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JSM Sexual Medicine

Research Article

The Effects of Exposure to Weather and Climate Variations on Human Semen Parameters: A Retrospective Cohort Study of Fertile Men Living in Different Altitudes of China

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Submitted: 26 April 2023

Accepted: 27 June 2023

Published: 27 June 2023

ISSN: 2578-3718

Keywords

- Male reproduction healthy
- Semen parameters
- Weather fluctuations
- Hypoxia

Abstract

Purpose: To estimate associations of weather and climate variation exposures with semen parameters.

Methods: We retrospective evaluated the associations of weather, climate and altitude variation with semen parameters of fertile male living in China from 2018 to 2021. All the weather and climate parameters were obtained from The National Meteorological Science Data Centre of China.

Results: The outcomes of exposure were evaluated by semen analysis, including sperm donors and healthy males. For the short-term exposure to daily weather fluctuations, the non-parameter spearman-test results only revealed the progressive motility (%) was correlation with all the weather factors, including pressure (ρ=-0.111, p= 0.000), temperature (ρ=0.076, p= 0.000) and moisture (ρ=0.046, p= 0.003). For the long-term exposure to climate, the Tibetan population living in the Qinghai Tibet Plateau showed superior concentration of semen (median=63.20 million/ml, p=0.000) and the males living in the Turpan Basin exhibited superior volume of semen (median=3.55ml, p=0.000) than others. Furthermore, combined all the climate and altitude factor, the generalized linear model between the climate variations and dependent variable semen parameters showed that the oxygen content (%) of different altitudes had significantly effects on all the semen parameters, especially on the volume (95% CI, 0.612-2.170, p= 0.000) . Conclusions: The data of fertile men living in different altitudes of china showed the semen parameters are sensitive to the temperature of the daily weather fluctuation, while the oxygen content were the most sensitive parameters

INTRODUCTION

Nowdays, semen analysis is usually the first and often the “must be” test used to evaluate the reproductive function of a male in infertility couples [1]. The adverse effect of seasonal exposure to ambient weather variations on semen quality is well documented [2-4]. Seasonal variations, especially those regulated the hypothalamic–pituitary–gonadal axis, manage the oestrus, and the subsequent birth rate exposure to this environment4. Unlike other mammalian species, humans do not strictly adhere to a season of fertility and can reproduce throughout the entire year [5,6]. Although numerous time-series studies have examined the associations between seasonal variations, most evidence has been found in studies in single cities or regions. There are also large challenges in analysing these data and obtaining valid results because of different complicated climate modelling and potential sampling bias. The above limitations can be solved by performing unbiased sampling, multicentre studies that adopt the same analytic protocol, and comprehensive statistical models to estimate representative associations of weather and climate variation exposures with semen parameters. We hypothesized that semen parameters are associated with daily weather fluctuations and also adapted to the long-term reginal climate where they lived from birth to adult. Given the completed evidence regarding their effects of semen, both the daily (defined as short exposure) and annual mean values (defined as long-term exposure) of temperature, atmospheric pressure, relative humidity, and oxygen content were collected, standard and analysed in this research. As far as global climate changing with human health are concerned, men's fertility lead to some specific questions requiring answers: (i) the effects on the semen characteristics of short time exposure to daily weather; (ii) the effects on the semen characteristics of long-term exposure to regional climate; and (iii) the outcomes of the duration of short and long term on men's health.

MATERIALS AND METHODS

Sampling

In this retrospective study, the outcomes of exposure were evaluated by semen analysis, including sperm donors and healthy males. A large series of qualified sperm donors admitted to the Obstetrics and Gynecology Hospital of Fudan University between June 2018 and June 2020 were analysed for short-term exposure to daily weather variations. The hospital is located in Shanghai in eastern China (Table 1), with a population of more than 2000 volunteers per year. For the long-term exposure to weather variations, of which annual mean weather parameters were calculated, three regional populations of pre-marriage and pre-pregnancy couples were screened by physical examination from Lhasa (native Tibetan residence), Turpan (native Uighur residence) or Shanghai (native Han population). The geographical location were Shanghai (30°40'N, 120°52'E; mean altitude: 4 m), Lhasa (29°41'N, 91°1'E; altitude range from 3650 to 5989 m) and Turpan (42°45'N, 86°37'E; altitude range from -103 to 3189 m) (Table 1 and Figure 1). The air temperature, atmospheric pressure, relative humidity, and oxygen content were obtained from the historical records of The National Meteorological Science Data Centre of China.

