Semen Pathology in Infertile Men: Correlation between Abnormal Sperm Morphology with Motility and Count

Aiad Abdullah Abdulrazak

Assistant Professor of Pathology, Department of Pathology, Tikrit College of Medicine, University of Tikrit, Iraq

Abstract

Introduction: About 50% of infertility is attributed to male factor. Semen analysis is the cornerstone of the diagnosis, and treatment of male infertility. The quality of semen varies from country to country. The present study was undertaken to evaluate semen abnormality of infertile Iraqi men as compared to other countries and to determine whether these parameters are correlated to each other.

Patients and Method: The seminal fluid profile was classified according to the WHO manual (2010). Briefly, asthenozoospermia (i.e. progressive motility of spermatozoa below 32%), oligozoospermia (i.e. spermatozoa concentration below $15x10^6$ per ml), teratozoospermia (i.e. morphologically normal spermatozoa below 4%), asthenoteratozoospermia, oligoasthenozoospermia, oligoasthenoteratozoospermia, oligoteratozoospermia, and azoospermia (absence of spermatozoa in the ejaculate)

Results: The most striking abnormality is the high percentage of patients withabnormally low morphology score (72.09%). The majority of cases have isolated abnormality (teratozoospermia; 48.84%). Asthenoteratozoospermia (ATZ) was found in 10.47% and oligoasthenozoospermia (OAZ) and oligoteratozoospermia (OTZ) in 8.14% of cases. The least common pattern was necroteratozoospermia (NTZ) and oligonecroteratozoospermia (ONTZ) 1% each. Azoospermia was encountered in 3.49% of cases.

Conclusion: Abnormalsperm morphology is the best indicator of infertility and teratozoosperma is the most common finding in abnormal spermiogram.

Keyword: *Semen parameters, sperm, morphology, motility, count.*

Introduction

More than 70 million couples suffer from infertility worldwide, the majority being residents of developing countries. Infertility is defined as the failure of a couple to conceive following 12 months of unprotected sexual intercourse. About 50% of infertility is attributed to male factor.[1]

The fertility potential of any male can be predicted through the evaluation of his semen, thus, Semen analysis is the cornerstone of the work up, diagnosis, and treatment of male infertility.[3] Male infertility is diagnosed in laboratory through descriptive semen analyses (count, motility, and morphology). Fertility is negatively affected if these parameters reduce to a level below a predictive threshold [2-4]

The quality of semen reportedly varies from country to country, suggesting the role of the geographic factors in male infertility. In order to establish evidence-based reference values for semen analysis, the World Health Organization (W.H.O) 2010 manual describes the values obtained in eight countries from 1953 men who became fathers with a time to pregnancy of <12 months. [5,6]

Regional differences in semen quality have been reported in the USA (Fisch et al.[7]), Europe (Jørgensen et al.[8,9]), Japan (Iwamoto et al. [10]), India (Adiga et al.[11]), China (Gao et al.[12]), and Tunisia (Feki et al).[13]

Corresponding Author:
Aiad Abdullah Abdulrazak
Assistant Professor of Pathology, Department of Pathology, Tikrit College of Medicine, University of Tikrit, Iraq
e-mail: aiadalkhalidi@gmail.com
Mobile: 00964-7710651794

The major causes of male infertility can be treatable and preventable. The root cause of this can be one or a combination of the following: low sperm concentration, poor sperm motility, or abnormal morphology. Therefore, understanding these conditions is foremost.[14] Examining the correlation between these parameters may help us understand the mechanism that controls these parameters.

The present study was undertaken to evaluate the pattern of anomalies in the semen of male partners of couples presenting with infertility, to determine whether these parameters were correlated to each other, and to determine the parameters that behave in a different or similar manner to currently reported figures worldwide.

Patients and Method

A retrospective study includes a total of 86 infertile men visiting a fertility clinic for the period from 15 October 2018-15 November 2018.

The medical records of infertile couples were reviewed and the data were retrieved. Information which was extracted from the records included semen analysis results (sperm count, volume, pH, viscosity, morphology, motility and vitality).

