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Review Article

MALE INFERTILITY**Afrim Zeqiraj¹, Sheqibe Beadini¹, Zehra Hajrulai-Musliu⁵, Nexhbedin Beadini¹, Hesat Aliu¹, Sadi Bexheti⁴, Zafer Gashi², Shkelzen Elezaj³, Agim Shabani⁶**¹Department of Biology, University of Tetovo, Republic of Macedonia²Department of Biochemistry, UBT Colleague, Prishtina, Republic of Kosovo³Faculty of Medicine, University of Zagreb, Croatia⁴Faculty of Medicine, University of Tetovo, Republic of Macedonia⁵Faculty of Veterinary Medicine, University Ss. Cyril and Methodius, Republic of Macedonia⁶Agim Shabani, Department of Chemistry, University of Tetovo,
Republic of Macedonia. Tel: 389-4435-6500. E-mail: agim.shabani@unite.edu.mk**Abstract:**

Infertility is defined as without the ability of a sexually active mate to reach a pregnancy despite regular and unprotected sexual intercourse for more than 12 months (Singh & Agarwal, 2011). Of all couples trying to have children, 17% -25% will be diagnosed as infertile, where about 50% of these cases are attributed to male infertility (Venkatesh et al., 2011). Of 25% of couples who do not get pregnant within a year, 15% of them seek medical treatment for infertility and less than 5% of them are left without children. Approximately 50% of the cases the basic etiology of infertility lies only with males (Poongothai et al., 2009). In addition, in approximately 60-75% of cases, no cause is found in males and is called idiopathic (unknown) factor. Male infertility may be the result of genetic damage, oxidative stress, tumors, BMI, urogenital tract infections, temperature increase, varicocele, hormonal disorders, smoking, drug-related toxicity (WHO, 2000). In men in whom the cause of infertility is idiopathic, there are no previous stories related to fertility problems and findings are normal in physical and hormonal examinations. Diagnostic processing of idiopathic cases involves the analysis of ejaculate which usually reveals the reduction of sperm count (oligospermia), decreased sperm motility (asthenospermia) or the presence of morphologically abnormal spermatozoa (teratospermia). If these anomalies occur together, the entirety of all these abnormalities is described as oligoasthenoteratospermia (OAT). The presence of genetic abnormalities in both chromosomal and gene levels is a major concern for couples choosing assisted reproduction techniques (ART), which offer the ultimate hope for these couples to have their descendants (WHO, 2010).

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INTRODUCTION:

Infertility is traditionally diagnosed based on a number of standard ejaculate parameters including volume, pH, morphology, mobility, and number, as recommended by the WHO manual, which focuses on human ejaculatory examination (World Health Organization, 2010), hereinafter referred to as instructions or manuals. Periodically, WHO's first manual was published in 1980, then amended in 1987, 1992, 1999 and the 5th edition in 2010 (Esteves; Zini et al., 2012). The 5th edition guidelines radically alter the interpretation of the ejaculate analysis so patients diagnosed with an abnormal ejaculatory analysis under the 4th edition guidelines can be diagnosed as having a normal ejaculate analysis using the criteria of the editions the 5th.

It is believed that approximately half of the couples returning to the assisted reproductive techniques do so because of factors of male infertility. Scientists have increasingly received male infertility problems for successful treatment of a couple with infertility.

Since in vitro fertilization rates (IVF) are still quite low, prognostic information for spousal couples is very helpful in making clinical decisions. Research has shown a significant increase in the appearance of gonad abnormalities over a relatively short period of time due to environmental factors rather than genetic factors. It is generally believed that pollution, smoking, oxidative stress, alcohol, and sexually transmitted diseases play a role in male infertility. In addition, studies have shown that masculine growth, body mass index (BMI), previous illnesses, medications, use of steroids, hormones and trauma in the testicles have also contributed to the reduction of sperm quality. Health problems such as mumps, kidney disease, hormone problems, medicines, radiation therapy, and chemotherapy for tumors can affect abnormal sperm production. In addition, obesity is directly associated with increased male infertility. The role in diagnosing male infertility (De Jonge, 2012) has its limitations. Research has shown that approximately 15% of infertile males are tested with normal ejaculate parameters (Ohl et al., 2010).

Cut-off reference values for semen characteristics as published in consecutive WHO manuals

Semen characteristics	WHO 1980	WHO 1987	WHO 1992	WHO 1999	WHO 2010
Volume (mL)	ND	≥ 2	≥ 2	≥ 2	≥ 1.5
Sperm count (10 ⁶ /mL)	20-200	≥ 20	≥ 20	≥ 20	≥ 15
Total sperm count (10 ⁶)	ND	≥ 40	≥ 40	≥ 40	≥ 39
Total motility (%)	≥ 60	≥ 50	≥ 50	≥ 50	≥ 40
Progressive motility	≥ 2	≥ 25%	≥ 25% (a)	≥ 25% (a)	≥ 32% (a+b)
Vitality (%)	ND	≥ 50	≥ 75	≥ 75	≥ 58
Morphology (%)	80.5	≥ 50	≥ 30	(14)*	≥ 4*
Leukocyte count (10 ⁶ /mL)	< 4.7	< 1.0	< 1.0	< 1.0	< 1.0

MATERIALS AND METHODS:

Sampling was done by 257 patients. For the control group (88 patients), patients with normospermia were taken, while for the working group (169 patients) patients were treated with asthenospermia, oligospermia, and oligoasthenospermia. Spermogram analysis was done according to WHO 2010 recommendations.

