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Original Article

Pathology Section

# Associated Factors with Male Infertility: A Case Control Study

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## ABSTRACT

**Objective**: Sperm analysis is an important step to evaluate and diagnose male's infertility. The present study aimed to determine associated factors with males' infertility by using semen analysis.

**Materials and Methods:** In this study 96 men were evaluated who attended to the infertility clinics of Ilam province, western Iran between May 2010 to May 2011. Semen analysis was done using the Weili Dynamic Sperm Analysis software adapted to the WHO classification. Based on movement and speed characters, sperms were classified to either A, B, C or D classes. Participants were stratified into two groups that called "Oligospermia (OS)" with sperm counts of less than 20 million in mL (n=48) and "Non-Oligospermia (NOS)" with values more than determined cutoff point (n=48).

**Results**: The Mean age ±SD for OS and NOS group were 29.9 ±5.1 y and 31.17 ±5.24 y, respectively (p>0.05). Overall, 62.5% of OS and 31.2% of NOS were clinically infertile (OR=3.6, CI, 1.5-8.5, p=0.01). A significant difference was found between job and live ratio(A+B+C) in NOS group (F=2.8, p<0.05).

**Conclusion**: Prevalence of infertility was higher in the OS men compared to the NOS group. The main risk factors in the OS group were History of Varicocele surgery and residence site of patients that are totally similar to the NOS men. Further case-control studies and clinical trials are recommended to recognize infertility causes in men.

**Keywords:** Infertility, Men, Oligospermia, Semen analysis

## INTRODUCTION

Infertility affects approximately 15% of couples. Men and women must be evaluated simultaneously, because male factors in 40-60% of cases are the major contributor causes [1]. Sperm analysis is the first step to diagnose male's infertility. Many factors can affect semen quality, therefore urological assessment and physical examination must be done in order to exclude the abnormal anatomy, genetic and endocrinology disorders, varicocele as well as obtaining complete patients history is necessary including history of previous genital tract surgery (cryptoorcidism or hernia), testicular trauma or history of exposure to heat and working condition requiring travel to tropical areas and history of taking certain medications such as Cimitidine , Spironolactone and anabolic steroids in these patients seem necessary.

Semen parameters could be changed in exposing to heavy metal such as lead, mercury and pesticides could be changed [2]. Although exposure to these substances has been introduced as destructive agent of spermatogenesis but data about their effects on men fertility are still controversial. Psychological stress and exposure to waves as well radiation are the other factors affecting men infertility.

Up to 9.8% of men who were referred to infertility clinics usually have some kind of chromosomal abnormality [3]. Some structural abnormalities of Y chromosome such as mutations that lead to micro deletion of certain genes are probably involved into the obstructive azospermia in men [4]. Life style factors such as smoking could result in dysfunction of leading cells secretions and decreased frequency of intercourse and finally result in semen quality and change in sperm morphology [5].

Thus, evaluating occupational parameters, drug history and reproductive disorders should be considered in order to correct spermogram interpretation and infertility treatment in patients who are attending for infertility treatments. On the other hand, techniques of collecting semen and laboratory analysis method can effect the results as well. Therefore, it is important to choose a comprehensive and reliable method for semen analysis.

The current study aimed to determine prevalence and major associated risk factors with males' infertility in Ilam province in the western Iran.

## MATERIALS AND METHODS

This was a descriptive analytic study of men who referred to the infertility clinics in Ilam province in the western Iran from May 2010 to May 2011. Participants were referred to the pathobiology laboratory for semen analysis after physical and urological examination.

During the study, 201 men referred to pathobiology laboratory for semen analysis. All participants gave a sample of semen. But 13 samples excluded from analysis, because their samples collected by condom or substandard plates (standard plate is a clean Glass or plastic plate with dilated and dry mouth which is heated at a temperature of 20-40°C without any detergent compounds or other toxic substances). Finally 188 samples remained. Of them, 49 cases had a sperm counts less than 20 million (Oligospermia) and 139 cases had a value above the cut of point. So, in order to assess the prevalence of Male infertility and associated factors, we selected 48 men with oligospermia (OS) and 48 men (NOS) that had a sperm counts more than 20 million (Nonoligospermia). Both groups were matched for smoking, age, Job, educational levels, BMI and exposure to radiation.