For the qualified sperm donors, clinical and laboratory reports, including age, education, body mass index (BMI), ejaculatory abstinence period, smoking history, semen parameters, and the date of semen analysis, were extracted from the sperm bank record database. For pre-marriage and pre-pregnancy males, limited clinical and laboratory reports, including age, ejaculatory abstinence period, and semen parameters, were extracted from the patients' record database. After reviewing the extracted medical data, healthy males found to have clinical oligozoospermia, asthenozoospermia, and azoospermia were not included in this study. All semen samples were evaluated according to the date of semen production, and the fertile men were selected as inclusion team finally (Figure2).

Semenanalysis

According to the World Health Organization guidelines (WHO, 2010), semen samples were obtained by masturbation into sterile plastic cups. Semen samples were allowed to liquefy for 30–40 min at 37 ℃. After liquefaction of fresh ejaculate, specimens were evaluated for andrology characteristics, including viscosity, pH value, volume, count, and motility. The qualified donors followed the National Sperm Bank reference for semen parameters (volume ≥ 2.0, concentration ≥ 60 million/ml, progressive motility ≥ 60%, normal sperm morphology ≥ 70%), while the premarriage or prepregnancy males adopted the WHO reference for semen parameters (volume ≥ 1.5, concentration ≥ 15 million/ml, progressive motility ≥ 32%). Normal sperm morphology was evaluated by the Diff Quick method according to Kruger's strict criteria (≥ 4%).

Statistical Analysis

For descriptive statistics, data are presented as the mean, standard deviation (SD), median, standard deviation, variance, full distance, sum value, minimum, and maximum value as appropriate. Histograms and the Kolmogorov-Smirnov test were used to assess the normality of the continuous variables. For the correlation test, we used the non-parameter spearman-test when non-normal distributions. The significance of difference were used the median test when non-normal distributions. We trained a generalized linear model on the 9 parameters, including pressure, temperature, humidity, oxygen's content, abstinence day, height, weight, age with Bonferroni correction to explore the possible relationship with semen parameters. A probability value of $p < 0.05$ was considered to indicate statistical significance. All statistical analyses were performed using SPSS software (SPSS, version 25: IBM Corporation).

Table 1: Geographical distributions of sampling hospitals and residence altitude of the study subjects

Characters		Age (year)	Height (CM)	Weight (kg)	Abstinence time (Day)	Volume (ml)	Concentration (million/ml)	Progress motile concentration (million/ml)	Progressive Motility (%)
N	Effective	2111	2111	2111	2111	2111	2111	2111	2111
	Missing	0	0	0	0	0	0	0	0
Mean		28.32	174.43	70.61	3.59	2.97	67.71	35.22	51.43
Median		27.00	175.00	70.00	3.00	2.80	65.00	36.00	50.00
SD		5.05	4.63	8.75	0.99	1.34	23.05	14.63	10.66
Minimum		20.00	165.00	50.00	2.00	0.20	7.00	1.00	5.00
Maximum		44.00	188.00	108.00	7.00	11.00	197.00	94.00	84.00

Note: SD, standard deviation.

