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Original Research Article

A study on the association of diabetes and semen quality in and around Chennai, Tamil Nadu, India

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ABSTRACT

Background: Globally prevalence of diabetes is gradually increasing in individual at reproductive stage. Uncontrolled blood sugar affects biological systems including reproductive. Thus, this study was aimed to analyze the association of diabetes and male infertility in and around Chennai.
Methods: Fifty-four male participants who visited the fertility clinic was grouped in two based on the sugar value. An anthropometric measurement, clinical, blood, seminal parameters and life style behaviors was analyzed. All study variables was analyzed to examine the association of diabetes and semen quality.
Results: Study results shows that people with diabetes had abnormal semen parameters as compared to non- diabetic study participants. Pearson's correlation between the semen parameters and blood sugar value of the study participants showed semen parameters: volume ($r=-0.28$, $p<0.05$), count ($r=-0.22$, $p<0.05$), and motility ($r=-0.23$, $p<0.05$), has a significantly week negative correlation with blood sugar level. Scatter plots also showed semen parameters: volume ($r^2=-0.079$), count ($r^2=-0.048$), and motility ($r^2=-0.053$), had a significantly week negative linear correlation with blood sugar level.
Conclusions: From the study it was concluded that the uncontrolled blood sugar levels affect the reproductive health of the study participants.

Keywords: Male infertility, Semen, Diabetes, HbA1c, Cholesterol, Cortisol

INTRODUCTION

Infertility is a disease of the human reproductive system defined as the inability to become pregnant after a year or more of regular unprotected sexual practice. Infertility is more than just a medical condition. However, it is a condition characterized by psychological, stress, economic, and social pressures on child-bearing.[1] A few emotions experienced by infertile couples include irrational rage, severe depression, self-blame, isolation from family members, societal pressure, and embarrassment in front of couples who are fertile.[2] Globally, male factors account for 40-50% of the fertility problem, affecting 10-15% of couples of reproductive ages.[3] The prevalence of male infertility varies between developed and developing countries, depending on the resources available for investigation and treatment. Every year, 60-80 million couples worldwide suffer from infertility, with 15-20 million from India.[4]

The prevalence of male infertility varies geographically. According to a study by WHO, the incidence of infertility in India is not yet clear. It is estimated that approximately 13 to 19 million couples are infertile.[5] Although diabetes is not known to directly affect fertility, some of its associated disorders have been shown to have an impact.

Diabetes can cause erectile dysfunction and retrograde ejaculation in men. These issues can contribute to a loss of interest in sex as well as difficulties in giving birth to a child. Furthermore, their sperm quality is inferior to that of normal men.[6]

During spermatogenesis, diabetes may alter the sperm's modification genes, and these changes may be passed on to the next generation through sperm, increasing the progeny's risk of developing diabetes.[7] Studies have shown that the ARTs successful outcome was less in diabetic male as compared to normal male.[8] Since sperm motility play an important role in deciding the appropriate ARTs. A study have shown that minimum 5 million, 2 million and less than 2 million progressive sperm required for IUI, IVF and ICSI respectively.[9]

Globally, the prevalence of diabetes is gradually increasing, thus this is crucial area of research. Studies have shown that anti diabetic drugs show adverse effect on semen quality.[10] Only few literatures available on the relationship between diabetes and semen quality and most of them are animal study. Various risk factors of diabetes also directly influence the semen quality. Thus, this study was aimed to study the effect of diabetes and risk factors on semen quality in diabetic infertile males in and around Chennai, Tamil Nadu.

METHODS

Study area

This randomized control trail was carried out at Fertility foundation centre in the department of andrology, Chennai, Tamil Nadu, India during 2017. The informal consent was obtained by each participant after explained the project and the study protocol was approved by institutional ethical committee, Chennai for conducting research study on human beings.

Sample size

Sample size was calculated using sample size determination (OpenEpi calculator) in health studies formula and a prevalence of 10% of male infertility.[11] A total 60 participants with fertility problem who visited the study center were approach randomly, out of which 54 willing participants were divided into two groups (27 participants with diabetes and 27 non-diabetic participants) based on their sugar level were recruited in the study. Infertile male participants aged between 25 and 50 years who had diabetes for more than one year and who sought treatment for infertility from the study center were included in the study.

