, and Australia (5th ed, 2010). This edition was criticised due to under-representation of the population from South America, Asia, and Africa. In the most recent edition of the manual (6th edition, 2021) these concerns have been partially addressed by adding 1789 more individuals in the data pool from Southern Europe, Asia, and Africa [14]. Interestingly, the representative population from Middle Eastern Region in the 6th edition consists of only 168 individuals from Iran. So far, there has been no representation from KSA, which is the largest country in the Middle East Region. Herein, we have analysed 9935 semen analyses from Saudi Arabia to report temporal changes in semen quality over 18 years (2004–2021).

2. Materials and methods

Semen analysis data of 9935 reports from men referred to Assisted Reproductive Technology (ART)/*In Vitro* Fertilization (IVF) Unit, King Faisal Specialist Hospital and Research Centre, Jeddah, Kingdom of Saudi Arabia, between 2004 and 2021 were analysed as per 4th edition of WHO manual. Data extraction was performed between 2021–2023. Irrespective of the quality of semen parameters, all the data from 2004–2021 was included. However, where there were rare sperm found in the ejaculate, morphology was not performed. The most common semen parameters which are clinically considered during the interpretation of the semen report, were included in this analysis. These include semen volume, sperm count, motility, and morphology. Semen reports were further categorised accordingly to single or multiple sperm abnormalities for each year (2004–2021) to assess the temporal changes. Briefly, wet smears were prepared for sperm motility assessment as per the 4th edition of WHO manual and were assessed by trained andrologists. Sperm concentration was reported as million/mL and sperm morphology was scored on fixed-stained slides. In samples with very low sperm count, morphology was not assessed.

Data was analysed by GraphPad Prism Version 10 software (GraphPad Software, Inc, San Diago, CA, USA) using either two-tailed t test, linear simple regression analysis or Pearson correlation with $p < 0.05$ as significant.

3. Results

In this study, semen parameters that are critical for natural fertilisation are analysed. Table 1 shows the yearly mean values of semen parameters from 2004 (start year of analysis) to 2021 (end year of analysis).

There was a statistically significant decrease in the mean values of semen parameters, except semen volume, in the end year when compared to the start year of the analysis (Fig. 1).

TABLE 1. Mean values of semen characteristics from 2004 to 2021.

Year	N (9935)	Volume (mL)	Concentration (million/mL)	Count (million/ejaculate)	Motility (%)	Morphology (%)
2004	245	2.9	51.3	148.2	53.9	15.5
2005	259	2.6	50.0	133.2	48.8	11.7
2006	195	3.2	62.9	201.8	53.8	10.0
2007	395	2.9	57.2	168.3	51.4	13.0
2008	394	2.9	48.6	140.8	49.4	10.6
2009	464	2.8	40.0	114.0	51.0	10.8
2010	499	2.6	33.7	87.4	47.2	11.1
2011	545	2.8	34.4	95.4	45.3	11.6
2012	688	2.6	48.7	128.2	47.5	8.6
2013	678	2.7	48.8	132.7	45.4	5.0
2014	566	2.5	39.5	100.8	41.8	5.0
2015	515	2.5	40.3	101.7	46.0	5.0
2016	608	2.6	41.2	107.1	44.2	5.9
2017	708	2.5	47.6	118.2	40.5	6.0
2018	655	2.5	39.8	101.7	42.1	6.2
2019	733	2.6	34.7	91.8	42.7	6.0
2020	656	2.6	38.5	99.7	43.1	5.9
2021	1132	2.7	39.8	107.4	43.5	6.3