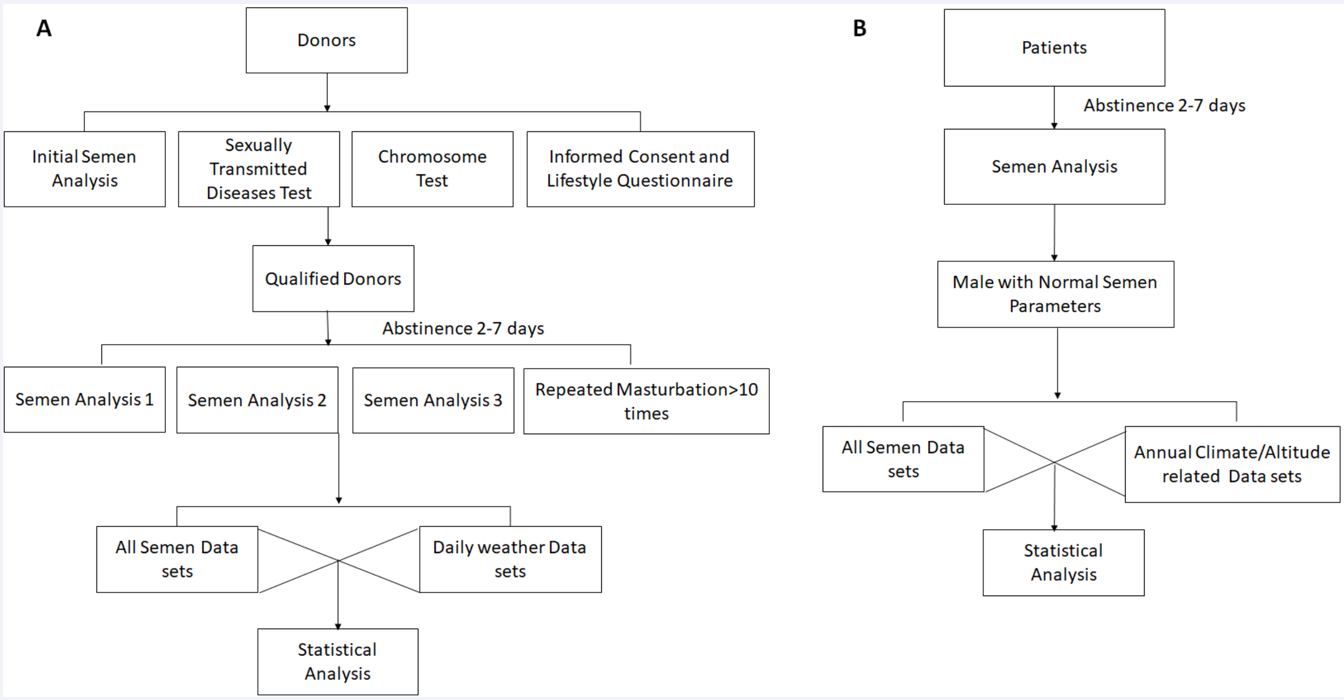

Figure 1 Geographical distributions of sampling hospitals and residence altitude of the study subjects in Shanghai, Lhasa and Turpan of China.