Anthropometric measurements

Anthropometric measurements were taken for all study participants. The height (cm) was taken using AnthroFlex wall mount stadiometer after ensuring the legs, arms, shoulders, and eyes are straight and relax. Weight (Kg) was taken using Healthgenie digital weight machine by keeping in smooth floor and after removing shoes. Blood pressure (mmHg) was taken in a sitting position on left hand using Dr. Morepen BP02 BP monitor in after removing watches, two readings were taking with five minutes gap and average was taken. Waist circumference (cm) was measured using non stretchable inch tape near to the navel point.

Blood parameters

Venous blood sample (5ml) was collected in all study participants. Random blood sugar level was analyzed using a semi-auto biochemistry analyzer (GOD/POD method). A blood sugar level of 200 mg/dL or higher indicates diabetes. Hemoglobin A1c (HbA1c) is used to monitor 3 months average blood sugar level in people with diabetes. HbA1c was measured by immune assay and level 6.5 above consider as diabetes. Total cholesterol level was measured by CHOD-POD method using fully automatic analyzer and cholesterol level of 200 mg/dL and above is consider as high. Serum cortisol is used as the stress marker and was measured in the serum sample of the study participants using immunoassay method and 5-25 mcg/dL was consider as normal and above 25 mcg/dl was considered as stressed.

Semen collection and processing

The participants were advised to collect their semen sample by masturbation in a separate room near to the analytical lab and the ejaculate was collected into sterile container. Data on any loss of fraction of the ejaculated during sample collection was also recorded and sample container was labelled with the study ID, date, time and taken for further analysis.

Semen analysis

Semen analysis was carried out as per WHO guidelines. Liquefaction time was measured by keeping the semen sample without disturbed for 15-30 minutes in a room temperature. The pH of the collected sample was measured using pH paper and sample was transferred into a sterile glass tube to determine the sample volume. Sperm concentration was measured using hemocytometer and the concentration of sperm was counted after 5 minutes in the central square of the chamber using light microscope at 20× and 40×. The concentration of sperm was calculated as million/mL of the semen sample. Immediately after liquefaction the semen was examined for motility. The slides were examined under microscopically at 20× and 40× magnifications to assess the different grades like progressive motility (PR), non-progressive motility (NP) and immotility (IM). The motility of sperm was calculated in percentage (%). Microscopic examinations for sperm morphology were analyzed using microscope and the

percentage of normal, dead, as well as live sperm were recorded.

Data collection and statistical analyses

Baseline data was collected through standardized questionnaire including age height, weight, infertility and diabetes duration, occupation, lifestyle, family history of diabetes, and other medical histories. Statistical analysis was carried out using the IBM statistical package of social sciences, (SPSS version 24). Unique study ID was given to each participant and a $p<0.05$ was considered statistically significant. The study interest is to determine the association of diabetes and semen quality in diabetic and non-diabetic infertile participants. Age, body weight, BMI, waist circumference, blood pressure, RBS, HbA1c, total cholesterol and serum cortisol are considered as the continuous variables. The life style and behavior changes and family history of diabetes were categorical variables. Descriptive data analysis was conducted to characterize the participants and independent test was used to assess the difference in the study outcome between study populations. Scatter plots and Pearson's correlation were used to measure the association of sugar level and semen parameters.

RESULTS

Totally 54 participants were recruited in the study and based on the sugar level the enrolled participants were grouped into group 1 (non-diabetic) and group 2 (diabetic). Table 1 represented the anthropometric measurements of the study participants and all variable shows statistically significant between study groups.

The average age of group 1 and group 2 participants ranged from 27-48 years and 26-51 years respectively and the mean age of group 2 was found higher (37.8) as compared to group 1 (34.7). The body weight of group 1 and group 2 participants ranged from 48-98 kg and 47-170 kg respectively and it was found that the group 2 (82.1 kg) participants mean body weight was greater than group1 (71.7 kg).

