

Men's Sleep Quality and Assisted Reproductive Technology Outcomes in Couples Referred to a Fertility Clinic: A Chinese Cohort Study

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Background: Poor sleep quality has been linked to lower semen quality, but it is unclear whether this result in decreased fertility. To address this question, we retrospectively evaluated the relationship between men's sleep quality and treatment outcomes in subfertile couples receiving assisted reproductive technology (ART).

Patient Enrollment and Methods: From September 2017 to November 2019, 282 subfertile couples referred to a Chinese fertility clinic and eligible for ART procedures were enrolled in our study. Sociodemographic characteristics, life habits, and sleep habits in the year prior to ART were recorded. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). We first divided the patients into two groups based on sleep quality (good sleep: PSQI < 5 and poor sleep: PSQI ≥ 5). Then, the ART outcomes (fertilization rate, good quality embryo rate, implantation rate, positive pregnancy rate, clinical pregnancy rate, live birth rate, miscarriage rate, and birth weight) of each group were analyzed. Finally, multivariate linear and logistic regression analysis were used to examine the relationship between sleep quality (discrete variable or dichotomous variable) and ART outcomes.

Results: The participants in the poor sleep group showed a lower fertilization rate of 60.13% (543/903) when compared with 67.36% for the good sleep group (902/1339), $P < 0.001$. The global PSQI score had a significant influence on birth weight (β , -63.81; 95% CI, -119.91- -8.52; $P = 0.047$), and live birth rate (OR, 0.88; 95% CI, 0.78- 0.99; $P = 0.047$) after adjusting for the interfering factors. Men's sleep quality was unrelated to good quality embryos rate, implantation rate, positive pregnancy rate, clinical pregnancy rate, or miscarriage rate.

Conclusion: Men's sleep quality was positively associated with fertilization rate, birth weight, and live birth rate among couples undergoing ART.

Keywords: sleep quality, PSQI, fertility, male reproduction, in vitro fertilization, intracytoplasmic sperm injection

Introduction

According to the World Health Organization (WHO), approximately 15% of the couples of childbearing age face fertility issues, and male factors contribute to 40%–50% of all infertility cases.^{1,2} The prevalence of infertility has increased significantly over the past decades, while the increasing prevalence of not optimal lifestyle factors such as obesity,^{3,4} tobacco⁵ or alcohol consumption. Because these lifestyle factors are modifiable, they represent an improved way of infertility management. In addition to the widely studied unhealthy lifestyle parameters associated with infertility, the short sleep duration and poor sleep quality⁶ were proved to be potential risk factors. Sleep is a naturally recurring state that is modulated by the circadian rhythm⁷ and homeostatic system.⁸ Inadequate sleep duration has been linked to adverse health outcomes, including all-cause mortality,⁹ cardiovascular diseases,¹⁰ hypertension,¹¹ and diabetes.¹²

Therefore, the influence of sleep on reproduction and fertility has aroused widespread concern in recent years.^{13,14} Goldstein et al¹⁵ previously reported that women's total sleep time was positively related to the oocytes retrieved during in vitro fertilization (IVF) treatment among 22 women presenting to an infertility clinic. Our previous studies in men confirmed those of other researchers, demonstrating that sleep quality^{16,17} and sleep duration^{17,18} are related to sperm

concentration and sperm motility. However, other studies have not validated this relationship.^{19,20} Therefore, it is unclear whether the recently described sleep-related variations in semen quality translate into diminished fertility. Moreover, one study to date has evaluated whether sleep impacts couple fecundity rather than semen quality. Wise²¹ and colleagues found that fecundability ratios (FRs) were 0.62 (95% CI 0.42–0.87) in men who slept less than 6 hours per night compared to men who slept 8 hours per night. To further understand how sleep impacts male fertility, we evaluated the association of men's sleep quality with infertility treatment outcomes of subfertile couples undergoing assisted reproductive technology (ART).

Materials and Methods

Study Population

This retrospective study was conducted on 342 infertile couples undergoing their first ART cycle with in vitro fertilization/ intracytoplasmic sperm injection (IVF/ICSI) in a reproductive medicine center from September 2017 to November 2019. Among couples attending the infertility clinic, the female partners were 20–42 years old. Of these 342 couples, 60 were excluded: 45 male partners used sperm retrieval techniques (testicular sperm extraction or percutaneous epididymal sperm aspiration), 4 male partners did not join the study, and 11 treatment cycles were canceled due to ovarian hyporesponse or natural pregnancy.

