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■ Original Research Article

Seminal Fluid Analysis Pattern of Infertile Couples: Does The World Health Organization Criteria Used Make a Difference?

Oni Olaolu.O, Ifebude Joshua. E, Bello Oluwasomidoyin.O, Saanu Olugbenga.O, Olayemi O.

Department of Obstetrics and Gynecology, University College Hospital, Ibadan

Abstract

Background: Male partners are key contributors to infertility in many couples because of the high incidence of abnormal sperm parameters. This study examined the semen parameters of couples evaluated for infertility in University College Hospital (UCH) over a 10-year period using different editions of World Health Organization (WHO) seminal fluid analysis (SFA) criteria. **Methodology:** This study was a retrospective study of SFA of male partners of infertile couples who presented at the gynecological clinic of UCH, Ibadan from 2011 to 2020. The SFA results were analyzed using the 1999, 2010 and 2021 editions of WHO SFA criteria for comparison. Data analysis was done using the Statistical Package for the Social Sciences version 25 software and a p-value of <0.05 was set for statistical significance. **Results:** The SFA of 2,055 male partners were examined with 17.5%, 46.3% and 46.7% of the men qualified as normal according to the WHO 1999, 2010 and 2021 criteria respectively. Also, 57.4%, 61.1% and 60.0% had single sperm parameter abnormality using WHO 1999, 2010 and 2021 criteria respectively. Some of the male partners had combined sperm abnormalities but only few had oligoasthenoteratozoospermia (OATS). Inferential statistical analysis shows statistically significant results (p =0.00) when WHO 1999 criteria was compared to 2010 and 2021 SFA criteria. **Conclusion:** The seminal fluid abnormalities were noted to have increased over the years and the 1999 WHO SFA criteria is significantly different compared to the 2010 and 2021 criteria and this might have relevant clinical significance.

Keywords: Seminal fluid analysis**,** male partners, infertile couples, WHO SFA criteria

Corresponding Author:

Dr. Oni O. Olaolu

Department of Obstetrics and Gynecology, University College hospital, Ibadan.
Phone numbers: +2348062087527
Mail: olaoluoni43@yahoo.com

INTRODUCTION

Infertility is defined as a couple's inability to conceive despite 12 months of uninterrupted, unprotected sexual activity.[1] In Nigeria, infertility is a widespread issue and because of the high value placed on childbearing in African cultures, childlessness might lead to marital strife.[2] Infertile marriages are usually blamed on the women particularly in Africa where male partners are absolved of the guilt so far the men can ejaculate and achieve erection.[3] Declaring a man sterile is even considered an abomination in certain cultures therefore women often bear the brunt of infertility without realizing that they might not be the cause.[4]

According to studies, the frequency of infertility in the general population is between 15% and 20%.[5] Thirty percent of infertility cases are caused by male factors, another 30 to 40% by female factors while 20 to 40 % are caused by a combination of male and female factors and unexplained infertility.[5,6] According to researchers, male partners are key contributors to infertility in many infertile couples because of the high

incidence of abnormal sperm parameters.[3,7,8] Since the quality of seminal fluid cannot be directly examined, medical laboratory intervention is frequently required.[3]
In the past, seminal fluid analysis (SFA) was regarded to be of little use, but it is now widely understood that any male infertility evaluation should begin with the fundamentals, which include a complete history, physical examination of the male partner and semen analysis.[6]

Poor semen quality and male factor infertility in general have also been associated with men's overall health and the likelihood of later life comorbid illnesses.[9,10] When it comes to semen analysis, fertile and sub-fertile men's semen evaluations overlap significantly[11], and there is significant variation both within and between individuals, mostly due to cultural, environmental, genetic, and laboratory-related factors.[11] Taking this into consideration, standard laboratory techniques for semen analysis are provided by the World Health Organization(WHO) laboratory manual for the examination and processing of human semen, which are widely applied in both clinical practice and research. The WHO manual's 6th edition was released in July 2021 and reports various changes from the previous edition which has been used in the past eleven years, which is significant from a clinical standpoint.[6,12]