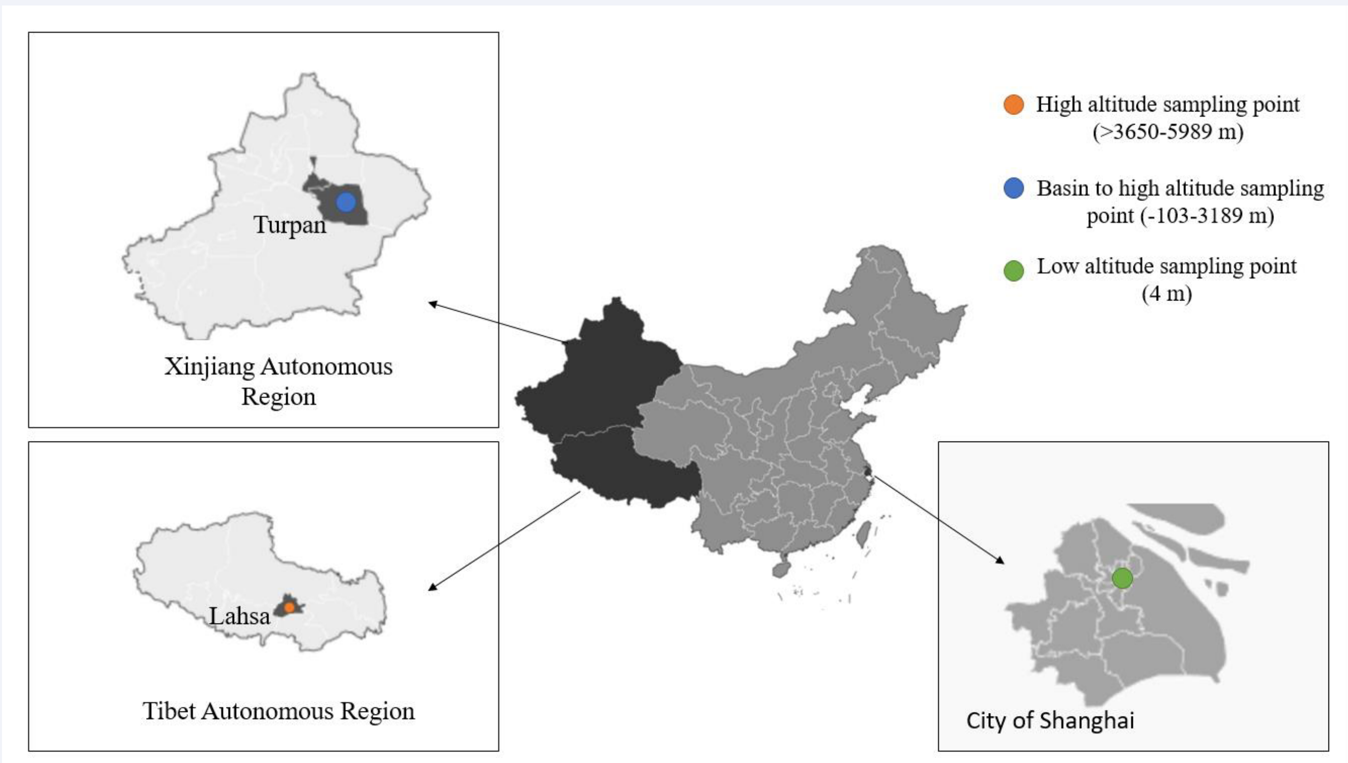

Figure 2 The design of study flow.

Ethics Statement

The Institutional Ethics Committee of the Obstetrics and Gynecology Hospital of Fudan University approved the study (approval number: FCKYY201801).

RESULTS

Descriptive Analyses

From June 2018 to June 2021, we recruited 6600 sperm donors from the Han population living in Shanghai for more than one year. Following the Chinese sperm bank screening process, including semen analysis, sexually transmitted diseases, and chromosome detection, only 320 donors (<5% pass rate followed the National Sperm Bank semen reference) qualified. Then, we collected 10 or more semen samples from each qualified volunteer with healthy hobbits excluding drinking alcohol, smoking, and lack of daily exercise time. Finally, the short-term analysis included 2111 sets of semen analyses from 192 qualified volunteers' continuous acquisition (mean 10.99 times/donors). The sequential semen parameters, including volume, concentration, progress motile sperm concentration, and progressive motility are shown in a line chart individually (Table 2 and Figure 3). In general, the mean volume of semen was 2.97 ml (median, 2.80 ml [range, 0.20 to 11.00]), the mean concentration was 67.71 million/ml (median, 65.00 million/ml [range, 7.00 to 197.00]), the mean progress motile sperm concentration was 35.22 million/ml (median, 36.00 million/ml [range, 1.00 to 94.00]) and the mean progressive motility was 51.4% (median, 50.0% [range, 5.0% to 84.0%]).

From Jan 2018 to May 2021, we recruited 6204 premarriage or prepregnancy males of the native Han population, Tibetan population, and Turban population. Following the premarriage or prepregnancy test process, including the semen test, sexually transmitted diseases test, and chromosome detection, only 2750 males (<50% pass rate following the WHO 5th semen reference) qualified to exclude infertile males with oligozoospermia, asthenozoospermia, teratozoospermia, or azoospermia [7]. Finally, the long-term analysis included 2310 sets of semen parameters from Shanghai (native Han population), 394 sets of semen parameters from Lhasa (native Tibetan population), and 46 sets of semen parameters from Turpan (native Uighur population), as shown in (Table 4). Compared the baseline of the semen parameters, the Tibetan population living in the Qinghai Tibet Plateau showed superior concentration of semen (median=63.20 million/ml, p=0.000), while the males living at the sea level exhibited superior progressive motility (%) of semen (median=54.1%, p=0.000), and the males living in the Turpan Basin exhibited superior volume of semen (median=3.55ml, p=0.000) than others (Table 4).