During the study period, the controlled ovarian stimulation protocols for women undergoing ART treatments included: long agonist protocol, antagonist protocol, ultra-long protocol. Only the first fresh embryo transfer cycle was analyzed in this study, and all the couples agreed to participate in this study with a signed informed consent form. This study was approved by the Research Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (No. 2017–708). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Questionnaire

Patient demographics, including age, education, occupation and duration of infertility, and lifestyle habits such as smoking, alcohol, coffee consumption, and exercise, were collected. Any history of chronic illness, urinary or reproductive disease, neurological or psychiatric condition, and a recent fever ($\geq 38^{\circ}\text{C}$ within the past 3 months) were also disclosed, and the Pittsburgh Sleep Quality Index (PSQI) was used to measure the sleep quality.²² The self-survey included 19 items reflecting the sleep quality of respondents in the past month. These items reflect sleep quality through seven components, namely: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component was scored between 0–3, and the overall PSQI scores ranged from 0 to 21.

Ovarian Stimulation and Outcome Survey

Women underwent one of three ovarian stimulation treatment protocols for ART: long agonist protocol, antagonist protocol, or ultra-long protocol. Briefly, gonadotropins were initiated on day 3 of induced menses or after 14 days of down-regulation, and the GnRH agonist or antagonist was continued or started according to the usual ovarian stimulation protocols.²³ The HCG trigger injection was administered when a transvaginal ultrasound revealed at least three dominant follicles (≥ 16 mm), and oocyte retrieval was completed after 36 hours. Oocytes underwent either conventional IVF or ICSI as clinically specified. The percentage of normally fertilized oocytes (2PN) in the inseminated oocytes was calculated as fertilization rate. The good-quality embryo rate was defined as the percentage of optimal embryos among the total number of cleavage embryos. Consequently, clinical outcomes were measured following the transfer of one or two embryos. The positive pregnancy rate referred to the percentage of positive pregnancies in the total fresh embryo transfer cycles, defined by an elevation in plasma β -HCG levels above 10 IU/L, measured 12 days after embryo transfer. The clinical pregnancy rate was defined as the percentage of clinical pregnancies in total fresh embryo transfer (ET) cycles, characterized by the presence of an intrauterine pregnancy confirmed by ultrasound at 6 weeks of gestation. The miscarriage rate referred to the percentage of early miscarriages in the clinical pregnancies, indicating pregnancy

termination before 12 gestational weeks. The live birth rate referred to the percentage of live births to fresh embryo transfer cycles, defined as the birth of a neonate on or after 24 weeks of gestation.

Statistical Analysis

Data were presented as frequencies and percentages for categorical variables and mean standard deviation (SD) for continuous variables. The participants were divided into two groups according to a previously validated^{24–26} cut-off point (PSQI= 5), namely the good sleep group and the poor sleep group. A total PSQI score of 5 or more points indicates poor sleep quality.^{24–26} The PSQI features a diagnostic sensitivity of 98% and a specificity of 55%.²⁴

We assessed the relationship between sleep quality and potential confounders using the Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables. To study the association of sleep quality (continuous variable or dichotomous variable, independent variables) with fertilization rate, good quality embryos rate, and birth weight (dependent variables), multivariate linear regressions were conducted. In contrast, binary logistic regressions were performed to study the relationship between sleep quality (continuous variable or dichotomous variable, independent variables) and positive pregnancy, clinical pregnancy, live birth, and miscarriage (dependent variables). Both continuous variable methods (general PSQI scores) and dichotomous variable methods (PQSI < 5 vs PQSI ≥ 5) were both employed to analyze sleep quality. Two models were created: an unadjusted model with only the sleep quality (independent variables); and a second model with the main effects adjusted for potential confounders (independent variables) associated with ART outcomes (dependent variables), such as paternal age, BMI, smoking, alcohol drinking, and maternal age, BMI, duration of infertility, type of ovarian stimulation protocol, the number of retrieved oocytes, oocyte insemination technique (IVF/ICSI), global PSQI score, duration of sleep (categorical variable), endometrial thickness, number of embryos transferred, embryo transfer day.

Throughout the study, to reduce the probability of obtaining false positive results, the *P*-value was adjusted using Benjamini-Hochberg False Discovery Rate (FDR).²⁷ Differences were considered to be statistically significant if *P* < 0.05. Statistical analyses were performed using the Statistical Package for the Social Sciences version 23.0 (SPSS, Inc., IBM) software.

Results

Oocyte retrieval was performed on all 282 participating females. A total of 274 cycles were successfully fertilized, while no oocyte was retrieved, or fertilization was failed in 8 cycles. In addition, embryo transfer was completed in 267 cycles but failed in 7 cycles (3 with no cleavage and 4 with poor embryo quality). Finally, 183 positive pregnancies were recorded, leading to 164 clinical pregnancies and 141 cycles with live birth (Figure 1).