The average BMI of group 1 and group 2 participants ranged from 15.0-30.0 kg/m^2 and 16.4-39.6 kg/m^2 respectively and the mean BMI of group 2 participants was significantly ($p<0.05$) higher (25.2 kg/m^2) as compared to group 1 participants (23.2 kg/m^2). The waist circumference of group 1 and group 2 ranged from 54.5-98 cm and 70.5-112.8 cm respectively. It is evident from the table that the mean waist circumference of group 2 was higher (91.3 cm) than group 1 (83.7 cm).

Average systolic BP for group 1 and group 2 ranged from 100-156 mmHg and 101-180 mmHg respectively and it was observed that the systolic BP of group 1 was significantly lower (125 mmHg) than the group 2 (135 mmHg). Similarly, the average diastolic BP of group 1 and group 2 ranged from 61-113 mmHg and 76-113 mmHg respectively and lower diastolic BP was observed in the group 1 (84 mmHg) as compared to the group 2 (90 mmHg).

The RBS of group 1 and group 2 participants ranged from 86.0-124.0 mg/dl and 200-280 mg/dl respectively and the mean blood sugar value was found significantly higher in group 2 (210.4 mg/dl) than group 1 (102.2 mg/dl). Similarly, the HbA1c of group 1 and group 2 ranged from 4.3-5.8% and 6.5-8.3% respectively and the mean HbA1c was observed higher (7.4%) in group 2 than group 1 (5.2%).

The average total cholesterol of group 1 and group 2 participants ranged from 100-189 mg/dl and 100-300 mg/dl respectively and the mean total cholesterol was higher (204.5 mg/dl) in group 2 than group 1 (139.9 mg/dl). The serum cortisol level of group 1 and group 2 participants ranged from 0.05-0.27 µg/dl and 0.05-0.55 µg/dl respectively and the serum cortisol level was observed maximum (0.21 µg/dl) in group 2 as compared group 1 (0.13 µg/dl) respectively.

The results of semen parameters for the study groups were shown in Table 2. The mean marriage history for group 1 and group 2 was 6.3 and 7.1 years respectively. The mean liquefaction time range was 24-30 minutes and 26-39 minutes for group 1 and 2 respectively and the average pH range was 7.5-8.2 and 7.2-8.1 for group 1 and 2. Semen volume of group 1 and 2 ranges from 1.2-5.0 ml and 1.0-4.0 ml respectively and regards to sperm count range from 1.8-105.3 million/ml and 1.7-97.4 million/ml respectively. The average motility of the sperm for group 1 and 2 range from 5-75% and 5-70% respectively. The average rapid, moderate and sluggish motility for group 1 ranges from 0-20%, 0-40% and 0-40% respectively and for group 2 ranges from 0-10%, 2-52% and 3-60% respectively. It was found that the average live and dead sperms percentage range from 62-94% and 6-38% for group1 and 18-93% and 7-82% for group 2 respectively. The study results show that the average live sperm count range from 1-22% for group 1 and 1-12% for group 2 respectively. It is evident from table 2 that the mean, pH, semen volume, sperm count, motility, live and normal sperm percentage was significantly higher in group 1 as compared to group 2 and also observed that the liquefaction time, sluggish and dead sperm percentage was found significantly higher in group 2 than group 1.

Life style behaviors of the study participants reported in Table 3. It was found that higher percentage of smokers (55.5%) in group 2 as compared group 1 (22.2%) but usage smokeless tobacco percentage was found higher in group 1 (7.4%) than group 2 (3.7%). 44.4% of group 2 participants was alcoholic and 37.0% in group 1. It was observed that maximum percentage of group 2 participants working IT sector and 48.2% of group 1 participants working in non-IT sectors. Nearly 40.7% of group 2 participants self-reported as stressed as compared to group 1 (29.6%) and also found that higher (59.3%) percentage

of group 2 participants was physically inactive than group 1 (29.6%). Around 3.7% and 44.4% of group 1 and 2 participants having strong family for diabetes and also observed that higher (63.0%) percentage of unhealthy eating habits in group 2 than group 1 (55.6%). It is evident from the table that higher percentage (81.5%) of group 2 participants not sleeping more than 8 hours as compared group 1 (70.4%).