The seminal fluid profile was classified according to the WHO manual (2010). Briefly, asthenozoospermia (i.e. progressive motility of spermatozoa below 32%), oligozoospermia (i.e. spermatozoa concentration below $15x10^6$ per ml), teratozoospermia (i.e. morphologically normal spermatozoa below 4%), asthenoteratozoospermia, oligoasthenozoospermia,oligoasthenoteratozoospermia, oligoteratozoospermia, and azoospermia (absence of spermatozoa in the ejaculate)[5]

Statistics: Correlation between some sperm parameters: count (millions/ml, total motility (%), Grade A motility (%) and normal sperm morphology (%) were assessed. The values were given as mean ±SD. The relation between the values was evaluated by correlation analysis. Medcalc® version 11.6.1 software and SSP (Smith statistical package) version 2.8 were used for the statistical analysis. The results were evaluated in 95% confidence interval and the statistical significance was defined as $p<0.05$

Results and Discussion

The incidence of male infertility differs significantly from one part of the world to another due to several underlying etiological factors, including social habits, genetic causes and environmental conditions such as underlying infections, chemicals, radiation, exposure to heat and frequency of intercourse.[26]

Although conventional semen analysis has been criticized as not a true test of sperm function based on its poor prediction of fertility when compared to more sophisticated tests such as sperm penetration, capacitation, acrosome reaction and, more recently, sperm chromatin structure assay (SCSA) for the detection of DNA integrity, [27] it provides clues to structural or hormonal dysfunction and it remains the basis of important decisions concerning appropriate treatment.[3]

Table (1) shows the mean and standard deviation of basic semen parameters (semen volume, sperm count, motility, and morphology). The dominant abnormality is the very low percentage of morphologically normal spermatozoa (2.03 ± 1.36).

We have found that the majority of cases have isolated abnormality (teratozoospermia; 48.84%). Asthenoteratozoospermia (ATZ) was found in 10.47% and oligoasthenozoospermia (OAZ) and oligoteratozoospermia (OTZ) in 8.14% of cases. The least common pattern was necroteratozoospermia (NTZ) and oligonecroteratozoospermia (ONTZ) 1% each. Azoospermia was encountered in 3.49% of cases.

Teratozoospermia is the most common single sperm abnormality (48.84) that could cause infertility in patients studied. This is in agree with Alenzi[28], Altken[29], and MacLeod [30], but much higher than figures reported in other studies Alesiea[19], Taha et al [21], Kumurga et al [22], Peter et al [23], Owolabi et al [24], Aulia et al [14], Karabulut et al [15], and Elhussein et al [25] .

The above discrepancy could be explained by the fact that each author has his specific way of defining abnormal spermatozoa. For the sperm morphology study and the classification of abnormal sperm forms we have followed the guide-lines of the W.H.O. Moreover, sperm morphology is affected by smearing technique, fixation, staining, mounting and the optics and the illumination used i.e. the quality of the microscope. Even the small artifacts [31]

Among the sperm characteristics, sperm morphology has usually played a key role in determining fertility potential.[32,33]

It has been well documented that morphology of spermatozoa used for injection is an indicator of the competence of sperm and therefore directly related to ICSI outcome including fertilization and pregnancy rates. [34]

Bartoov and colleagues introduced a new technique called motile sperm organelle morphology examination (MSOME).Combination of this technique with routine ICSI gave rise to a new technique called intracytoplasmic morphologically selected sperm injection (IMSI), which enabled the selection of morphologically 'perfect' sperm during microinjection. [35]

In our study, 22.09 % of patients have sperm count below the WHO2010 threshold (i.e., < 15 million/ ml). Isolated sperm count reduction (oligospermia) was found in 2.33% of cases, in agreement with Taha et al [21], Alesiea[19], and AlEnizi[28], but less than figures reported by Peter [23], and Owolabi[24]. The total absence of spermatozoa in seminal fluid (azoospermia) was encountered in (3.49%) of cases, comparable with figures reported by Peter [23], and Owolabi[24], but much lower than figures reported by Razzak[36], Alesiea[19], Aulia[14], and Elhussein[25].Combined low sperm count with other abnormalities of seminal fluid was found in 19.76% of cases in accord with Razzak[36], but disagree with Alesiea[19], Peter [23] and Aulia[14].