The demographic characteristics are displayed in Table 1. The study population included 282 participants, with a mean age of 32.49 ± 4.98 years and a BMI of 24.11 ± 3.45 kg/m². The median PSQI score was 4 (interquartile range, 3–6), and the mean PSQI score was 4.02 ± 2.42, with an average sleep duration of 7.44 ± 0.94 hours. A total of 110 participants (39%) were classified into the poor sleep group (general PSQI scores ≥ 5). Compared with the good sleep group, they experienced a shorter sleep duration (7.06 ± 1.04 hrs), while their female partners had higher general PSQI scores (4.06 ± 2.39). In Table S1, we re-grouped according to PSQI > 5 as cut-off, a total of 62 participants (21.99%) were classified into the poor sleep group (PSQI > 5). Compared with the good sleep group (PSQI ≤ 5), they experienced a shorter sleep duration (6.69 ± 1.00 hrs), while their female partners had higher general PSQI scores (4.44 ± 2.31). Out of 282 female partners (mean age = 30.05 ± 3.76 years; BMI = 22.28 ± 3.46 kg/m²), 267 completed assisted reproductive technology- embryo transfer (ART-ET) cycles and retrieved 7.95 ± 3.85 oocytes. Consequently, embryo transfer failed in 15 (5.32%) cases, and 18.79% (53/282) couples reported a primary diagnosis of male factor infertility.

Table 2 shows the laboratory and clinical outcomes of ART for both groups. The comparison showed that the fertilization rate (60.13%) of the poor sleep group (PQSI ≥ 5) participants was significantly lower than those in the good sleep group (PQSI < 5) (67.36%) (*P* = 0.001). In Table S2, we re-grouped according to PSQI > 5 as cut-off, the poor sleep group (PSQI > 5) had a significantly lower fertilization rate (55.01%) when compared with the good sleep group (PSQI ≤ 5) (67.22%) (*P* < 0.001). However, there was no statistically significant difference between the two groups in good quality embryos rate, implantation rate, positive pregnancy rate, clinical pregnancy rate, live birth rate, miscarriage rate, and birth weight.