Pearson's correlation between the semen parameters and blood sugar level of the study participants shown in Table 4. It is evident from the table that semen parameters include volume (r=-0.28, p<0.05), count (r=-0.22, p<0.05), and motility (r=-0.23, p<0.05), shows significantly week negative correlation with blood sugar level. Scatter plots show that semen parameters include volume (r^2=-0.079), count (r^2=-0.048), and motility (r^2=-0.053), shows significantly week negative linear correlation with blood sugar value (Figure 1-3).

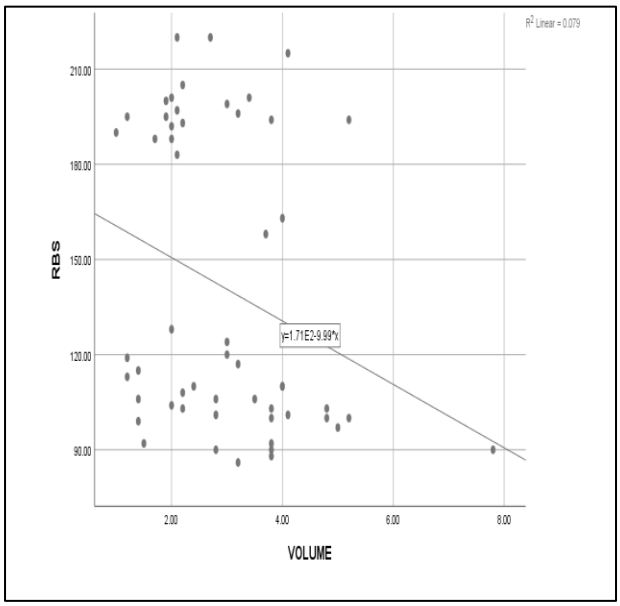

Figure 1: Scatter plots and linear regression lines of blood sugar level and semen volume of study participants.

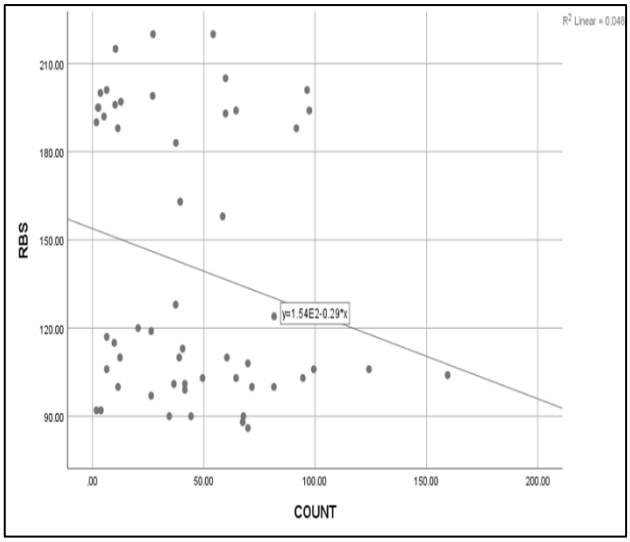

Figure 2: Scatter plots and linear regression lines of blood sugar level and sperm count of the study participants.

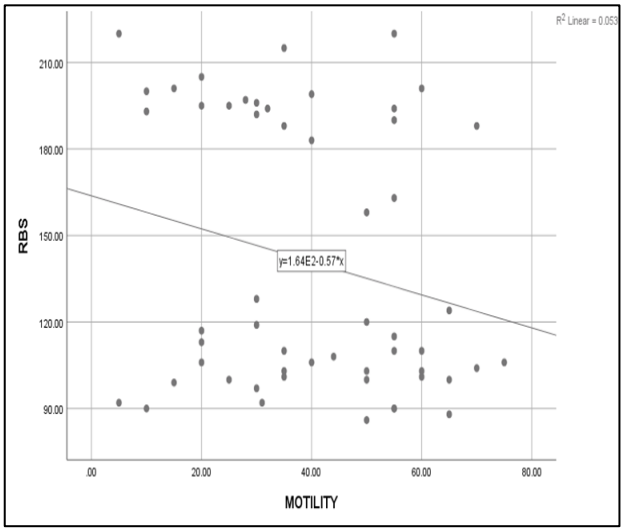

Figure 3: Scatter plots and linear regression lines of blood sugar level and sperm motility of study participants.