In fact, the lower fifth percentile of this distribution has been regarded as a true threshold limit for normal versus abnormal semen parameters since the 5th edition presented the distribution of values from approximately 1800 men who contributed to a natural conception within 12 months of trying.[6] Data from the fifth version of the WHO Manual have been extensively assessed and supplemented in the sixth edition with information from over 3500 more males in 12 countries.[12,13] Noteworthy are minor variations in reference values (lower 5th percentile) from the previous edition.[6,12]

The classification of semen parameters as normal or abnormal (according to the 5th percentile) is still of paramount clinical relevance in the routine management work-up of these males, despite evidence from both the WHO manual itself and clinical practice highlighting that the lower 5th percentile of data from men in the reference population does not represent a limit between being fertile or infertile.[14] Semen quality severity is really taken into account by recent guidelines to help determine the indication for diagnostic tests and to recommend suitable infertility treatment choices.[15,16]

A considerable percentage of infertile males are unable to impregnate their female partners because of lack of sperm (azoospermia) or inadequate sperm (oligozoospermia) or/and poor motility (asthenozoospermia). There is evidence that sperm counts have fallen in the last 50 years, leading to a rise in male infertility.[17,18] Semen samples with various abnormalities have been found to have a low fertilizing ability. As a result, a one-factor anomaly is associated with a better prognosis than a two-factor abnormality, which is a valuable guide to prognosis which is in turn better than a three-factor abnormality.[19]
As seen in the table below, the WHO 2010 semen parameters differ from the WHO 1999 and WHO 2021 criteria:

WHO 1999, 2010, 2021 SFA reference values

Seminal fluid parameters	WHO 1999	WHO 2010	WHO 2021
Seminal volume (ml)	≥2	≥1.5	≥1.4
Concentration(million/ml)	≥20	≥15	≥16
Total motility (%)	≥ 50	≥40	≥42
Progressive motility (%)	≥ 50	≥32	≥30
Morphology (%)	≥14	≥4	≥4

Volume, pH, sperm concentration, motility, morphology, and vitality are all features of seminal fluid.[6] On semen analysis, men who have male infertility exhibit observable abnormalities[20], therefore a thorough evaluation of the semen parameters may reveal various reasons of male infertility.

While the WHO 2021 criteria of SFA seems to be less stringent criteria compared to that of 1999 and even that of 2010 criteria in evaluation of these semen parameters, the incidence of the male factor infertility tends to be on the increase in recent time among apparently normal looking male partners.[5,21] This study therefore looked at semen parameters of couple evaluated for infertility in UCH over a 10-year period, their pattern and assessed if the edition of WHO criteria used played a significant role in labeling male partners as infertile or not.

METHODOLOGY

This was a retrospective study of seminal fluid analyses of male partners of infertile couples presenting at the gynecological clinic of University College Hospital, Ibadan, Nigeria from 2011 to 2020. The University College Hospital (UCH) is strategically located in Ibadan, bridging the urban Ibadan North and the semi-urban Ibadan Central areas. It serves as a referral center for surrounding and distant hospitals in the state and nation in general. The gynecological clinic complex was the site of sample collection for patients who met the inclusion criteria.

Gynecology outpatient and the SFA registers were retrieved. A total of 2,800 cases of infertile couples were seen from January 2011 to December 2020. Only 2196 of the male partners presented their semen for analysis. All the infertility cases that were managed at UCH, Ibadan during the study period were retrieved. Proforma were used to collate information on the seminal fluid parameters of the men. All the male partners with complete seminal fluid analysis results were included for the study while those without the seminal fluid analysis results or with incomplete seminal fluid analysis results were excluded. Therefore, out of 2,800 cases of infertile couple seen during the period, only SFA of 2,055 male partners were analyzed. The SFA results were analyzed using the 1999, 2010 and 2021 editions of WHO SFA criteria for comparison. Statistical analysis was done using the Statistical Package for the Social Sciences version 25 software (SPSS Inc., Chicago, IL, USA). McNemar Test (exact) was used for the comparison of the criteria and the p-value of less than or equal to 0.05 was considered statistically significant.