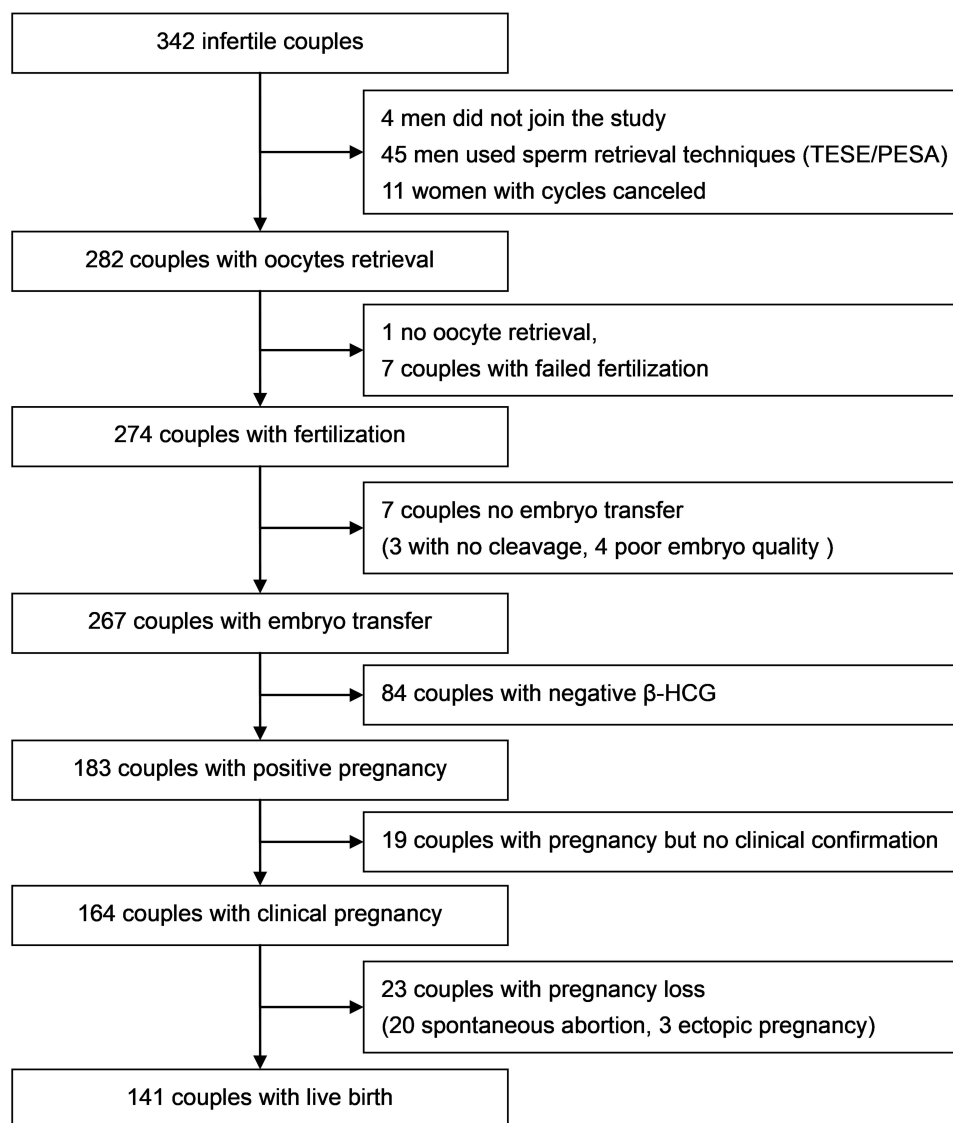


Figure 1 A cohort study population flowchart.

Abbreviations: TESE, testicular sperm extraction; PESA, percutaneous epididymal sperm aspiration; HCG, human chorionic gonadotropin.

Regression analysis is shown in [Table 3](#). In crude analyses, linear regression analysis illustrated that the global PSQI score had a negative influence on fertilization rate (β , -1.43 ; 95% CI, -2.67 - -0.19 ; $P = 0.045$), and birth weight (β , -55.08 ; 95% CI, -104.70 - -5.46 ; $P = 0.045$) ([Figure 2A](#) and [C](#)). After adjustment for confounders, the global PSQI score had a negative influence on birth weight (β , -63.81 ; 95% CI, -119.91 - -8.52 ; $P = 0.047$). Moreover, binary logistic regression analysis demonstrated that the global PSQI score was negatively associated with the live birth (OR, 0.88 ; 95% CI, 0.78 - 0.99 ; $P = 0.047$) ([Figure 2D](#)). In addition, we observed an inverse association between poor sleep group ($PQSI \geq 5$) and the fertilization rate, both before and after the adjustments. In [Table S3](#), we also found the same conclusion, although we grouped according to $PSQI > 5$ as cut-off. In contrast, regression analysis found no relationship between sleep quality and good quality embryos rate, positive pregnancy, clinical pregnancy, and miscarriage.

Discussion

We retrospectively assessed the relationship between men's sleep quality and treatment outcomes in their partners who underwent ART. We found that a higher global PSQI score was related to lower fertilization rate, birth weight, and live