The mean sperm count in our current study was 42.86 ± 33.24 that is above the WHO2010 threshold (i.e, 15 million/ml). This is in greement with Najam[17], Karabulut[15], Gowri[16], Alemanji[18], Alesiea[19], Feki[13], and Guzik[6], but disagree with Lackner[20].

The difference between present results and other researchers' reports is probably due to different exposure to the above risk factors and of course different genetic, racial and environmental backgrounds, Moreover, some cases of male infertility that were attributed to the low number of spermatozoa could be due the female factor[17].

About one fifth of our patients (20.93%) has low total sperm motility (i.e< 40%, WHO2010 threshold). The mean of percentages of Grade A (progressive motility) was 31.42 ± 14.8 which is slightly below the WHO2010 threshold (i.e., < 32%). Our results are comparable to Taha et al [21], Aulia[14], and Karabulut[15] but, lower than those reported by Alesiea[19] and Peter.[23]

This difference is due to the subjectively evaluated motility in some studies, which is overestimated by 15-20% compared with objectively assessedmotility.

Correlation coefficient and p values of the semen parameters including count (million/ml), total motility (%), Grade A motility (%), and normal morphology (%) rates with each other is shown in table 3. There is a statistically significant positive correlation of each semen parameter with other parameters. The strongest correlation observed was between total motility (%) and grade A (progressive) motility (%).

This is in agreement with Vaidya etal1996 who found a positive relationships between a falling sperm count, and decrease in motility and total motile counts. Also, they found that abnormal morphology increased with lower sperm counts.[37]

Hellstrom et al 2006 found that sperm motility and sperm morphology were associated with each other and with higher sperm concentrations. Total sperm count was positively correlated with semen volume, sperm concentration, sperm motility, and sperm morphology.[38] This in agreement with previous reports.[39,40]

- Our average of abnormal forms is higher as compared with those in other studies. This may be attributed to the way in which normal and abnormal spermatozoa are defined, which is specific to each author.
- Correlation between sperm concentration and percent of motility found by us is similar to that found by Rehan et al. [41]

In conclusion:Abnormalsperm morphology is the best indicator of infertility and teratozoosperma is the most common finding in abnormal spermiogram.

We hope that this study will inspire further studies that include larger number of patients recruited for longer period of time from multiple infertility clinics and preferably compared to fertile men.

Table 1; Basic semen parameters

Parameter	**Mean ± SD**
Semen volume (mL)	2.25 ± 0.96
Sperm count (million/mL)	42.86 ± 33.24
Total sperm motility (%)	40.32 ± 17.58
Grade A (progressive) sperm motility (%)	31.42 ± 14.8
Normal sperm morphology (%)	2.03 ± 1.36

Table 2: Seminal fluid abnormalities

Semen parameter	**WHO 2010 threshold**	**Semen abnormality in this study**			**No; (%)**		**Total**
Count	15 million/ml	Low sperm count	Isolated oligospermia		2 (2.33%)		19 (22.09%)
			Combined	OAZ	7 (8.14%)	17 (19.76%)	
				OATZ	2 (2.32%)		
				ONTZ	1 (1.16)		
				OTZ	7 (8.14%)		
			Azospermia		3 (3.49%)		-
Motility (total)	40%	Low sperm motility	Isolated asthenozoospermia		0		18 (20.93%)
			Combined	OAZ	7 (8.14%)	18 (20.93%)	
				OATZ	2 (2.32%)		
				ATZ	9 (10.47%)		
Morphology	4% (normal morphology)	Abnormal sperm morphology	Isolated teratozoospermia		42 (48.84%)		62 (72.09%)
			Combined	NTZ	1 (1.16%)	20 (23.25%)	
				OATZ	2 (2.32%)		
				ONTZ	1 (1.16)		
				OTZ	7 (8.14%)		
				ATZ	9 (10.47)		