A standard questionnaire was used for collecting demographic characteristics and clinical data such as age, height, weight, occupational state, past medical history and urological surgery as well as drug history and exposure to environmental toxins were obtained.

Semen samples were collected according to the WHO guideline, by masturbation after avoidance of intercourse or ejaculation for 3 to 5 days.

Density, vitality and motility percentiles were recorded by using dynamic sperm analysis via Weili software (WLJY9000). Magnified microscopic image of moving sperm sample by camera were recorded in this software, then signal of image were analysed and information about sperm vitality and motility percentile were evaluated. In this software based on movement and speed characters, sperms are classified to either A.B.C or D classes. Class A related to sperm which has sufficient speed and good movement directly, class B related to those that has less speed or minor deviation in direction, class C related to sperm that has spiral movement and class D is

| | | BMI | | Weight | | Age Height | | BMI | |
|---|---|---|---|---|---|---|---|---|---|
| | | r | p value | r | p value | r | p value | r | p value |
| Class A | Cases | 0.08 | 0.56 | -0.066 | 0.56 | 0.064 | 0.66 | 0.089 | 0.54 |
| | Control | -0.314 | 0.03 | 0.023 | 0.87 | 0.106 | 0.47 | 0.119 | 0.41 |
| Class A+B | Cases | 0.076 | 0.6 | -0.005 | 0.97 | 0.165 | 0.26 | 0.098 | 0.5 |
| | Control | -0.417 | 0.003 | -0.045 | 0.75 | 0.039 | 0.79 | 0.076 | 0.6 |
| Live Ratio | Cases | -0.043 | 0.76 | 0.022 | 0.88 | 0.143 | 0.33 | 0.061 | 0.67 |
| | Control | -0.426 | 0.003 | 0.018 | 0.9 | 0.015 | 0.91 | 0.017 | 0.91 |

**[Table/Fig-1]:** Correlation between anthropometric measurements and A class, A+B and Live Ratio classes of semen analysis in case and control groups

related to sperm that has no movement. Live Ratio(A+B+C) was used for evaluation of infertility in the system, the first group was accumulation of class "A,B,C" that infertility scale and percentiles of active sperm were less than 60% in the group, and other groups were class A+B and class A that less than of 50% and less than of 25% to be considered as infertile scale in the person, respectively.

Collected data was analysed by using SPSS software (Version 17).The Kolmogorov-Smirnov test used for normality distribution of data. For abnormal data, nonparametric tests such as Mann-Whitney, Kruskal-Wallis and Spearman correlation were used and for normal data, parametric tests such as t test, ANOVA, Pearson correlation were used. According to The Kolmogorov-Smirnov test age, height, Weight and BMI had totally a normal distribution.

## RESULTS

Mean age ± standard deviation for OS and NOS were 29.9 ±5.1 y and 31.17 ±5.24 y respectively with no significant difference. More than one-fourth of samples (27.7%) in the both groups had an educational level less than Diploma. Both groups had same jobs.

Overall, 3 of OS group (6.2%) and 1 of NOS group had noted history of infertility in their family. Exposure to X-Ray radiation was reported in 8.34% and 6.2% of participants in OS and NOS group. There was significant differences were observed in the surgical and urological diseases between OS group (45.8%) and NOS group (18.8%).

Infertility according to percentage of class A, class A+B and Live Ratio(A+B+C) was 75%, 77.1% and 62.5% in OS group and 50%, 45.8% and 31.2% achieved for the NOS group. There was a significant difference between OS and NOS group in class A (OR=3, CI, 1.2-7.1, p=0.01), Class A+B (OR=3.9, CI, 1.6- 9.5, p=0.002) and Live Ratio(A+B+C) (OR=3.6, CI, 1.5-8.5, p=0.002).