Table I Demographic and Reproductive Characteristics of Study Populations

Characteristics	Total (n= 282)	Good Sleep (n= 172)	Poor Sleep (n= 110)	P value ^a
Age (year) ^b	32.49 ±4.98	32.35 ±4.75	32.69 ±5.32	0.812
BMI (kg/m ²) ^b	24.11 ±3.45	24.24 ±3.21	23.91 ±3.78	0.199
Duration of infertility (years) ^b	3.30 ±2.18	3.08 ±1.91	3.65 ±2.51	0.152
College and higher, n (%)	126 (44.68)	80 (46.51)	46 (41.82)	0.439
Employed, n (%)	263 (93.26)	160 (93.02)	103 (93.64)	0.841
Smoking, n (%)	107 (37.94)	66 (38.37)	41 (37.27)	0.853
Drinking alcohol, n (%)	55 (19.50)	37 (21.51)	18 (16.36)	0.287
Drinking coffee, n (%)	27 (9.57)	16 (9.30)	11 (10.00)	0.846
Physically activity, n (%)	78 (27.66)	52 (30.23)	26 (23.64)	0.227
Fever, n (%)	10 (3.55)	6 (3.49)	4 (3.64)	1.000
Global PSQI score ^b	4.02 ±2.42	2.49 ±1.20	6.42 ±1.83	< 0.001
Duration of sleep (hours) ^b	7.44 ±0.94	7.68 ±0.78	7.06 ±1.04	< 0.001
Primary infertility diagnosis, n (%)				0.315
Male factor	53 (18.79)	28 (16.28)	25 (22.73)	
Female factor	206 (73.05)	128 (74.42)	78 (70.91)	
Ovulation disorders	24 (11.65)	15 (11.72)	9 (11.54)	
Diminished ovarian reserve	26 (12.62)	14 (10.94)	12 (15.38)	
Tubal	113 (54.85)	71 (55.47)	42 (53.85)	
Endometriosis	27 (13.11)	16 (12.50)	11 (14.10)	
Uterine	16 (7.77)	12 (9.38)	4 (5.13)	
Unexplained	23 (8.16)	16 (9.30)	7 (6.36)	
No. of embryos transferred, n (%)				0.014
No embryos transferred	15 (5.32)	5 (2.91)	10 (9.09)	
1 embryo	56 (19.86)	29 (16.86)	27 (24.55)	
2 embryos	211 (74.82)	138 (80.23)	73 (66.36)	
Embryo transfer day, n (%)				0.078
No embryos transferred	15 (5.32)	5 (2.91)	10 (9.09)	
Day 2	37 (13.12)	20 (11.63)	17 (15.45)	
Day 3	219 (77.66)	141 (81.98)	78 (70.91)	
Day 5	11 (3.90)	6 (3.49)	5 (4.55)	
ICSI, n (%)	46 (16.37)	23 (13.45)	23 (20.91)	0.099
Female partner characteristics				
Age (year) ^b	30.05 ±3.76	29.98 ±3.63	30.16 ±3.97	0.772
BMI (kg/m ²) ^b	22.28 ±3.46	22.28 ±3.25	22.28 ±3.77	0.732
Endometrial thickness (mm) ^b	10.45 ±1.80	10.34 ±1.67	10.62 ±1.97	0.116
Oocytes retrieved (n) ^b	7.95 ±3.85	7.78 ±3.82	8.21 ±3.90	0.388
Global PSQI score ^b	3.62 ±2.21	3.34 ±2.04	4.06 ±2.39	0.011
Duration of sleep (hours) ^b	7.55 ±1.65	7.64 ±1.50	7.40 ±1.86	0.478

Notes: ^aComparison between each group: continuous variable (Kruskal–Wallis test), categorical variables (χ^2 or Fisher's exact test). ^bData were expressed as mean± standard deviation.

Abbreviations: BMI, body mass index; PSQI, Pittsburg Sleep Quality Index; ICSI, intracytoplasmic sperm injection.

birth rate. However, men's subjective sleep quality was unrelated to good quality embryos rate, implantation rate, positive pregnancy rate, clinical pregnancy rate, or miscarriage rate.

Previous studies mostly focused on the potential effect of sleep quality on male reproduction and its relation with semen quality. We found that men with poor sleep quality had fewer spermatozoa with lower motility and lower normal sperm morphology than men who slept well.¹⁶ However, sleep quality was unrelated to ejaculate volume in a cross-

Table 2 Laboratory and Clinical Outcomes of ART in Each Group According to the Paternal Global PSQI Scores

Characteristics	Total (n = 282)	Good Sleep (n = 172)	Poor Sleep (n = 110)	P value ^a
Fertilization rate % (n) ^c	64.45 (1445/2242)	67.36 (902/1339)	60.13 (543/903)	0.001
Good quality embryos rate % (n) ^d	57.05 (813/1425)	55.77 (498/893)	59.21 (315/532)	0.255
Implantation rate % (n) ^e	45.82 (219/478)	46.89 (143/305)	43.93 (76/173)	0.533
Positive pregnancy rate % (n) ^f	68.54 (183/267)	71.26 (119/167)	64.00 (64/100)	0.259
Clinical pregnancy rate % (n) ^g	61.42 (164/267)	64.07 (107/167)	57.00 (57/100)	0.293
Live birth rate % (n) ^h	52.81 (141/267)	56.29 (94/167)	47.00 (47/100)	0.188
Miscarriage rate % (n) ⁱ	12.20 (20/164)	10.28 (11/107)	15.79 (9/57)	0.349
Birth weight (g) ^b	2926.84 ±596.61	2990.74 ±604.53	2799.02 ±565.18	0.089

Notes: ^aComparison between each group: continuous variable (Kruskal–Wallis test), categorical variables (χ^2 -test). P value was adjusted using Benjamini-Hochberg False Discovery Rate(FDR). ^bData were expressed as mean± standard deviation. ^cFertilization rate: normally fertilized oocytes/inseminated oocytes; ^dGood quality embryo rate: optimal embryos/cleavage embryos; ^eImplantation rate: number of gestational sac/ number of embryos transferred; ^fPositive pregnancy rate: positive β -HCG/fresh embryo transfer cycles; ^gClinical pregnancy rate: clinical pregnancies/fresh embryo transfer cycles; ^hLive birth rate: live births/fresh embryo transfer cycles; ⁱMiscarriage rate: miscarriages/clinical pregnancies.