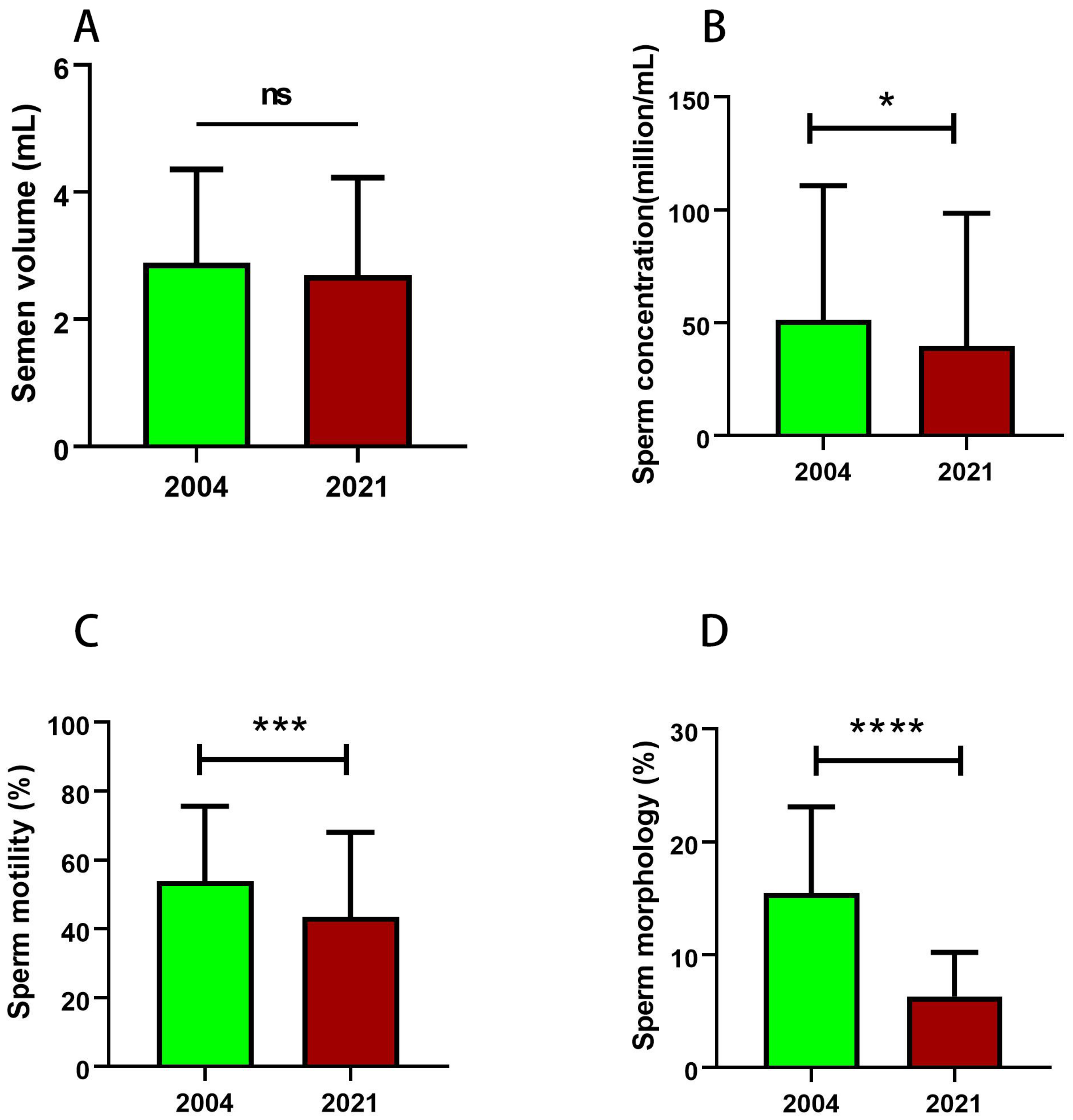
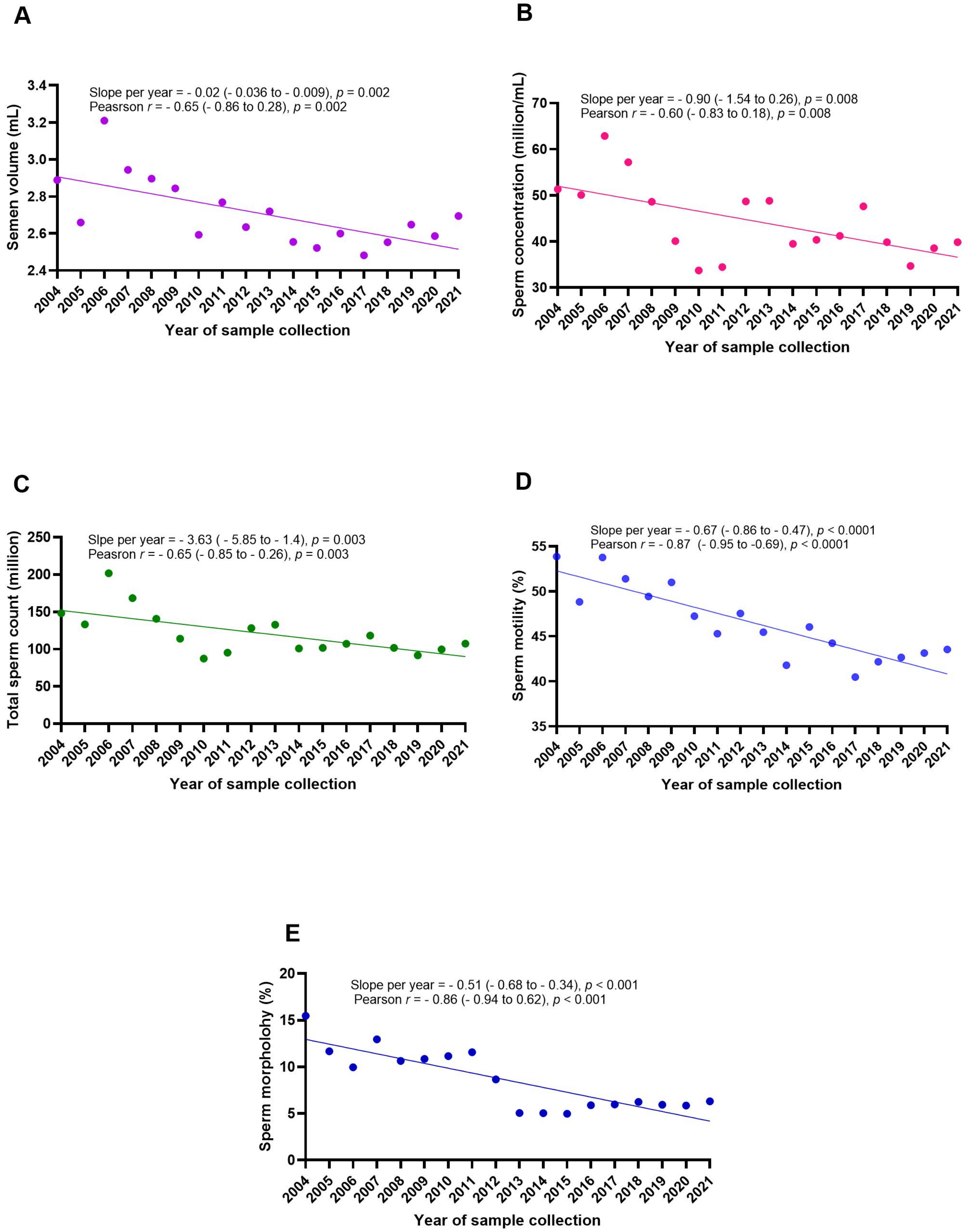