AZ (azoospermia); NTZ (necroteratozoospermia); OAT (oligoasthenozoospermia); OATZ (oligoasthenozoospermia); ONTZ (oligonecroteratozoospermia); OTZ (oligoteratozoospermia; ATZ (asthrnoteratozoospermia); OZ (oligozoospermia; TZ (teratozoospermia

Table 3: Correlation between semen parameters

	Total motility (%)	**Normal morphology (%)**	**Grade A motility (%)**
Count (million/ml)	r = 0.3766 p = 0.0004	r = 0.4401 P < 0.0001	r = 0.3390 P = 0.0014
Total motility (%)		r = 0.4196 P = 0.0001	r = 0.9176 P < 0.0001
Normal morphology (%)			r = 0.4338 P < 0.0001

Table 4: Comparison of semen parameters in different studies

Author	Country	No;	Age (year)	Mean Semen Volume (ml)	Mean sperm count x 10^6/ ml	Motility %	Normal sperm Morphology %
Present study, 2020	Iraq	86	-	2.25±0.96	42.86±33.24	40.32±17.58	2.03±1.36
Karabulut et al[15] (2017)	Turkey	1404	-	-	78.67±81.39	66.1±19.85	2.3±2.46
Gowri et al[16] (2010)	Oman	67 (Primary infertility)	32.72±8.08	2.54±1.4	32.05±59.19	30.62±26.74	73.49
		31 (secondary infertility)	36.71±10.09	3.39±4.12	27.66±37.61	32.71±19.83	60.77
Najam[17] (2012)	Iraq	50	30.56±5.41	2.25±0.42	51.75±8.5	35±5.4	58.88±6.5
Alemanji et al [18] (2000)	Nigeria	100	100	2.26	57.05	62.02	65.2
Aleisa[19] (2012)	KSA	160	35.65±8.67	2.97±1.61	39.38±49.54	39.28±19.58	29
Adiga et al. [11] (2008)	India	1610	-	2.64	26.61	47.14	19.75
Guzick et al. [6] (2001)	USA	765	34.7±4.9	-	52±42	49±15	11±6
Lackner et al. [20] (2005)	Austria	7,780	31.6	-	10.25	21	15
Feki et al. [13] (2009)	Tunisia	2940	36.0±6.9	3.2±1.6	96.1±88.2	44.2±12.7	25.0±16.5

Table 5: Comparison of semen profile in different studies

Study	Country	Oligozoospermia (%)	Asthenospermia (%)	Oligoasthenospermia (%)	Teratozoospermia (%)	Azoospermia (%)
Present study, 2020	Iraq	2.33	-	8.14	48.84	3.49
Alesiea, [19] (2012)	Saudi Arabia	5.7	35.5	21.5	-	26
Taha et al, [21] (2011)	Iraq	1.35	10.81	2.16	2.43	11.62
Kumurya et al,[22] (2018)	Nigeria	11.7	52.3	10.8	55	14.4
Peter et al, [23] (2016)	Nigeria	34.9	26.6	14.2	6.5	3.5
Owolabi et al, [24] (2013)	Nigeria	25.6	11.5	3.2	18.5	6.2
Aulia et al, [14] (2017)	Indonesia	39.7	5.9	17.8	2.6	24.4
Karabulut et al, [15] (2017)	Turkey	14.3	13.4	9.4	9.1	-
Elhussein et al,[25] (2019)	Sudan	15.85	17.96	-	5.28	26.41