Abbreviations: ART, assisted reproductive technology; PSQI, Pittsburg Sleep Quality Index.

sectional analysis among men from the Reproductive Medicine Center in Zhejiang. Chen HG et al¹⁷ studied the sperm samples from 842 healthy potential sperm donors and reported that poor sleep quality was associated with lower total sperm count, total motility, and progressive motility. Furthermore, Jensen et al²⁸ reported that sleep disturbance was negatively related to sperm concentration, total sperm count, and percentage of normal sperm morphology in a 953 Danish men's case-control study. These three findings are in accordance with our analysis and infer strong associations between sleep quality and semen quality.

This study illustrates an inverse relationship between the global PSQI score and outcomes in ART cycles and supports the previous reports of a negative association between the general PSQI scores and sperm morphology.¹⁶ Such

Table 3 Linear and Logistic Regression Analysis of the Association Between the Paternal Sleep Quality and Laboratory and Clinical Outcomes

	The Global PSQI Score				Good Sleep vs Poor Sleep			
	u- β / OR (95% CI)	P value ^a	a- β / OR (95% CI)	P value ^a	u- β / OR (95% CI)	P value ^a	a- β / OR (95% CI)	P value ^a
Fertilization rate (%) ^{bf}	-1.43 (-2.67, -0.19)	0.045	-1.33(-2.62, -0.04)	0.059 ^d	-8.19 (-14.32, -2.05)	0.018	-8.06(-14.38, -1.75)	0.026 ^d
Good quality embryos rate (%) ^{bg}	0.56 (-0.98, 2.09)	0.475	0.57(-1.02, 2.17)	0.479 ^d	-0.55 (-8.21, 7.11)	0.888	0.30(-7.60, 8.20)	0.940 ^d
Birth weight (g) ^b	-55.08 (-104.70, -5.46)	0.045	-63.81(-119.11, -8.52)	0.047 ^e	-191.72 (-400.76, 17.31)	0.108	-200.77(-429.48, 27.93)	0.113 ^e
Positive pregnancy ^{ch}	0.92 (0.83, 1.03)	0.166	0.92(0.82, 1.03)	0.188 ^e	0.72 (0.42, 1.22)	0.271	0.71(0.40, 1.28)	0.308 ^e
Clinical pregnancy ^{ci}	0.92 (0.83, 1.02)	0.153	0.91(0.81, 1.02)	0.135 ^e	0.74 (0.45, 1.23)	0.301	0.73(0.41, 1.28)	0.316 ^e
Live birth ^{ci}	0.91 (0.83, 1.01)	0.109	0.88(0.78, 0.99)	0.047 ^e	0.69 (0.42, 1.13)	0.189	0.57(0.33, 1.01)	0.078 ^e
Miscarriage ^{ck}	1.15 (0.92, 1.44)	0.268	1.24(0.90, 1.70)	0.217 ^e	1.64 (0.63, 4.22)	0.359	2.31(0.64, 8.35)	0.250 ^e

Notes: ^aP value was adjusted using Benjamini-Hochberg False Discovery Rate(FDR). ^bMultiple linear regression analysis; ^cBinary logistic regression analysis; ^dRegression coefficients were adjusted for paternal age, BMI, smoking, alcohol drinking, and maternal age, BMI, duration of infertility, type of ovarian stimulation protocol, the number of retrieved oocytes, oocyte insemination technique (IVF/ICSI), global PSQI score, duration of sleep (categorical variable). ^eRegression coefficients were adjusted for paternal age, BMI, smoking, alcohol drinking, and maternal age, BMI, duration of infertility, type of ovarian stimulation protocol, the number of retrieved oocytes, oocyte insemination technique (IVF/ICSI), global PSQI score, duration of sleep (categorical variable), endometrial thickness, number of embryos transferred, embryo transfer day. ^fFertilization rate (continuous variables): normally fertilized oocytes/inseminated oocytes; ^gGood quality embryo rate (continuous variables): optimal embryos/cleavage embryos; ^hPositive pregnancy (dichotomous variables): 12 days after embryo transfer, the level of plasma β -HCG above 10 IU/L; ⁱClinical pregnancy (dichotomous variables): at 6 weeks of gestation, the presence of intrauterine pregnancy by ultrasound; ^jLive birth (dichotomous variables): the birth of a neonate on or after 24 weeks of gestation; ^kMiscarriage (dichotomous variables): pregnancy termination before 12 gestational weeks.

