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Risk Factors Associated with Abnormal Semen Parameters: Case-Control Study at a Tertiary Hospital in Eastern Nepal

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ABSTRACT

Background: Infertility is a global problem. Male factors are estimated to be the cause of up to 50% of infertility cases. A variety of identifiable and reversible etiological factors are involved in male factor infertility. This study aimed to compare the risk factors in men who have abnormal semen parameters with those with normal parameters.
Methodology: This was a case-control study. The male partners of the infertile couples presenting for infertility evaluation were advised for semen analysis and based on the report they were divided into control (normal parameters) and case (abnormal parameters) groups. A detailed interview of each subject was conducted focusing on risk factors causing different semen parameter abnormalities and the risk factors in both groups were compared.
Results: There were 50 subjects in each group. The mean age was 31.02 ± 5.183 years and the mean BMI was 24.824 ± 2.438 kg/m^2. The mean duration of infertility for those in the case group was significantly higher (p-value 0.006). Mean sperm concentration and sperm motility were 33.492 ± 30.306 million/ml and 38.1% ± 18.893 respectively. 40 subjects had oligozoospermia and 36 had asthenozoospermia. Age (OR1.464), the habit of cigarette smoking (OR 37.946), and the presence of past medical conditions (0R 534.82) were significantly associated with abnormal semen parameters. Service-holder men were significantly less likely to develop semen abnormalities (OR 0.087).
Conclusion: Age, cigarette smoking, and presence of past medical history are associated with abnormal semen parameters thus contributing to male factor infertility.

Keywords: male infertility, risk factors, oligozoospermia, asthenozoospermia

INTRODUCTION

Infertility is defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.[1]

Recent global demographic surveys indicate that infertility remains an ongoing reproductive problem.[2] Based on the current world population, it is estimated that 72.4 million people are currently infertile.[3]

Male infertility refers to a male's inability to result in pregnancy in a fertile female.[4] At least 30 million men worldwide are infertile.[5] Half of the infertile couples have a component of male factor infertility and almost 30% solely are caused by a male factor.[6]

"Male factor" infertility is seen as an abnormality in sperm concentration and/or motility and/or morphology in sperm

analysis. Semen quality is used as a surrogate measure of male fecundity.[7] Therefore, semen analysis is the initial and most essential step of infertility evaluation.[8] Although normal semen analysis does not necessarily implicate fertility, abnormal semen analysis has been found to be strongly associated with male infertility.[9]

A variety of etiological factors are involved in male factor infertility. The various risk factors associated with male infertility include tobacco use, alcohol consumption, obesity, history of varicocele, orchitis, scrotal trauma, increased caffeine intake, etc.[9] Studies have also shown the effects of environmental factors, such as toxic materials, pesticides, and radiation, and demonstrated that toxic materials and pesticides could cause a decrease in sperm concentration.[10]

Amongst these various associated factors, some are identifiable and reversible. Thus, it is important to identify the cause and correct it accordingly.

This study aims to compare the risk factors in the male partners of infertile couples who have abnormal semen parameters with those who have normal semen parameters thus, identifying the correctable causes of male infertility and offering timely treatment.

General Objectives:

- To identify the different types of semen parameter abnormalities.
- To evaluate the presence of risk factors associated with semen parameter abnormalities and compare them between the case and control groups.

MATERIALS & METHODS

This Case-control study was conducted in the Department of Obstetrics and Gynecology from April 2021 to March 2022 after obtaining ethical clearance from the Institute Research Committee (IRC) of B.P. Koirala Institute of Health Sciences. This study involved the male partners of infertile couples who presented to the Outpatient Department for evaluation of infertility.

Those male partners of the infertile couples were advised for a semen analysis test as a part of a routine infertility workup. The semen sample was collected after three days of sexual abstinence by masturbation into a sterile wide-mouth plastic container and analyzed within an hour of collection at the Central Laboratory of the institute by an automated semen analyzer according to the WHO criteria.[11] The semen analysis report was interpreted as per WHO sperm reference values 2010.

- **Normal semen parameters:**
  - Sperm concentration ≥15 million/ml
  - Sperm motility ≥40%
  - Sperm with normal morphology ≥4%.
- **Abnormal semen parameters**
  - Oligozoospermia: Sperm concentration <15 million/ ml
  - Asthenozoospermia: Sperm motility <40%
  - Teratozoospermia: Sperm with normal morphology <4%

Based on the semen analysis report, after taking informed written consent, those men who met the inclusion criteria and had any semen parameter abnormality were enrolled as cases whereas those with normal semen parameters were recruited as control.