Correlation Test

As the semen parameters of the donors were non-normal distribution, we used the non-parameter spearman-test to explain correlation between the daily weather and semen parameters. The results revealed a weakly correlation between semen volume with daily temperature (ρ=0.043, p= 0.048); the concentration was correlation with daily temperature (ρ=0.053, p= 0.015) and pressure (ρ=-0.055, p= 0.012); the progressive

Table 2: Descriptive analyses of the body characteristics and semen parameters of 192 qualified volunteers

Sampling Hospitals	Residents Nationality	Total Number (inclusion patient)	Mean Altitude (m)	Annual mean Pressure (KPa)	Annual mean oxygen content (%)	Max Temperature (℃)	Min Temperature (℃)
Shanghai	Han	2310	4.53	100.53	20.95	37.0	-2.0
Lhasa	Tibet	395	3658.10	65.25	19.90	23.5	-7.5
Turpan	Uygur	46	34.55	90.76	15.09	41.0	-10.0

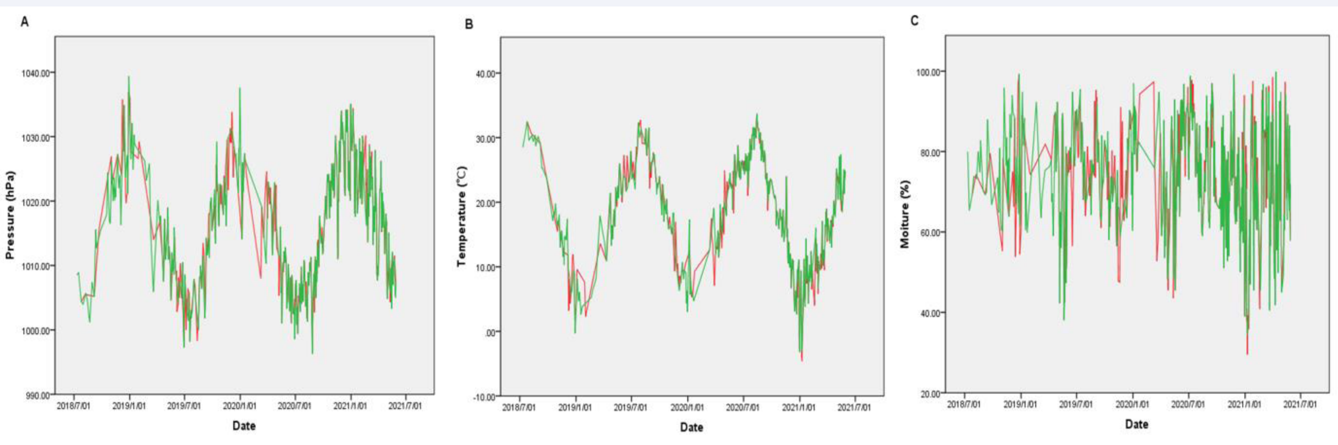

Figure 3 The distribution of excellent semen quality (green line) or not (red line) of 192 qualified volunteers obtained in 6 months are shown in (A) with daily pressure state and (B) with daily temperature state and (C) with daily moisture state.

Table 3: The generalized linear model between the weather variations and dependent variable semen parameters of 192 volunteers

Cross -Parameters	Optimized Parameter Distribution	Calculated coefficient	SD	95% Wald CI		Hypothesis Test		
				upper	lower	Wald chi-square	df	Sig.
Volume-Pressure	Gamma	.011	.0059	.000	.023	3.561	1	.059
Volume-Temperature		.024	.0065	.011	.037	13.777	1	.000***
Volume-Humidity		.001	.0021	-.003	.005	.401	1	.527
Volume-Abstinence time		.453	.0303	.394	.513	223.004	1	.000***
Volume-Height		.036	.0068	.023	.049	28.318	1	.000***
Volume-Weight		-.011	.0035	-.018	-.004	9.368	1	.002**
Volume-Age		-.024	.0052	-.034	-.014	21.371	1	.000***
Concentration-Pressure		-.002	.0006	-.004	-.001	16.427	1	.000***
Concentration-Temperature		.000	.0007	-.001	.001	.069	1	.793
Concentration-Humidity		.000	.0002	-.001	9.594E-005	2.256	1	.133
Concentration-Abstinence time		.032	.0026	.027	.037	144.622	1	.000***
Concentration-Height		-.001	.0006	-.003	.000	5.046	1	.025*
Concentration-Weight		.001	.0003	.000	.001	2.339	1	.126
Concentration-Age		.005	.0005	.004	.006	74.458	1	.000***
PR-Pressure	Poisson	-.003	.0007	-.004	-.002	18.415	1	.000***
PR-Temperature		-.002	.0008	-.003	.000	4.451	1	.035*
PR-Humidity		-8.484E-005	.0002	-.001	.000	.125	1	.724
PR-Abstinence time		-.003	.0031	-.009	.003	.921	1	.337
PR-Height		.000	.0007	-.001	.002	.461	1	.497
PR-Weight		.001	.0004	.000	.002	9.018	1	.003**
PR-Age		-.003	.0006	-.004	-.001	16.796	1	.000***