FIGURE 1. Comparison of mean values of semen parameters between 2004 (start year) and 2021 (end year). (A) Semen volume, (B) sperm concentration, (C) sperm motility, (D) sperm morphology. *$p < 0.05$; ***$p < 0.001$; ****$p < 0.0001$; ns: non significant.

Although there was a significant decline in the critical sperm parameters in the end year, this did not really tell us if the same declining trend existed in the years between 2004 and 2021.

To assess this change, we performed Pearson correlation and linear regression analysis (Fig. 2). These further analyses showed a significant negative correlation of semen parameters with the year of analysis indicating a temporal negative change in the semen parameters over the 18 years (2004–2021). Average slope per year and 95% confidence interval calculated through linear regression analysis further confirmed this trend in all the semen parameters (Fig. 2).

Next, we categorised semen reports according to semen/sperm abnormalities (single or multiple) as given in Table 2. There was a heterogeneous expression of semen abnormalities over 18 years, but it showed a general increasing trend in percentage of single as well as multiple sperm abnormalities as the year of analysis progressed (Table 2). The heatmap (Fig. 3A) shows yearly change in the semen abnormalities over the 18 years of analysis. The percentage abnormalities of start year compared with end year (Fig. 3B) showing sperm morphology alone and combined with count and motility, were the most affected sperm abnormalities between the 2 years. A significant temporal change in the increase in semen abnormalities was evident after correlation and linear regression analyses (Fig. 4).



F I G U R E 2. Temporal changes in the mean semen values assessed by correlation and linear regression analyses from 2004 to 2021. A temporal change was observed in all the semen parameters; semen volume (A), sperm concentration (B), total sperm count (C), sperm motility (D) and sperm morphology (E) from the start to end year of analysis.