There was an inverse significant correlation between class A, class A+B and Live Ratio(A+B+C) with age in NOS group [Table/Fig-1]. The Kruskal-Wallis test showed a significant relationship between job and Live Ratio in NOS group [Table/Fig-2].

There was a significant difference in class A, class A+B and Live Ratio of men who had a history of varicocele surgery in both group. The mean percentage of class A, class A+B and Live Ratio of them (men with history of varicocele surgery) in OS group was significantly higher compared to NOS group (p<0.001) [Table/Fig-3].

Men who lived in urban areas had a high percentage of class A, class A+B and Live Ratio compared to men who lived in rural areas. There was a significant relationship between class A, class A+B and Live Ratio in the OS and NOS group who lived in Urban area (p<0.05) [Table/Fig-3].

## DISCUSSION

Quality of semen might be affected by occupational and environmental exposures along with genetics factors, so determining a unique factor involving with semen quality seems to be difficult. Jobs that require working in hot environments or mechanical trauma and physical load on the pelvic contents can reduce semen quality.

| | | | Mean ± STD | f | p-value | CI 95% |
|---|---|---|---|---|---|---|
| Case | Class A | Clerk | 33.00±30.77 | 6.43* | 0.09 | 10.98-55.01 |
| | | business | 12.08±10.73 | | | 7.05-17.01 |
| | | Militarist | 17.75±22.17 | | | -7.90-36.29 |
| | | worker | 16.60±9.44 | | | 9.85-23.35 |
| | Class A+B | Clerk | 49.25±33.14 | 2.02 | 0.124 | 25.55-72.96 |
| | | business | 27.91±18.93 | | | 19.05-36.77 |
| | | Militarist | 29.09±25.42 | | | 7.83-50.35 |
| | | worker | 34.47±16.32 | | | 22.79-46.15 |
| | Live ratio | Clerk | 59.77±33.60 | 0.80 | 0.498 | 35.72-83.81 |
| | | business | 46.33±31.47 | | | 31.60-61.06 |
| | | Militarist | 40.46±26.71 | | | 18.12-62.80 |
| | | worker | 44.16±18.75 | | | 30.74-57.57 |
| Control | Class A | Clerk | 28.87±10.08 | 2.32 | 0.088 | 21.66-36.08 |
| | | business | 28.36±12.77 | | | 22.38-34.34 |
| | | Militarist | 18.83±11.58 | | | 9.14-28.52 |
| | | worker | 19.73±11.02 | | | 11.84-27.62 |
| | Class A+B | Clerk | 56.86±14.78 | 2.62 | 0.062 | 46.28-67.44 |
| | | business | 53.37±13.30 | | | 47.14-59.59 |
| | | Militarist | 42.46±23.01 | | | 23.22-61.70 |
| | | worker | 40.32±16.94 | | | 28.20-52.44 |
| | Live ratio | Clerk | 79.84±17.34 | 2.80 | 0.050 | 67.43-92.25 |
| | | business | 74.88±13.36 | | | 68.62-81.14 |
| | | Militarist | 62.77±29.79 | | | 37.86-87.68 |
| | | worker | 57.74±24.18 | | | 40.44-75.04 |

**[Table/Fig-2]:** Comparison between different jobs and classification of semen analysis

Reduced spermatogenesis and semen quality in workers, welding or drivers who travel to tropical areas have already been reported [6,7]. Psychological stress and febrile illness have a great impact decreasing semen parameters [8]. Stress itself can affect sperm parameters and reduces sperm morphology [2].

Although, in the present study, no significant correlation was found between subjective report of psychological stress at work places or in family, but Giblin and colleagues [9] found that stress significantly reduces sperm movement and morphology in infertile men. A negative effect of stress on decreasing levels of testosterone, progesterone, cortisol and prolactin have also been reported [10].