Ethical Clearance: Taken from the research ethics committee in Tikrit university/College of Medicine.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Mossa M. Marbut, Azzawi M. Hadi, Dekhel H. Hadri. Ginger as a single agent in treatment of male infertility. Tikrit Medical J. 2011; 17(1): 1-5.
2. Fido A. Emotional distress in infertile women in Kuwait. Int J FertilWomens Med 2004;49(1):24-28
3. Lewis SE. Is sperm evaluation useful in predicting human fertility? Reproduction 2007;134:31-40.
4. Tomlinson M, Lewis S, Morroll D. British Fertility Society. Sperm quality and its relationship to natural and assisted conception: British Fertility Society guidelines for practice. Hum Fertil (Camb).201316: 175-193.
5. World Health Organization. WHO Laboratory Manual for the Examination and Processing of Human Semen, 5th ed. Cambridge: Cambridge University Press; 2010.
6. Guzick, D.S., Overstreet, J.W., Factor-Litvak, P., Brazil, C.K., Nakajima, S.T., et al. Sperm

morphology, motility, and concentration in fertile and subfertile men. N. Engl. J. Med. 2001345, 1388–1393.

7. Fisch, H., Feldshuh, J., Goluboff, E.T., Broder, S.J., Olson, J.H., et al.,. Semen analyses in 1,283 men from the United States over a 25-year period: no decline in quality. Fertil. Steril. 1996;65, 1009–1014.
8. Jørgensen, N., Andersen, A.G., Eustache, F., Irvine, D., Suominen, J.S.S., et al. Regional differences in semen quality in Europe. Hum. Reprod. 2001;16, 1012–1019
9. Jørgensen, N., Carlsen, E., Nermoen, I., Punab, M., Suominen, J., et al. East-West gradient in semen quality in the NordicBaltic area: a study of men from the general population in Denmark, Norway Estonia and Finland. Hum. Reprod. 2002;17, 2199–2208.
10. Iwamoto T, Nozawa S, Yoshiike M, Hoshino T, Baba K, Matsushita T, Tanaka SN, Naka M, Skakkebaek NE, Jørgensen N. Semen quality of 324 fertile Japanese men. Hum Reprod. 2006; 21(3):760-5.
11. Adiga, S.K., Jayaraman, V., Kalthur, G., Upadhya, D., Kumar, P. Declining semen quality among south Indian subfertile men: A retrospective study. J. Hum. Reprod. Sci. 2008;1, 15-18.
12. Li, Y., Lin, H., Ma, M., Li, L., Cai, M., et al. Semen quality of 1346 healthy men, results from the Chongqing area of southwest China. Hum. Reprod. 2009;24, 459–469.
13. Feki, N.C., Abid, N., Rebai, A., Sellami, A., Ayed, B.B., et al., Semen quality decline among men in subfertile relationships: experience over 12 years in the South of Tunisia. J. Androl. 2009; 30, 541–547.
14. Aulia SN, Lestari SW, Pratama G, et al; The pattern of abnormalities on sperm analysis: A study of 1186 infertile male in Yasmin IVF clinic Jakarta. IOP Conf. Series: Journal of Physics: Conf. Series. 2017; 884: 012138
15. Karabulut S, Keskin I, Sagiroglu Y. Relationship between Semen Parameters in Samples Obtained from Sub-fertile Patients. Andrology (Los Angel) 2017;6: 1000180.
16. GowriV,Venkiteswaran KP, Al-Zakwani I: Comparison of the Demographics, Semen Parameters and Hormone Profiles in Men with Primary and Secondary Infertility
17. Najam WS: Significant value of hormonal assays as a marker for Male Infertility in Tikrit city. Tikrit Medical Journal 2012;18(2):314-321
18. Alemnji GA, Thomas KD, Oyelese AO, Ojedije TO. The semen of fertile black males: analysis of 100 consecutive cases. Ann Saudi Medicine. 2002; 22:94-7.
19. Aleisa NAS; Semen characteristics of fertile and subfertile men in a fertility clinic and correlation with age. Journal of King Saud University – Science. 2013; 25, 63–71
20. Lackner, J., Schatzl, G., Waldho¨ r, T., Resch, K., Kratzik, C., et al. Constant decline in sperm concentration in subfertile males in an urban population: experience over 18 years. Fertil. Steril2005; 84, 1657–1661.
21. Taha, A., & Rashid, K.. Etiology of infertility in couples attending maternity hospital in Erbil. Zanco J Med Sci, 2018; 17(1), 322-330.
22. Kumurya, A. S., Dogo, E. B. & Abdukadir, G. Semen parameters of some infertile patients attending Aminu Kano Teaching Hospital, Kano, Nigeria DUJOPAS.2018;4(2): 281 - 290,
23. Peter AO, Temi AP, Olufemi AP, et al; Pattern of Semen Parameters and Factors Associated with Infertility in Male Partners of Infertile Couples in Nigeria. Andrology (Los Angel) 2016, 5:1:161
24. Owolabi AT, Fasubaa OB, Ogunniyi SO. Semen quality of male partners of infertile couples in Ile-Ife, Nigeria. Niger J ClinPract 2013;16:37-40.
25. Elhussein OG, Ahmed MA, Suliman SO, et al; Epidemiology of infertility and characteristics of infertile couples requesting assisted reproduction in a lowresource setting in Africa, Sudan. Fertility Research and Practice.2019; 5:7 page number
26. Lunenfeld B, Steirteghem VA. Infertility in the third millennium: Implications for the individual, family and society: Condensed meeting report from the bertarelli foundation's second globalconference. Hum Reprod Update 2004;10:317-326.
27. Weber RF, Dohle GR, Romijn JC. Clinical laboratory evaluation of male subfertility. AdvClinChem 2005;40:317-364.
28. AlEnezi H, Isa AM, Abu-Rafea B, et al: Pattern of semen fluid abnormalities in male partners of infertile couples in Riyadh, Saudi Arabia. Can J Urol 2014;21(3):7322-7325