TABLE 2. Single and multiple sperm abnormalities from 2004–2021.

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total
Total SA	245	259	195	395	394	464	499	545	688	678	566	515	608	708	655	733	656	1132	9935
Azoo-spermic	51	55	31	51	74	74	71	112	173	163	175	113	109	152	168	229	135	325	2261
Azoo-spermic (%)	20.8	21.2	15.9	12.9	18.8	15.9	14.2	20.6	25.1	24.0	30.9	21.9	17.9	21.5	25.6	31.2	20.6	28.7	22.8
HS	35	35	22	50	67	76	93	94	151	94	135	122	130	158	146	151	140	207	1912
HS (%)	14.3	15.8	11.3	12.7	17.0	16.4	18.6	17.2	21.9	13.9	23.9	23.7	21.4	22.3	22.3	20.6	21.3	18.3	19.2
Total SA	194	203	184	344	331	391	428	433	610	513	401	402	482	523	462	493	512	774	7680
Oligo-spermic	79	79	77	155	147	193	199	240	319	259	219	206	241	274	265	314	280	418	3964
Oligo-spermic (%)	40.7	38.9	41.8	45.0	44.4	49.4	46.5	55.4	52.3	50.5	54.6	51.2	50.0	52.4	57.4	68.0	54.7	54.0	51.6
Astheno-spermic	71	93	72	145	153	171	208	227	297	281	226	207	279	317	276	285	291	437	4036
Astheno-spermic (%)	36.6	45.8	39.1	42.2	46.2	44.0	48.6	52.3	48.7	54.8	56.4	51.5	57.9	60.7	59.7	57.9	56.8	56.5	52.6
Total SA	148	182	139	258	250	309	320	308	410	363	248	272	335	330	269	261	311	470	5183
Terato-spermic	60	107	96	138	133	168	186	179	303	331	233	256	308	306	240	237	299	434	4014

SA: Semen analysis; HS: Hypospermia.

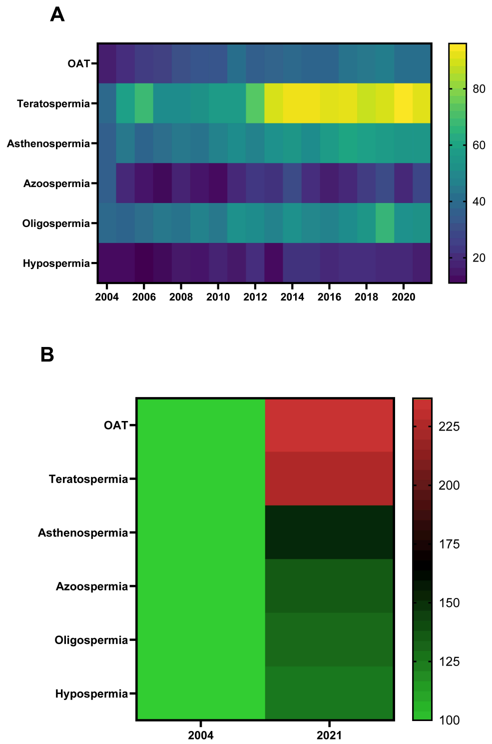


FIGURE 3. Heat map of percentage semen abnormalities. (A) shows yearly percentage of semen abnormalities from 2004 to 2021; (B) shows percentage change in the semen abnormalities between the start year (2004) and the end year (2021). Values in 2004 were given a score of 100 as base value and compared with relative increases in the corresponding abnormality in year 2021. Hypospermia (low volume), Oligospermia (low count), Azoospermia (no sperm in ejaculate), Asthenospermia (low motility), Teratospermia (low morphology), Oligoasthenoteratospermia/OAT (low count, motility, and morphology).

4. Discussion

In this study nearly 10,000 semen reports were analysed (WHO 4th edition) and a temporal change (positive or negative) was assessed over 18 years of period from 2004 to 2021. Though, the results agreed with earlier reported studies [1, 5, 6, 15, 16] showing a declining trend in the semen parameters over time, the changes observed in this study are major. Irrespective of the semen parameter, our results show significant declining trend from 2004 to 2021 where semen volume is relatively less affected, and sperm morphology is the most affected sperm parameter. In addition to the overall decline in sperm quality the single and multiple sperm anomalies showed strong temporal association indicating deterioration in the semen quality. Our results are in contrast with the similar recent study which has reported relatively stable sperm count from 2000 to 2019 [17]. Our results also refute observations from other studies indicating either no change or improvement in the semen quality over time [18].