Table 1: Anthropometric measurements of the study participants by group.

Variables	Group 1, non-diabetic (n=27), mean ± SD	Group 2, diabetic (n=27), mean ± SD	*P value
Age (Years)	34.7±5.2	37.8±7.0	0.028
Weight (Kg)	71.7±11.4	82.1±12.2	0.011
BMI (Kg/m^2)	23.2±3.8	25.2±4.1	0.032
Waist circumference (cm)	83.7±10.1	91.3±12.4	0.018
Systolic BP (mmHg)	125±14	135±22	0.050
Diastolic BP (mmHg)	84±13	90±9	0.049
Blood sugar (mg/dl)	102.2±9.9	210.4±14.9	0.001
HbA1C (%)	5.2±0.3	7.4±0.5	0.001
Total cholesterol (mg/dl)	139.9±23.8	204.5±31.9	0.008
Serum cortisol (µg/dl)	0.13±0.05	0.21±0.13	0.010

*p<0.05 value denotes significance between groups.

Table 2: Semen parameters of the study participants by group, (n=27).

Semen analysis	Group 1, non-diabetic, mean ± SD	Group 2, diabetic, mean ± SD	*P value
Marriage history (Years)	6.3±1.1	7.1±1.5	0.05
Liquefaction (Minutes)	28.3±1.7	30.0±1.4	0.043
pH	7.9±0.1	7.7±0.1	0.442
Volume (mL)	3.3±1.3	2.5±1.0	0.030
Count (million/mL)	50.5±7.5	37.7±5.8	0.047
Motility (%)	41.5±10.3	37.7±7.9	0.020
Rapid (%)	12.5±2.5	9.3±1.2	0.001
Moderate (%)	20.2±3.4	13.8±3.0	0.002
Sluggish (%)	18.0±1.5	21.0±1.9	0.001
Live (%)	81.8±8.1	66.3±4.8	0.001
Dead (%)	17.4±1.6	33.6±4.6	0.001
Normal (%)	7.5±0.2	7.0±0.1	0.044

*P<0.05 value denotes significance between groups.

Table 3: Life style behavior measures of the study participants by group.

Variables		Group 1, non-diabetic (n=27), (%)	Group 2, diabetic (n=27) (%)
Smoking	Yes	22.2 (6)	55.5 (15)
	No	77.8 (21)	44.5 (12)
Pan gutkha	Yes	7.4 (2)	3.7 (1)
	No	92.6 (25)	96.3 (26)
Alcohol	Yes	37.0 (10)	44.4 (12)
	No	63.0 (17)	55.6 (15)
Occupation	IT	51.8 (14)	66.6 (18)
	Non-IT	48.2 (13)	33.4 (9)
Stress	Yes	29.6 (8)	40.7 (11)
	No	70.4 (19)	59.3 (16)
Physically active	Yes	70.4 (19)	40.7 (11)
	No	29.6 (8)	59.3 (16)
Diabetes family history	Yes	3.7 (1)	44.4 (12)
	No	96.3 (26)	55.6 (15)
Healthy diet	Yes	44.4 (12)	37.0 (10)
	No	55.6 (15)	63.0 (17)
Sleep >8 Hours	Yes	29.6 (8)	18.5 (5)
	No	70.4 (19)	81.5 (22)

Table 4: Association of blood sugar level and semen parameters of the study participants.