RESULTS

The total number of samples analyzed in this study was 2055. It shows that 17.5% of the men qualified as normal according to the WHO 1999 criteria, whereas 46.3% qualified as normal using WHO 2010 reference values and 46.7% of the men were classified as normal according to 2021 criteria as shown in Table 1.

Table 1: Seminal fluid analysis findings

Variable	WHO 1999 n (%)	WHO 2010 n(%)	WHO 2021 n(%)
Semen characteristics			
Normal	360(17.5)	951(46.3)	959(46.7)
Abnormal	1695(82.5)	1104(53.7)	1096 (53.3)
Total	2055	2055	2055

Semen analyses of the study population were also categorized based on each SFA parameter analyzed using WHO 1999, 2010 and 2021 criteria (Table 2). This analysis revealed that of the abnormal semen samples, 40.4% had abnormal sperm concentration, 76.0% had abnormal sperm motility and only 7.3% had abnormal sperm morphology using 1999 WHO criteria, while 34.2% had abnormal sperm concentration, 48.8 % had abnormal sperm motility and 2.0% had abnormal sperm morphology using the 2010 WHO criteria. However, according to WHO 2021 criteria, 35.3% had abnormal sperm concentration, 64.3% had abnormal sperm motility and 2.0% had abnormal sperm morphology (Table 2).

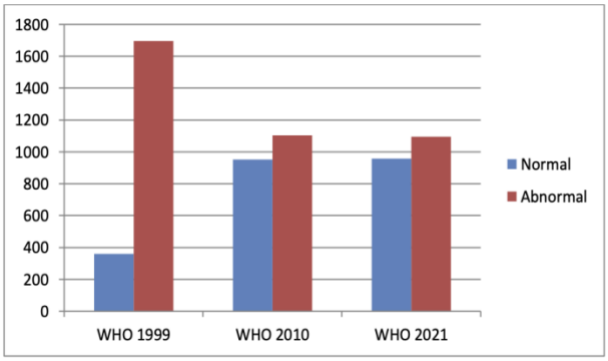

Fig 1: Semen characteristics based on three different WHO criteria.

Table 2: Type of abnormal semen characteristics

Variable	WHO 1999 n (%)	WHO 2010 n (%)	WHO 2021 n (%)
Azoospermia			
Yes	127 (6.2)	127 (6.2)	127 (6.2)
No	1928 (93.8)	1928 (93.8)	1928 (93.8)
Total	**2055**	**2055**	**2055**
Motility			
Normal	463 (24.0)	987 (51.2)	689 (35.7)
Abnormal	1465 (76.0)	941 (48.8)	1239 (64.3)
Total	**1928**	**1928**	**1928**
Morphology			
Normal	1787 (92.7)	1889 (98.0)	1889 (98.0)
Abnormal	141 (7.3)	39 (2.0)	39 (2.0)
Total	**1928**	**1928**	**1928**
Total sperm count			
Normal	1149 (59.6)	1269 (65.8)	1248 (64.7)
Abnormal	779 (40.4)	659 (34.2)	680 (35.3)
Total	**1928**	**1928**	**1928**

Table 3: Classification of abnormal semen characteristics

Variable	WHO 1999 n (%)	WHO 2010 n (%)	WHO 2021 n (%)
Abnormal types			
Azoospermia	127 (7.5)	127(10.8)	127(11.6)
Oligozoospermia	91(5.4)	220(21.5)	317(28.9)
Asthenozoospermia	757(44.5)	321(28.5)	212(19.3)
Teratozoospermia	0(0.0)	3(0.3)	2(0.2)
Astheno/oligo	681(40.2)	397(35.8)	400(36.5)
Oligo/teratozoospermia	0(0.0)	3(0.3)	4(0.4)
Astheno/teratozoospermia	3(0.2)	0(0.0)	1(0.1)
Oligo/astheno/teratozoospermia	36 (0.2)	33(2.8)	33(3.0)
Total	1695	1104	1096

A sub-classification based on the sperm parameter abnormalities occurring as single abnormalities or combined (i.e, oligozoospermia,

asthenozoospermia, teratozoospermia, oligoasthenozoospermia, oligoteratozoospermia, oligoasthenoteratozoospermia) is depicted in Table 3. A clear shift in the respective total numbers of patients as well as the percentage of patients belonging to a specific group can be noticed from WHO 1999.