This is interesting but difficult to explain why all semen parameters have shown significant negatives changes over time in Saudi population. Sperm concentration declined 29%, sperm morphology 145%, motility 24% and volume 7% from 2004 to 2021. The reasons for general decline in semen quality are not fully known but rapidly changing lifestyle, environmental factors and diet have been considered as contributing factors [9, 19, 20]. Endocrine disrupting chemicals (EDC) have shown to play a negative role in male reproductive health including spermatogenesis [10, 21]. Sedentary lifestyle is also linked to poor semen quality and male reproductive potential [22, 23]. The climate conditions in Saudi Arabia are intense with extreme hot temperature in most part of the country with maximum dense population areas. This impacts the lifestyle of Saudi population with either restriction to most indoor activities or becoming physically inactive. Twenty years ago, 39–99% physical inactivity was reported in Saudi Population [24] which has not changed recently and still reported around 36 to 83% in male population [25]. Based on the literature evidence increased prevalence of physical inactivity could be one of the contributors to poor semen quality in Saudi population. Arguably, diet may be another factor impacting male reproductive health and semen quality depending on the type of food consumed [26, 27]. Reportedly, Saudi Arabia has notably higher prevalence of obesity compared to global average (35% *vs.* 13%) leading to higher obesity related mortality [28]. Conflicting evidence regarding association of obesity and semen quality have been reported in the literature. Some report a negative impact of high body mass index (BMI) on sperm count [29–33] sperm motility [31, 33–35] sperm morphology [36, 37] other report no association of these parameters with BMI [38–43]. Though conflicting but substantial evidence exists suggesting potential impact of higher BMI on overall semen quality.

Regardless of the cause of decline in semen quality reported in this study, the changes in sperm parameters in the past 2 decades are significant. This adds to the existing knowledge that sperm quality is variable and in addition to factors de-