29. Altken RS, Besr FS, Richardson DN. An analysis of sperm functions in cases of unexplained infertility capacity. FertilSteril 1982;30:212-214.
30. MacLeod J, Gold RZ. The male factor in fertility and infertility. II- spermatozoa count in 1000 men of known fertility and in 1000 cases of infertile marriage. J Urol 1951;66(3):436-449
31. NAFA–ESHRE. Manual on basic semen analysis 2002:19-21
32. Bartoov B, Berkovitz A, Eltes F, Kogosowski A, Menezo Y, Barak Y. Real-time fine morphology of motile human sperm cells is associated with IVFICSI outcome. J Androl. 2002; 23(1):1-8.
33. Kohn TP, Kohn JR, Lamb DJ. Role of sperm morphology in deciding between various assisted reproduction technologies. EurUrol Focus. 2018; 4(3): 311-3.
34. De Vos A, Van de Velde H, Joris H, Verheyen G, Devroey P, Van Steirteghem A: Influence of individual sperm morphology on fertilization, embryo morphology, and pregnancy outcome of intracytoplasmic sperm injection. FertilSteril 2003, 79:42–48
35. Bartoov B, Berkovitz A, Eltes F, Kogosovsky A, Yagoda A, Lederman H, and Barak Y. Pregnancy rates are higher with intracytoplasmic morphologically selected sperm injection than with conventional intracytoplasmic injection. FertilSteril.2003;80, 1413-9
36. Razzak A.H., Wais S.A. The infertile couple: A Cohort study in Duhok, Iraq. East Mediterr Health J, 2002; 8 (2-3): 234-8.
37. Dua A A, Vaidya S R. Sperm motility and morphology as changing parameters linked to sperm count variations. J Postgrad Med 1996;42:93-6
38. Hellstrom, WJG, overstreet JW, sikka SC, et al: Semen and Sperm Reference Ranges for Men 45 Years of Age and Older. J Androl 2006;27:421–428
39. Panidis DK, AsseoPP,Papaloucas AC: Semen parameters in 114 fertile men. Europ. J. Obstet. Gynec. reprodBiol, 1984., 16/6, 411-420
40. Makler, A., Itskovitz. J.. Branded, J.M. and Paldi, E.: Sperm velocity and percent of motility in 100 normospennic specimens analysed objectively by the multiple exposure photography (MEP) method. Fertil. andsteril. 1979;31. 155-161.
41. Rehan NE Sobrero AJ, Fertig JW: The semen of fertile men: statistical analysis of 1300 men. FertilSteril.1975;26:492,