Semen parameters	RBS (mg/dl), Pearson correlation (r) (p value)
Volume (mL)	-0.28 (0.039)
Count (million/mL)	-0.22 (0.010)
Motility (%)	-0.23 (0.48)

DISCUSSION

Present study reported role of diabetes in male infertility by examining anthropometric measurements, clinical, blood, semen parameters and life style behaviors. In our study group 2 participants had higher age than group 1. Study reported most of semen parameters were decreased along with increased age in male which supports our findings.[12]

In the present study the mean body weight was 15.4% higher in group 2 than group 1 participants. Studies have shown a substantial association between body weights and diabetes mellitus, with the majority of T2DM patients being overweight or obese and having a higher chance of getting the disease.[13] Spermatogenesis and semen quality depends on the testosterone level and higher body weight lowering the testosterone level leads to poor semen quality. A review study indicate that obesity with diabetes decrease the semen quality and similar results were also observed in our study that group 2 participant's shows abnormal semen parameters as compared group 1 participants.[14] Our study results observed that group 2 participants are greater BMI than group 1 and supportive results also found in a large population study where the

higher BMI shows negative association with semen parameters.[15] Apart from BMI, waist circumference also plays an important role in male infertility. It was found that group 2 participants have slightly higher waist circumference than group 1 participants. A study conducted in 81 infertile male shows the negative correlation between the waist circumference and semen parameters.[7] Prevalence of hypertension was also increased with prevalence of obesity and diabetes. An Italian study reported that the hypertensive male has higher percentage of abnormal sperm morphology than normal males.[23] and similar results also found in our study.[16]

Higher blood cholesterol reduces the blood flow thus shows the negative impact on semen quality. A study reported that the high fat diet consumption was negatively associated with sperm count and concentration.[17] Elevated serum cortisol is one of the risk factor for developing diabetes but the actual mechanism not yet studied.[18] Similarly in our study people with diabetes with higher serum cortisol level than non-diabetic population. A study conducted in 91 male shows that higher cortisol level shows adverse effect on sperm count and motility, thus supporting our findings that people with diabetes shows higher cortisol level with showing abnormal semen parameters.[19]

Our study shows that the semen pH of the diabetes group slightly lower than the non-diabetes group, and also observed the liquefaction time was nearly 30 minutes in diabetes group. Similar results were also reported in a study conducted in 60 diabetes infertile male.[20] Our studies shows that the seminal volume is lower (0.8 ml) in diabetes group than non-diabetes group and similar results were also reported by a studies conducted in infertile diabetes male.[21-22] A study has shown that infertile couples with diabetes male partner decreased sperm motility and also irregular sperm morphology.[23] Similar to our results, a study reported significant reduction of sperm motility in 52 diabetic men.[24] Another study shows that semen volume, sperm count, motility, and morphology reduced in diabetes patients as compared to non-diabetics.[25]

Unhealthy life style behaviors also affect the semen quality. Studies showed that smoking directly influence the sperm motility viability and sperm count.[26-28] Our results shows that diabetes group have higher alcohol consumption which directly impact of semen quality supportive results also reported by other studies.[29-30]

Risk factors include, fertility testing and treatment, less sex drive, work, family and social pressure reasons for stress in infertility males.[31] Studies have shown that higher stress changes the sex hormones and lead to poor semen quality.[32]

A study shown that stress scale scores have negative correlation with semen parameters include count and motility[33] In contrast no significant changes in semen volume and sperm morphology.[34] Role of physical activity on semen parameters are still in controversial. Studies have reported that the association of physical activity and semen parameters were positive and few studies reported negative correlation.[35-37] Analyzing the dietary patterns is very important parameter to describe the exact role of each nutrient in reproductive health. Study reported that consumption of animal products like dairy, meat and red meat shows decline in semen quality.[38] Studies reported that sweet, snacks, sweetened drinks and carbohydrate food were associated with increase prevalence rate of male infertility.[39] In overall reproductive health, sleep plays an important role. A study conducted on 970 patients reported that poor sleep quality leads to abnormal semen parameters include motility, count and morphology.[40]

Limitation

Our study had some limitations. We used moderate sample size and tested only in infertile male in and around Chennai. Hence larger sample size and cross-states appropriateness is yet to be evaluated.

CONCLUSION

This study concludes that multiple factors bring poor changes in the semen quality in group 2 participants compared to group1. It was observed that random blood sugar level and abnormal semen parameters was significantly shows linear negative correlation.

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