Abbreviations: PSQI, Pittsburg Sleep Quality Index; u- β / OR, unadjusted beta coefficient/odds ratio; a- β / OR, adjusted beta coefficient/odds ratio; 95% CI, 95% confidence intervals.

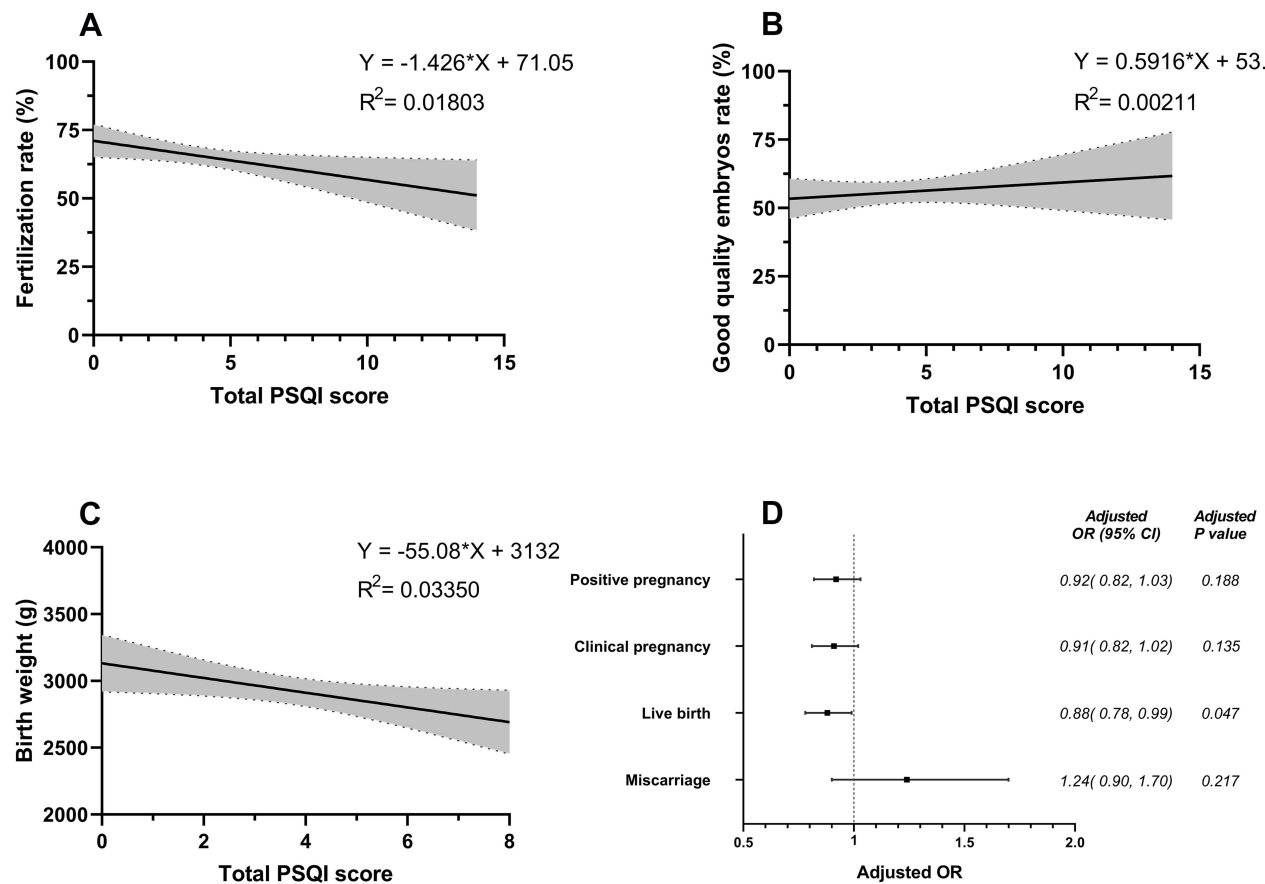


Figure 2 The paternal total PSQI score and ART outcomes. (A–C) respectively illustrate the linear regression analysis result between the global PSQI score and fertilization rate (N= 281), good quality embryos rate (N= 272); and birth weight (N= 141). The black line indicates the linear regression result, and the shaded area represents the 95% confidence interval. (D) shows the logistic regression analysis results between the global PSQI score and positive pregnancy (N= 183), clinical pregnancy (N= 164), live birth (N= 141), and miscarriage (N= 20).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ART, assisted reproductive technology; OR, odds ratio; 95% CI, 95% confidence intervals.

a relationship was expected since sperm morphology is associated with ART outcomes.²⁹ However, whether sleep quality has an impact on semen quality has yet to be elucidated.