Note: SD, standard deviation; PR, progressive motility (%); *p<0.05 or **p<0.01 or ***p<0.001 significant by chi-square analysis.

Table 4: Descriptive body and semen analyses of 2311 native fertile males from Shanghai, Lhasa, and Turpan

City	Parameters	Age (year)	Volume (ml)	Total sperm count (million)	Concentration (million/ml)	Progressive Motility (%)	Abnormal Sperm morphology (%)
shanghai	Mean	30.9593	2.8498	180.8188	64.2810	54.1320	93.7978
	N	2310	2310	2310	2310	2310	2310
	SD	4.65381	1.26395	110.80011	28.93105	9.69560	1.95251
	Median	30.0000	2.5000	154.0000	60.0000	54.0000	94.0000
	minimum	18.00	1.50	25.50	15.00	33.00	80.00
	maximum	56.00	10.00	1020.00	224.00	84.00	96.00
	ANOVA coefficient	21.658	1.598	12276.664	837.006	94.005	3.812
Lhasa	Mean	30.8203	3.6167	259.2108	74.3218	47.6481	93.7597
	N	395	395	395	395	395	395
	SD	4.97411	1.50877	169.89148	45.15565	11.17909	3.48609
	Median	30.0000	3.3000	212.1600	63.2000	45.3000	95.1000
	minimum	19.00	1.50	38.85	15.00	32.00	78.00
	maximum	50.00	9.20	1041.03	358.80	83.50	96.90
	ANOVA coefficient	24.742	2.276	28863.116	2039.032	124.972	12.153
Turpan	Mean	33.5217	3.6478	179.0889	52.7761	48.1087	92.8261
	N	46	46	46	46	46	46
	SD	4.73164	1.40629	115.88002	37.72732	11.63563	3.81403
	Median	32.5000	3.5500	153.2750	43.7000	46.0000	94.0000
	minimum	27.00	1.50	32.80	15.20	32.00	82.00
	maximum	48.00	8.40	575.12	205.40	71.00	96.00
	ANOVA coefficient	22.388	1.978	13428.178	1423.350	135.388	14.547
All	Mean	30.9822	2.9732	192.0457	65.5303	53.1003	93.7761
	N	2751	2751	2751	2751	2751	2751
	SD	4.71254	1.33409	124.17574	32.14566	10.22893	2.27940
	Median	30.0000	2.7000	160.0000	60.0000	53.0000	94.0000
	minimum	18.00	1.50	25.50	15.00	32.00	78.00
	maximum	56.00	10.00	1041.03	358.80	84.00	96.90
	ANOVA coefficient	22.208	1.780	15419.615	1033.343	104.631	5.196

Note: SD, standard deviation; *p<0.05 or **p<0.01 or ***p<0.001 significant by chi-square analysis.

Table 5: The generalized linear model between the weather variations and dependent variable semen parameters of 2311 native fertile males from Shanghai, Lhasa, and Turpan