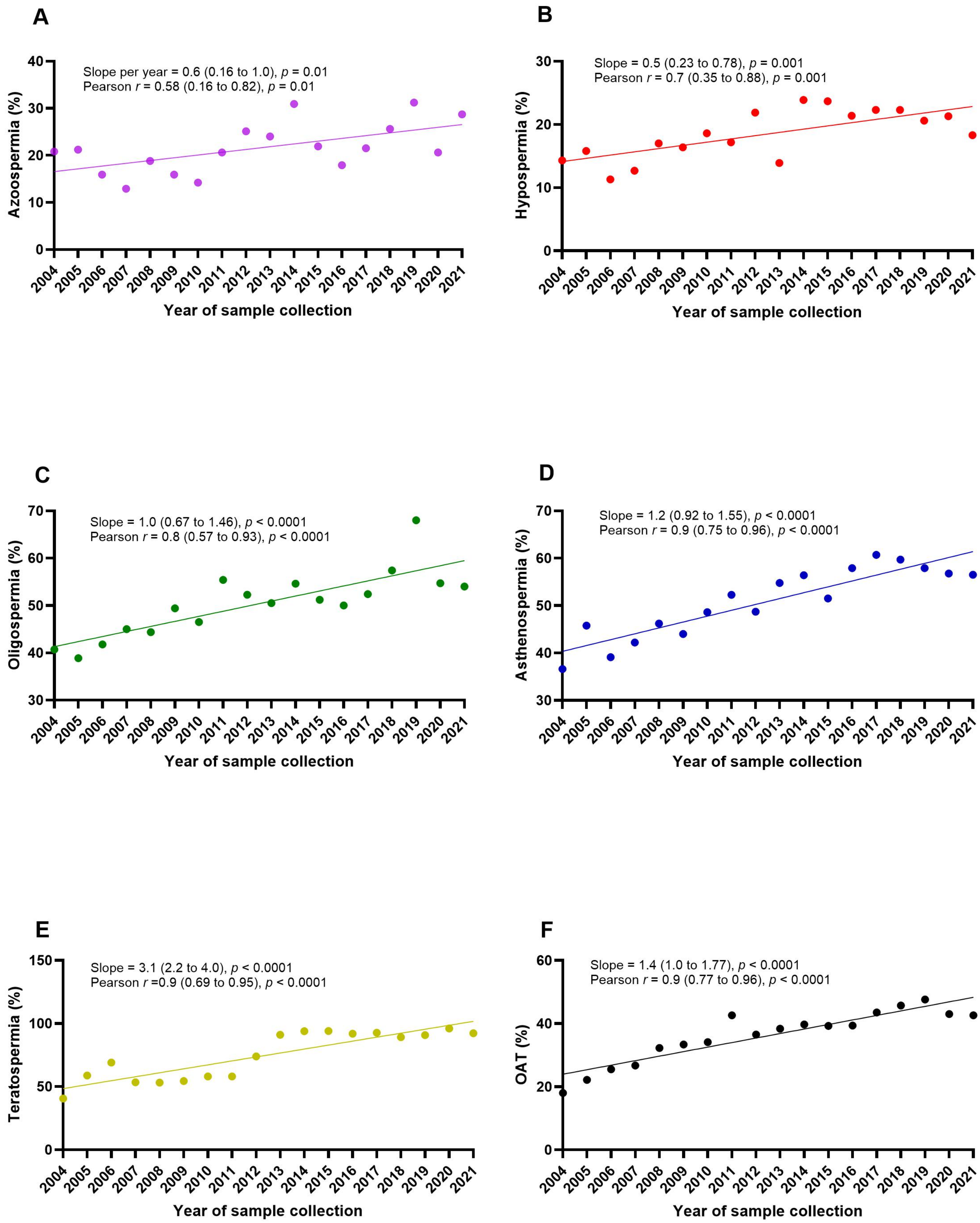


FIGURE 4. Correlation and linear regression analysis of percentage semen abnormalities from 2004 to 2021. The panels represent increase in the percentage of men with Azoospermia (A), Hypospermia (B), Oligospermia (C), Asthenospermia (D), Teratospemria (E) and Oligoasthenoteratospermia/OAT (F).

scribed above geographical location of the population may have variable semen parameters so is the impact on the quality. For example, Levine *et al*. [4] in a meta-analysis reported 52.4% decline in sperm concentration from 1970 to 2010 in Western men compared to 29% in our study from 2004 to 2021. Notably, Levine *et al*. [4] did not report other sperm parameters (motility, morphology) in their study and only decline in the sperm count in Western men compared to other population was reported. This endorses the above argument that ethnicity and geographic location may be another contributing factor. This requires attention when selecting the cutoff or normal reference values for the interpretation of semen analysis in the WHO manual. After strong critical response to WHO 5th edition from the scientific community for just relying on the data from Australia, North America, and Norther Europe, data from other countries were included in the 6th edition. This still does not truly represent the global population as data of <200 men were added from Middle Eastern region. Therefore, the current study may offer a prospect to include population from highly under-represented regions to better represent the reference values globally.

Nevertheless, demographic data of large number of patients was not available and is not presented in this study, which is one of the main limitations of this study. Furthermore, several factors including lifestyle [44], diet [45], smoking [46], medical conditions such as varicocele [47] that have shown to impact semen quality were not considered in this study. Additionally, the results of this study may not be applicable to general Saudi population because these are based on infertile cohort of men and not the normal donors.

5. Conclusions

Despite of the limitations mentioned above, this is the largest and first study on Saudi men reporting significant decline in semen quality over the 18 years period. Most of the published studies have reported the temporal impact on either sperm count or motility or both parameters. However, our results show that all essential sperm parameters were negatively impacted over time. The significant change in semen quality reported in current and earlier studies warrants further investigations to understand the main cause leading to deterioration of the semen quality.

AVAILABILITY OF DATA AND MATERIALS

All the data sets on which conclusions of this manuscript were drawn are included in the submitted article.

AUTHOR CONTRIBUTIONS

NI, IJ—Concept; supervision; data curation; writing. AAF, DMS, YHA, MT—Data curation; analysis. GA—Concept; data analysis; writing; supervision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The scientific and ethical approvals were obtained by the King Faisal Specialist Hospital and Research Centre (Gen. Org.), Jeddah, Kingdom of Saudi Arabia Institutional Review Board (approval number: IRB 2020-32). All data included in this manuscript was deidentified thus informed consent was not required by the Institutional Review Board (King Faisal Specialist Hospital and Research Centre).

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Gulfam Ahmad is serving as one of the Guest editors of this journal. We declare that Gulfam Ahmad had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to BB.

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