Notably, few previous studies have evaluated the association between men's sleep and infertility treatment outcomes. Interestingly, a study examined the association between male sleep and fecundability ratios (FRs) in a population-based cohort of 1176 couples who were attempting to conceive without using contraception or fertility treatment.²¹ In this study, multi-variable-adjusted FRs for participants with <6 hours of sleep per night were 0.62 (95% CI 0.42–0.87) when compared to peers with 8 hours of sleep per night. This study reached a similar conclusion as our findings, that is, compared with men who had no trouble sleeping, the FRs for men who had difficulty sleeping less than half the time was 1.06 (95% CI 0.85–1.31), and the FRs for men who had trouble sleeping more than half the time was 0.93 (95% CI 0.72–1.20).

The mechanisms by which poor sleep quality can reduce male fertility remain unclear. Several studies support the testosterone hypothesis; Andersen ML et al, Leproult R et al, and Jankowski KS et al^{30–32} found that poor sleep quality was associated with lower semen quality and/or lower testosterone levels. However, Jensen et al, Chen Q et al, Du CQ et al, and Morten Ruge et al^{16,28,33,34} found little connection between sleep quality and testosterone in their studies. The discrepancy in the results from various studies may reflect the complexity of the involved mechanisms. The circadian rhythm system may partially account for our observations. This system, regulated by the solar light and dark cycle, controls vital aspects of our physiology, including body temperature, heart rate, hormone secretion and cellular metabolism.^{7,35} Therefore, the circadian rhythm plays an essential role in the mature sperm production process.^{36–39} Unhealthy sleep habits disrupt the expression of circadian rhythm genes and have adverse effects on the male reproductive system.^{40,41} Since melatonin regulates the sleep-

wake cycle of the circadian rhythm, the inhibition of melatonin and cortisol production by endogenous circadian rhythm disorders may cause a disruption of the cycle.⁴² Additional functions of melatonin include the regulation of gonadotropin and testosterone secretion, promotion of testicular maturation and free radical scavenging, thus preventing testicular injury.⁴³ Therefore, the potential impact of sleep on male fertility deserves further investigation.

This study features a number of notable aspects. Our study was retrospectively designed and used a previously validated PSQI, and the participating couples were followed up during pregnancy until the babies were born. Furthermore, we examined multiple factors that could affect semen quality and ART outcomes, such as paternal age, paternal BMI, smoking, alcohol drinking, and maternal age, maternal BMI, global PSQI score, duration of sleep (categorical variable), duration of infertility, type of ovarian stimulation protocol, the number of retrieved oocytes, oocyte insemination technique (IVF/ICSI), endometrial thickness, number of embryos transferred, and embryo transfer day. Moreover, direct and objective measures of male fertility were selected, including fertilization rate, good quality embryos rate, implantation rate, live birth rate, and miscarriage rate. This is a novel approach that improves on the traditional semen quality parameters to assess male fertility. However, the present research also has some limitations. Firstly, sleep quality is a self-reported subjective indicator, and measurement errors cannot be completely excluded. Secondly, the participants were recruited from a single fertility clinic and were limited in number, raising the possibility of selection bias. Lastly, we only investigated the sleep quality before entering the ART cycle, without dynamically detecting the sleep quality, without considering the influences of anxiety and obstructive sleep apnea (OSA) on sleep quality, and only selected the data of the fresh embryo transfer cycle, which may cause some deviations in the results.

Sleep is closely related to quality of life and mental health. Some researchers have proposed that psychological stress negatively affects sperm parameters.^{44–46} Furthermore, psychological stress is associated with sleep disturbance and is more common in infertile couples than in fertile couples.⁴⁷ So, it should be emphasized that the relationship between sleep disturbances and male fertility may be bidirectional. Therefore, it will be interesting to include these confounding factors in future studies. Efforts to improve sleep can also be incorporated into global and individualized preconception care plans for infertile couples.⁴⁸

Conclusion

In this retrospective study, we present evidence that poor sleep quality is correlated with adverse pregnancy outcomes. This suggests a greater male reproductive potential with better sleep quality. Our study extends the current literature on the relationship between sleep quality and male fertility. In view of the growing global evidence that human semen quality is declining, and poor sleep quality is becoming more common, further research is needed to explore the underlying mechanisms and confirm our findings.

Acknowledgments

The authors are grateful to colleagues from Reproductive Medicine Center of The First Affiliated Hospital, College of Medicine, Zhejiang University for providing direct assistance and constructive suggestions for this research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no potential conflicts of interest with respect to the research, authorship and publication of this article.

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