Case:

- **Inclusion Criteria:**
  - Male partners of infertile couples with abnormal semen analysis parameters.
- **Exclusion Criteria:**
  - Men who did not maintain abstinence for at least three days before testing.
  - Men who incorrectly collected the semen.
  - Men who refused to consent to the study.

Control group:

- **Inclusion criteria:**
  - Male partners of infertile couples whose semen analysis parameters were within normal limits.

- **Exclusion Criteria:**
  - Men who refused to consent to the study.

Sample size calculation

This study considered a 95% confidence interval and 80% power to estimate the sample size. Due to its multiple negative effects on sperm quantity and quality, cigarette smoking is considered one of the major risk factors for semen parameter abnormalities. Therefore, sample size estimation for this study was done using the odd's ratio of smoking for semen parameter abnormalities, 1.17, reported by a study conducted in Nepal in 2019.[9]

Considering the above-mentioned data and the case-control ratio to be 1:1, the following formula was used to estimate the sample size:

$n = [Z_{\alpha/2}^2 / \log^2(1\text{-}RP)] * [1/X + 1/Y]$

n = 15 in each group

Since the above-calculated sample size was the minimum sample required, this study considered 50 cases and 50 control subjects.

Sampling technique: The samples were recruited using a systematic random sampling technique.

A detailed interview of each case and control group member was conducted about the socio-demographic characteristics and various risk factors known to be associated with different semen parameter abnormalities.

Statistical Analysis

The responses were recorded in a pre-designed proforma, entered into MS Excel 2010, and converted to SPSS 11.5 for further analysis. For descriptive statistics, mean (±SD), frequency, and percentage were calculated. Categorical variables were analyzed using the Chi-square test, and a p-value ≤0.05 was considered statistically significant. Binary logistic regression was used to investigate the potential risk factors associated with abnormal semen parameters.

RESULT

A total of 100 subjects meeting the inclusion criteria were enrolled in the study, 50 each with normal and abnormal semen parameters.

The mean age was found to be 31.02 years (SD ± 5.183). The mean BMI of the subjects was 24.824 kg/m^2 (SD ± 2.438).

A total of 83 subjects had primary subfertility whereas 17 had secondary subfertility. The mean duration of infertility among 100 subjects was 5.04 years (SD ± 3.321).

The demographic characteristics like type of infertility, ethnicity, educational status, and address were comparable between the case and control groups.

Table 1: Duration of infertility

	Control		Case		P value	Remarks
	Mean	SD	Mean	SD		
Duration of infertility (y)	4.14	2.70	5.94	3.66	**0.006**	**S**

Comparing the duration of infertility between the two groups, it was noted that the duration of infertility for subjects in the case group was significantly higher than those in the control group (p-value 0.006) suggesting that those with abnormal semen parameters were more likely to have infertility.

The case group included 50 subjects with abnormal semen parameters in terms of either sperm concentration, sperm motility, or sperm morphology. The subjects with low sperm concentration, low sperm motility, and low normal morphology were termed oligo/azoospermia, asthenozoo-spermia, and teratozoospermia respectively.

Mean sperm concentration and sperm motility were calculated to be 33.492 M/ml (SD ± 30.306) and 38.1% (SD ± 18.893) respectively.

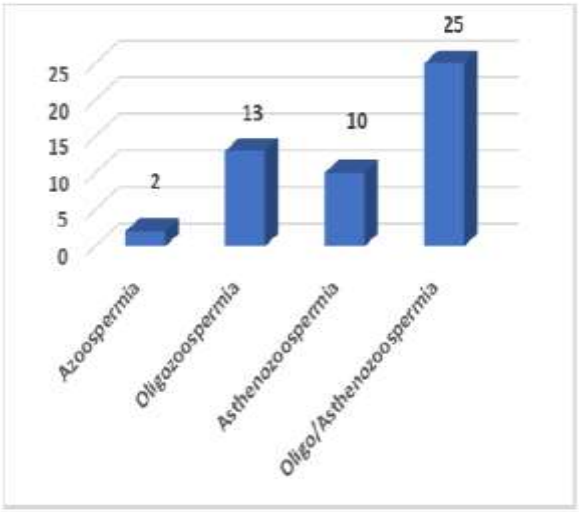

Figure 1: Type of semen parameter abnormalities

Of the 50 cases, 15 (30%) had oligozoospermia (of which 2 (4%) had azoospermia) and 10 (20%) had asthenozoospermia whereas 25 (50%) had both oligozoospermia as well as asthenozoospermia. The criteria for teratozoospermia were only fulfilled by the two subjects with azoospermia.

The mean age of the subjects in the control group was 29.90 ± 4.04 years whereas that in the case group was 32.14 ± 5.95 years. The subjects in the case group were significantly older than those in the control group (p-value 0.030). Also, the older men were found to have significantly higher odds (1.464) of having abnormal semen parameters (p-value 0.011).