All analyzes were performed at the Biolab Zafi Laboratory in Peja.

RESULTS:

Table 1. Comparison of parameters between the study group and the control group

Parameters	Study group (Mean \pm SD)	Control group (Mean \pm SD)	Tests	P-value
N	169	88		
Nr. sperm in 1 mil	19.25 \pm 19.45	61.43 \pm 34.48	U'=13215	P < 0.0001
General Mobility of spermatozoa (%)	28.37 \pm 17.86	57.15 \pm 10.83	U'=13761	P < 0.0001
Progressive Movement (a), (%)	13.37 \pm 11.85	25.51 \pm 7.47	U'=12210	P < 0.0001
Medium Movement (b + c) (%)	15.39 \pm 11.37	31.74 \pm 10.10	U'=12630	P < 0.0001
Not mobile (%)	70.98 \pm 17.58	42.67 \pm 10.88	U'=13753	P < 0.0001
Normal morphology (%)	15.85 \pm 13.48	42.58 \pm 15.21	U'=13426	P < 0.0001
Abnormal morphology (%)	84.09 \pm 13.51	57.67 \pm 15.24	U'=13365	P < 0.0001

Men of the study group has fewer sperm compared to men in the control group with significant statistical significance (Mann-Whitney test, U '= 13215, P <0.0001).

In the study group males, total sperm mobility was lower compared to those in the control group, with significant statistical significance (Mann-Whitney test, U '= 13761, P <0.0001).

In the study group males, the progressive mobility of the spermatozoa was lower than those of the control group, with significant statistical significance (Mann-Whitney test, U = 12210, P <0.0001).

In the male study group, secondary sperm mobility was lower compared to those of the control group, with significant statistical significance (Mann-Whitney test, U = 12630, P <0.0001).

All the patients studied were from the Republic of Kosovo.

The statistical processing of the data is done with the statistical package SPSS 22.0.

The difference is significant if P <0.05.

In the study group males, the proportion of immobile sperm was greater compared to those of the control group, with significant statistical significance (Mann-Whitney test, U '= 13753, P <0.0001).

In the study group males, the percentage of sperm with normal morphology was lower compared to those of the control group, with significant statistical significance (Mann-Whitney test, U '= 13426, P <0.0001).

In the study group, the percentage of sperm with abnormal morphology was greater compared to those of the control group, with significant statistical significance (Mann-Whitney test, U = 13365, P <0.0001).

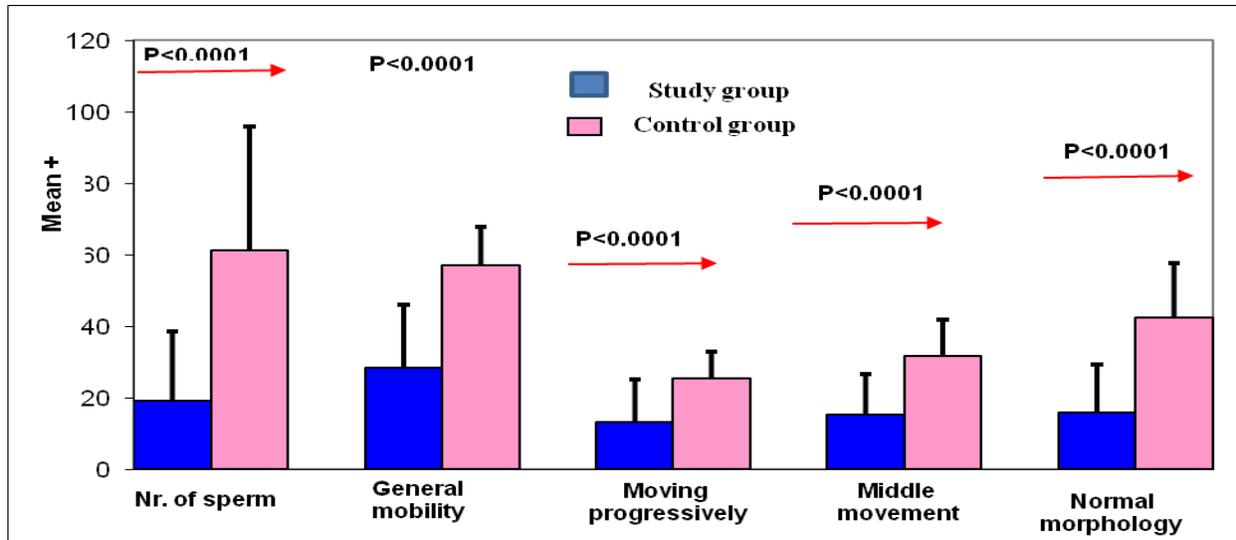


Chart 1. Comparison of the average number of sperm counts, their mobility and their morphology among groups

Chart 1 shows that average sperm count values, the percentage of general mobility of sperm, progressive and medium mobility, and the percentage of normal morphology have been lower in the study group compared to that of the control. All the differences were of significant statistical significance.