Weight gaining in men and increased body mass index potentially can alter the secretion of sexual hormones and leading to decrease testosterone – estradiol ratio and poor semen quality as [11-14]. However, in present study, no significant association was observed between BMI and poor semen quality in both OS and NOS probably due to sample size limitation.

There is evidence indicating that varicocele is a destructive agent on men fertility. Prevalence of varicocele in general population is 15-20% but this rate in infertile men is increasing upto 30-40%. The association between reduction in volume of testis and varicocele as well as improvement of semen quality after varicocele repairing has frequently been reported [15,16], which is consistent with the results of the present study that showed a significant relationship between having a history of varicocele repairing and semen quality and quantity in both OS and NOS group. Meanwhile, varicocele repairing had improved sperm morphology and LR in men with

| | | | Class A | | | | Class A+B | | | | Live Ratio | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Case | Control | p-value | CI 95% | Case | Control | p-value | CI 95% | Case | Control | p-value | CI 95% |
| Varicocele | Yes | Mean | 9.06 | 43.89 | <0.001 | -17.81-19.45 | 24.93 | 63.87 | <0.001 | -19.59-10.76 | 44.50 | 80.18 | 0.001 | -37.12-12.78 |
| | | STD | 5.72 | 23.09 | | | 12.96 | 19.25 | | | 28.90 | 19.38 | | |
| | No | Mean | 13.29 | 34.98 | <0.001 | -17.17-5.32 | 30.59 | 63.02 | <0.001 | -30.43-11.93 | 46.28 | 81.67 | <0.001 | -40.50-18.28 |
| | | STD | 7.23 | 7.81 | | | 15.77 | 9.74 | | | 23.23 | 11.98 | | |
| Residence | Urban | Mean | 21.48 | 25.59 | 0.04 | -13.55-5.33 | 39.10 | 50.77 | 0.05 | -23.34-0.00 | 53.06 | 71.28 | <0.001 | -31.74-4.70 |
| | | STD | 21.84 | 12.66 | | | 25.39 | 18.41 | | | 29.17 | 21.68 | | |
| | Rural | Mean | 12.57 | 24.38 | 0.001 | -20.12-3.49 | 24.47 | 47.86 | <0.001 | -34.49-12.28 | 37.92 | 68.98 | <0.001 | -46.79-15.31 |
| | | | 13.07 | 11.83 | | | | 15.30 | | | | 20.75 | | |

**[Table/Fig-3]:** Clinical and environmental factors and classification of semen analysis

higher sperm count. Lund and colleagues [17] have reported that varicocele repairing might be effective on improvement of semen quality.

With respect to effects of exercise and vigorous physical activity was, it has been demonstrated that cyclists [18] and workers [1] are at risk for decreasing sperm count possibly due to increasing mechanical trauma of testis and pelvic. In the present study, there was a significant difference was observed between employees and self-employed workers as well as militarist and non-militarist in terms of movements and optimal sperm speed. Therefore, it seems militarists and workers are more at risk for infertility disorders and reduced semen quality due to specific working condition and probably repeated physical trauma.

Environmental pollutants and pesticides have potential toxic effect on germinal cells [19,20]. In this study men who lived in rural areas that are likely be exposed to toxic substance and pesticides, had less LR than men who lived in urban areas.

It has been observed that sperm movement and semen volume was decreased in men by getting old [21]. The present study found that getting old had a negative effect on optimal sperm speed (class A), which is consisted with other reports [22].

Furthermore, according to the similar study, male infertility due to spermatogenesis defects could be associated with endocrinology disorders, varicocele, environmental factors or impaired sperm conduction as well as congenital anomalies or neurological and immunological factors [23].

## CONCLUSION

It seems that prevention of occupational and environmental risk factors, change in lifestyle such as smoking cessation, weight loss, improved nutritional status and proper treatment of varicocele can lead to improvement of semen quality in infertile men. Accurate assessment of semen quality using a comprehensive laboratory system which provides scientists to compare data in different laboratory can improve treatment methods and correct spermogram interpretations. Further case-control studies and clinical trials are recommended to recognize infertility causes in men.


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