Table 2: Comparison of age, BMI, and sedentary lifestyle

		Group		P value	Odds Ratio	95% C.I.	P value
		Control	Case				
Age (in years)	Mean ± SD	29.0 ± 4.04	32.14 ± 5.95	**0.030**	1.464	1.093-1.962	**0.011**
BMI	Mean ± SD	25.27 ± 2.71	24.38 ± 2.07	0.068	1.045	0.725-1.509	0.812
Sedentary lifestyle	No	43 (53.1%)	38 (46.9%)	0.202	2.104	0.158-28.086	0.574
	Yes	7 (36.8%)	12 (63.2%)				

The BMI and sedentary lifestyle of the subjects in both groups were found to be comparable.

Table 3: Risk factors associated with different habits

		Group		P value	Odds Ratio	95% C.I.	P value
	Category	Control	Case				
Cigarette smoking	No	42 (60.9%)	27 (39.1%)	**0.001**	3.193	0.242-42.201	**0.005**
	Yes	8 (25.8%)	23 (74.2%)				
Tobacco chewing	No	39 (54.2%)	33 (45.8%)	0.181	0.143	0.013-1.577	0.112
	Yes	11 (39.3%)	17 (60.7%)				
Regular alcohol intake	No	43 (49.4%)	44 (50.6%)	0.766	1.268	0.266-6.041	0.766
	Yes	7 (53.8%)	6 (46.2%)				
Substance abuse	No	46 (48.9%)	48 (51.1%)	0.400	0.268	0.020-3.639	0.323
	Yes	4(66.7%)	2 (33.3%)				
Coffee (>2 cups/ day)	No	46 (50%)	46 (50%)	1.000	1.631	0.265-10.049	0.598
	Yes	4 (50%)	4 (50%)				

Amongst the 100 subjects, 28% were tobacco chewers, 31% were cigarette smokers, 13% were regular alcohol users and 6% were substance abusers. The mean use duration for each was 12.35 ± 4.296 years, 11.81 ± 5.186 years, and 13.33 ± 2.582 years respectively. It was also seen that cigarette smokers smoked 8.97 ± 5.225 cigarette sticks per day. Also, the substances of abuse noted were marijuana and narcotics.

Comparing each of these habits among the subjects of each group, it was noted that cigarette smoking subjects were significantly more in the case group (p-value 0.001). Smoker men were three times more likely to have abnormal semen parameters and the association was statistically significant (p-value 0.005).

Further comparison of the duration of smoking revealed no significant difference between the two groups (p-value 0.668).

However, the subjects with a habit of tobacco chewing, regular alcohol intake, substance abuse, and drinking >2 cups of coffee per day were comparable between

both groups. The duration of use of each of these was also compared between both the groups which were also not statistically significant.

Table 4: Occupation

	Category	Group		P value	Odds Ratio	95% C.I.	P value
		Control	Case				
Occupation	Policeman	4 (66.7%)	2 (33.3%)	0.400	0.475	0.082-2.748	0.406
	Service holder	15 (71.4%)	6 (28.6%)	**0.027**	0.087	0.008-0.992	**0.049**
	Farmer	10 (100%)	0 (0%)	**0.001**	-	-	-
	Driver	7 (33.3%)	14 (66.7%)	0.086	0.501	0.049-5.089	0.559
	Laborer	3 (23.1%)	10 (76.9%)	**0.037**	3.193	0.242-42.201	0.378
	Unemployed	0 (0%)	6 (100%)	**0.012**	-	-	-
	Painter	0 (0%)	7 (100%)	**0.006**	-	-	-
	Carpenter	11 (68.8%)	5 (31.2%)	0.102	0.181	0.013-2.426	0.197

Upon comparison of the different occupation categories, it was found that there were significantly more service holders and farmers in the control group. Furthermore, service-holder men were significantly less likely to have abnormal semen parameters. However, risk association for farmers could not be analyzed due to the lack of subjects in the case group.

At the same time, laborers, painters, and unemployed subjects were significantly higher in number in the case group. The risk association of laborer men with abnormal semen parameters was not statistically significant. However, risk analysis for painters and unemployed subjects could not be conducted due to the lack of subjects in the control group.

Table 5: Occupational exposures

	Category	Group		P value	Odds Ratio	95% C.I.	P value
		Control	Case				
Occupational exposure to heat to the scrotum	No	39 (60%)	26 (40%)	**0.006**	2.658	0.216-32.738	0.445
	Yes	11 (31.4%)	24 (68.6%)				
Exposure to heavy metals/dyes/ pesticides	No	39 (52%)	36 (48%)	0.488	1.379	0.555-3.427	0.489
	Yes	11 (44%)	14 (56%)				

Further comparing the subjects of both the groups based on occupational exposures, it was found that occupational exposure to heat to the scrotum was significantly higher in the case group. However, the risk association was not statistically significant.