Cross-Parameters	Optimized Parameter Distribution	Calculated coefficient	SD	95% Wald CI		Hypothesis Test		
				upper	lower	Wald chi-square	df	Sig.
Volume-Abstinence time	Gamma	.209	.0138	.181	.236	228.225	1	.000***
Volume-Annual mean pressure		-.026	.0066	-.039	-.013	15.591	1	.000***
Volume-Annual mean oxygen content		1.391	.3975	.612	2.170	12.250	1	.000***
Volume-volume Age		-.019	.0042	-.027	-.010	19.715	1	.000***
Concentration-Abstinence time	Poisson distribution	.054	.0013	.052	.057	1754.407	1	.000***
Concentration-Annual mean pressure		-.004	.0014	-.007	-.001	9.021	1	.003**
Concentration-Annual mean oxygen content		.237	.0852	.070	.404	7.745	1	.005**
Concentration-Age		.003	.0005	.002	.004	39.755	1	.000***
PR-Abstinence-time	Poisson distribution	-.008	.0014	-.011	-.005	31.919	1	.000***
PR-Annual mean-pressure		.002	.0006	.000	.003	7.955	1	.005**
PR-Annual mean-oxygen content		-.083	.0343	-.150	-.015	5.799	1	.016*
PR-Age		-.003	.0005	-.004	-.002	38.391	1	.000***
Absperm-Abstinence time	Poisson distribution	.000	.0011	-.002	.002	.063	1	.801
Absperm-Annual mean pressure		.000	.0004	-.001	.001	.308	1	.579
Absperm-Annual mean oxygen content		-.014	.0245	-.062	.034	.319	1	.572
Absperm-Age		6.248E-005	.0004	-.001	.001	.028	1	.866

Note: SD, standard deviation; PR, progressive motility (%); *$p<0.05$ or **$p<0.01$ or ***$p<0.001$ significant by chi-square analysis.

motility (%) was correlation with all the weather factors, including daily pressure (ρ=-0.111, p= 0.000), temperature (ρ=0.076, p= 0.000) and moisture (ρ=0.046, p= 0.003). In the opposite, the volume of semen was strongly correlated with abstinence day (ρ=0.321, p=0.000) and the age (ρ=-0.105, p=0.000). Meanwhile, the correlation values of concentration (or progressive motility) with abstinence day (or the age) were weaker than 0.01. Other correlations between daily semen parameters and weather variations are summarized in (Table 3).

Regression Analyses

In Shanghai, Lhasa, and Turpan, there was a correlation between semen volume and annual mean pressure (independent variable gamma distribution, 95% CI, B = -0.026, P = 0.000) and annual mean oxygen content (independent variable gamma distribution, 95% Ci, B = 1.391, P = 0.000). Semen concentration was correlated with annual mean atmospheric pressure (independent variable gamma distribution, 95% CI, B = -0.004, P = 0.003) and annual mean oxygen content (independent variable gamma distribution, 95% CI, B = 0.237, P = 0.005). Progressive motility was correlated with annual mean atmospheric pressure (independent variable Poisson distribution, 95% CI, B = 0.002, P = 0.005) and oxygen content (independent variable Poisson distribution, 95% CI, B = -0.083, P = 0.016). The abnormal morphology rate was not correlated with any weather variations (Table 5). Above all, combined all the climate and altitude factor, the generalized linear model between the weather variations and dependent variable semen parameters showed that the oxygen content (%) of different altitudes had significantly effects on all the semen parameters.

DISCUSSION

Our study retrospective analysed multisite data on weather, climate and altitude variations with semen quality across three typical locals in China, although these cities spanned multiple longitudes and latitudes in the Northern Hemisphere. The short-term weather response analysis included 2111 sets of semen analyses from qualified volunteers' continuous acquisition (mean 10.99 times/donors), so the results of multiple analyses of semen are more stable and scientific for evaluating semen parameters. As the long-term climate response of populations from each city were analysed according to the same semen laboratory protocol, the estimate of the association between weather and "normal" semen parameters was based on a consentient dataset [7]. We evaluated associations of weather, climate and altitude variation with semen of fertile men. It provided evidence of short-term and long-term climate exposure with semen quality differentiation. In the analysis of weather-response fluctuations, we observed a weakly correlation between semen parameters and daily temperature or atmospheric pressure. The situation of the association is generally similar to previous findings in other single-city or sperm donor studies. For example, the U-shaped exposure-response relationships between air temperature exposure and all semen quality parameters (either qualified sperm donors or not qualified sperm donors) were revealed in China of Wuhan sperm bank, with generally the threshold of 13 °C, and the relationship was close to linearity when the exposure was lower or higher than the threshold [8]. In Europe, a similar study in Italy enrolled both infertile and fertile men and demonstrated a direct relationship between environmental temperatures and both total sperm number and concentration in the winter season in the same geographical area of northern Italy [9]. Other wisely, the former evident showed the temperature was only correlated for semen quantity-related parameters (i.e. Volume and Concentration) either not for semen quality (Progressive Motility and Morphology) which seem not to be influenced by seasons. In our repeat sampling of qualified sperm donor data, the temperature was positively correlated with all semen parameters. Furthermore, atmospheric pressure was weakly correlated with most semen parameters except for the volume of semen. Recently, eight years of Turkey research revealed that the temperature and temperature-humidity index were negatively correlated with semen parameters [4].