Table 2. Comparison of the number of sperm counts, sperm motility among male groupage

Parameters	<30 years (mean ± SD)	30-39 years (mean ± SD)	40+ years (mean ± SD)
N	32	73	64
Nr. sperm in 1 mil	19.38 ± 20.01	18.85 ± 19.56	19.63 ± 19.35
Comparative test	KW=0.003, P=0.998		
General Mobility of spermatozoa (%)	29.75 ± 17.41	27.84 ± 17.81	28.30 ± 18.38
Comparative test	KW=0.243, P=0.885		
Progressive Movement (a), (%)	14.13 ± 16.10	12.41 ± 10.53	14.09 ± 10.87
Comparative test	KW=0.858, P=0.651		
Medium Movement (b + c) (%)	17.53 ± 11.91	15.64 ± 11.53	14.03 ± 10.88
Comparative test	KW=2.101, P=0.349		
Not mobile (%)	70.56 ± 17.31	70.63 ± 17.24	71.59 ± 18.34
Comparative test	KW=0.118, P=0.943		

In the study group males we did not distinguish between significant statistical significance in these parameters by age group; (KW = 0.243, P = 0.885), Progressive Mobility (KW = 0.858, P = 0.651), Medium Movement (KW = 2.201, P = 0.885), Secondary Semiotics (KW = 0.003, P = 0.998), Total Spermatozoid Movement (KW = 0.349) and the percentage of uninhabited spermatozoa (KW = 0.118, P = 0.943), (Table 2).

Table 3. Comparison of morphology parameters by age group in the male study group

	<30 years (mean \pm SD)	30-39 years (mean \pm SD)	40+years (mean \pm SD)
N	32	73	64
Normal morphology (%)	13.84 \pm 12.13	15.79 \pm 13.22	16.91 \pm 14.47
Comparative test	KW=0.418, P=0.811		
Abnormal morphology (%)	86.16 \pm 12.13	84.05 \pm 13.28	83.09 \pm 14.47
Comparative test	KW=0.440, P=0.802		

The morphological data of the study group sperm did not have significant differences with age increase (normal morphology P = 0.811 and abnormal morphology P = 0.802), (Table 3).

DISCUSSION:

The results of this study confirm that measurements of sperm concentration, motility, and morphology all provide useful information for diagnosing male infertility. Sperm morphology, as measured according to strict criteria, appears to be the most informative semen measurement for discriminating between fertile and infertile men. However, none of the measures, alone or in combination, can be considered diagnostic of infertility.

Semen analysis remains the first laboratory test a clinician will order after completing a detailed medical history and physical examination for the male partner of an infertile couple. The standardization of the routine semen analyses (semen volume, sperm count, motility, and morphology) allows for comparison across laboratories. Reference range based on fertile men has been developed and generally adopted by most clinicians working with an infertile couple. The lower limit thresholds may not be applicable to every man, but can be used as guidance for determining the next step in the diagnosis and treatment. A semen analysis that is within the reference range (e.g., >5th percentile of the WHO recommended values) indicates that the male partner may not be the primary problem for the infertile couple. Focus should be first on the female partner. Whereas a semen sample that has triple defects—low sperm count, poor motility, and abundance of abnormal sperm morphology—indicates that male factor infertility is likely. Although specific approaches to the treatment of

male factor infertility are very few, they need to be investigated during the workup of the female partner. Male infertility is best tested by determining the ability of sperm to achieve a successful pregnancy. Nowadays, the analysis of seminal fluid is evaluated according to the World Health Organization criteria including semen volume, sperm concentration, total number of spermatozoa, total motility, sperm morphology, and viscosity (WHO, 2010).

Similar results with our results have also been gained (Jansen et al., 2019), which has gained high scores on the significance scale between the study group and the study group taken in the study.

Similar results with our results have also been gained (Jansen et al., 2018), which has obtained high scores on the significance scale between the study group and the study group taken in the study.

CONCLUSIONS:

Our data suggest that care should be taken in the interpretation of sperm analysis. Although low values for each measurement increase the likelihood that a male factor contributes to infertility. Thus, the low values for sperm concentration, motility and morphology are reliable indicators of male infertility. It is recommended that clinicians should advise and recommend patients presenting for infertility to undergo sperm analysis, hormonal analysis (fsh, lh, prolactin, testosterone) as well as sperm DNA fragmentation.

Conflicts of interest:

The Authors declare that there are no conflicts of interest.

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