Meanwhile, the comparison of occupational exposure to dyes/ heavy metals/ pesticides and their risk association between the subjects of the two groups was not statistically significant.

Table 6: Past medical and surgical history.

	Category	Group		P value	Odds Ratio	95% C.I.	P value
		Control	Case				
Past medical history	No	48 (59.3%)	33 (40.7%)	**0.000**	534.82	12.788-22366.87	**0.001**
	Yes	2 (10.5%)	17 (89.5%)				
History of Scrotal surgery	No	50 (51%)	48 (49%)	0.153	-	-	-
	Yes	0 (0%)	2 (100%)				

Of the 100 subjects, 19 had a history of past medical conditions like hypertension (13), hepatitis (4), and diabetes mellitus (2). Amongst 13 hypertensive subjects, 4 were under anti-hypertensive medications. Also, two subjects had undergone scrotal surgery for hydrocele.

Comparing the presence of past medical history amongst the subjects in both the groups, it was noted that subjects in the control group had a significantly higher number of subjects with chronic medical conditions (p-value 0.000), and the risk association was also found to be significant (p-value 0.001). The risk analysis for each

disease could not be carried out due to the small sample.

On the other hand, both the subjects who had undergone surgical intervention in the past belonged to the case group, but the data was not statistically significant and risk association could not be analyzed due to the lack of subjects in the control group.

This study also included regular hot baths, a history of chemotherapy/ radiotherapy, and a family history of infertility in first-degree male relatives as some of the risk factors. None of the subjects in either of the groups had any of these risk factors present.

DISCUSSION

This study demonstrated that the men with abnormal semen parameters were more likely to have infertility, analyzed in terms of duration of infertility. A similar observation was made by Shrivastava T et al in 2018 whereby it was concluded that abnormal semen analysis is strongly associated with male infertility.[9]

As observed in this study, another study by Kidd SA et al in 2001 also concluded that the trend towards later fathering appears to come with risks for diminished semen quality and fertility.[12]

Studies have indicated that high BMI affects sperm production and extreme levels of obesity negatively influence male reproductive potential.[13] Meanwhile, it was noted in this study that BMI in both the case and control groups were comparable. This observation could have been a result of the relatively small sample size and the presence of most normal BMI subjects in both groups.

It was concluded by Gaskins AJ et al that higher moderate-to-vigorous activity was significantly associated with higher total sperm count and sperm concentration.[14] However, this study did not reveal significant differences between the subjects of the case and control groups with sedentary lifestyles. Such a difference in observation could again be attributed to the small sample size included in the study.

It was observed in this study that cigarette smoking is significantly associated with abnormal semen parameters. Similar conclusions were made by other studies which suggested that sperm concentration, motility, and morphology were significantly affected in smokers and tobacco chewers.[15]

Subjects with occupational exposure to heat to the scrotum were significantly higher in the case group. Jung A et al also concluded that the fertility parameters of professionals with exposure to high temperatures and professional drivers with long periods of sitting in vehicles were found to be impaired.[16]

It was also observed in this study that the presence of past medical history like diabetes mellitus and hypertension was strongly associated with the subjects with abnormal semen parameters. However, the association of specific diseases with semen abnormality could not be analyzed due to the small sample size.

Observations made by Long L et al suggested that chronic diseases like type 2 diabetes mellitus could cause testicular damage and induce male infertility.[17] Similarly, men diagnosed with hypertension have a lower semen volume, sperm motility, total sperm count, and motile sperm count.[18]

CONCLUSION

This case-control study compared the presence of risk factors in the subjects with abnormal semen parameters (cases) with those having normal semen parameters (control). The risk association of each of those factors with abnormal semen parameters was also calculated.

It was noted that age, cigarette smoking, and the presence of past medical history (diabetes mellitus/ hypertension) were significantly associated with abnormal semen parameters.

Subjects with occupational exposure to heat to the scrotum were significantly higher in the subjects with abnormal semen parameters, however, the association was not statistically significant.

Service holders were significantly less likely to have abnormal semen parameters as compared to men with other occupation categories.

Limitation

This study had a relatively small sample size due to which statistical association for all the risk factor categories could not be satisfactorily analyzed. A larger sample size would have provided an opportunity to analyze each risk factor with specific sperm abnormalities as well.

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Conflict of Interest: None

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Ethical Approval: Approved by the Institutional Review Committee of B.P. Koirala Institute of Health Sciences.

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