In the analysis of long-term climate and altitude adaption, 2750 fertile males with semen parameters higher than the baseline value according to the World Health Organization included the native Han population, native Tibetan population, and native Uighur population7.The descriptive quantity data showed that the total sperm count and concentration of Tibet were 259.34±169.89 and 74.32±45.16, respectively, which were the highest of the three loci. In the quality way, progressive motility of the Shanghai was 54.1±9.7 and the abnormal sperm morphology rate of Turpan was 92.8±3.8, which were superior of the three sampling locus. This situation reflects that fertile Tibetan males prepared better sperm quantity, while Han and Uygur males prepared better sperm quality. Similar to previous findings in Zheng et al. and Gu et al. [10,11], the sperm concentration of Chinese soldiers was decreased significantly after 3 months of high-altitude exposure, and immigrated Hans exhibited higher sperm motility than native Tibetans [11,12].To explain the differences between the three populations' semen characteristics, we trained the general linear statistical model of the climate variations obtained from annual reports. We observed that most semen parameters, except for abnormal morphology rate, were correlated with annual mean pressure and air oxygen content in long-term analysis. Compared with residents at Shanghai or Turpan, where the annual mean atmospheric PO2 is 150 or 130 mm Hg, residents of the Tibetan highlands, where the PO2 is 98 mm Hg or less, live under conditions of chronic hypoxia and have evolved unique adaptations to their climate environment. The typical oxygen homeostasis system emphasizes the elements currently known to be involved in high-altitude adaptation. In the adapted Tibetan population, these physiological responses to hypoxia are not obvious, and many Tibetans have normal pulmonary arterial pressure and haemoglobin levels. The oxygen homeostasis system depends on the oxygen cascade, including oxygen sensing, blood vessels, red blood cells and haemoglobin concentration [13,14]. In earlier studies, hypoxia-inducible factor (HIF)-1 was found to be a transcriptional regulator of genes involved in oxygen homeostasis. This demonstrated that HIF-1 regulates core processes such as oxygen transport, angiogenesis, and glycolytic capacity in tissues. However, there have been no reports on the oxygen cascade of human sperm reproduction. Recently, testis-specific isoforms of HIF-1a were described and identified at the human sperm tail, especially at the mid-piece. In contrast, HIF-1a knockout mice do not show any obvious phenotype and are normally fertile [14,15].

CONCLUSIONS

The data of fertile men living in different altitudes of China showed the semen parameters are sensitive to the temperature of the daily weather fluctuation, while the oxygen content were the most sensitive parameters to semen in the long-term climate changing combined altitude effect. Our findings provide evidence for population settlement in different altitudes bypass the adaptation of climate and hypoxia, and also provides optimized statistical method to construct multifactorial–response functions of semen quality.

Funding

This project was supported by Shanghai Municipal Science and Technology Major Project (2017SHZDZX01) and Research and Development Centre Project of Serve China (2019001YZGT).

ACKNOWLEDGEMENTS

The authors would like to thank Can Sun, Ya-Dong Li, Hai-Tao Ma, Jie Ren and Bai-Lan Feng of Fudan University for his assistance in data collection.

Authorship contribution statement

Conceptualization: YZ, FZ, and FJ; Data curation: ZWT, FL, LO, and XJW; Formal analysis: YZ, and ZWT; Investigation: YZ, and FJ; Methodology: YZ, and FJ; Project administration: YZ, and FJ; Software: ZWT, and YZ; Supervision: YZ, and FJ; Validation: YZ, and FJ; Visualization: YZ, FZ, and FJ; Roles/Writing - original draft: YZ, and FJ; Writing - review & editing: YZ, FZ, and FJ; All authors reviewed the manuscript.

Data availability: Data will be made available on request.

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