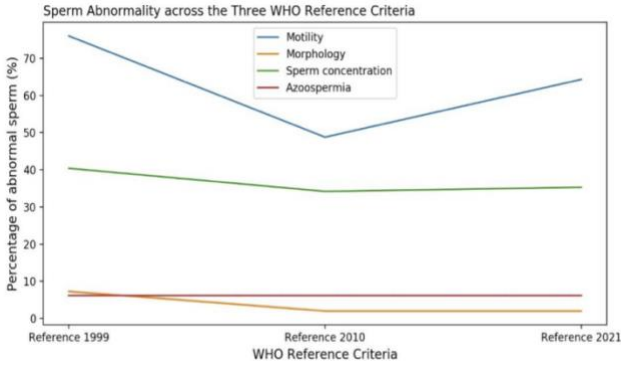

Fig 2: Percentage of abnormal sperms using the three WHO reference criteria

Table 4: Inferential statistical analysis for comparison

Cross-tabulation of reference criteria 1999-edition against 2010-edition					
		RC-1999			
		Normal	*Abnormal*	*Total*	P-value
	Normal	360	591	951	.000
RC-2010	*Abnormal*	0	977	977	
	Total	360	1568	1928	
Cross-tabulation of reference criteria 1999-edition against 2021-edition					
		RC-1999			
		Normal	*Abnormal*	*Total*	P-value
	Normal	359	600	959	.000
RC-2021	*Abnormal*	1	968	969	
	Total	360	1568	1928	
Cross-tabulation of reference criteria 2010-edition against 2021-edition					
		RC-2010			
		Normal	*Abnormal*	*Total*	P-value
	Normal	884	75	959	.557
RC-2021	*Abnormal*	67	902	969	
	Total	951	977	1928	

McNemar Test (exact) p = .000 statistically significant, p = .557 not statistically significant. RC-1999: WHO reference criteria 1999 edition, RC-2010: WHO reference criteria 2010 edition, RC-2021: WHO reference criteria 2021 edition. Distribution used = Binomial

to WHO 2010 to WHO 2021 criteria. When sperm parameter abnormalities (concentration, motility, normal sperm morphology) were taken into consideration, either as single abnormal parameter or multiple abnormal parameters, of the 2055 semen analyses, a total of 1695, 1104 and 1096 were regarded as abnormal using WHO 1999, 2010 and 2021 respectively.

Out of these 2055 men, 57.4%, 61.1% and 60.0% had single sperm parameter abnormality (azoospermia, oligozoospermia, asthenozoospermia or teratozoospermia) using WHO 1999, 2010 and 2021 respectively. Using 1999 criteria, 681(40.2%) had abnormal sperm concentration and motility together (astheno/oligo), no semen fluid analysis had oligo/teratozoospermia together, only 3 (0.2%) had (astheno/teratozoospermia) abnormal sperm motility and morphology together. Using 2010 criteria, the number of those with abnormal sperm concentration and motility (astheno/oligo) reduced to 397(35.8%) while 3 (0.3%) had abnormal sperm concentration and morphology (oligo/teratozoospermia) together and none had abnormal motility and morphology together. However, using 2021 criteria, 400 (36.5%) had abnormal sperm concentration and motility (astheno/oligo) together and 4 (0.4%) had abnormal sperm concentration and morphology (oligo/teratozoospermia) together. Only 1(0.1%) had abnormal motility and morphology (astheno/teratozoospermia) (Table 3).

Notably, those with oligoasthenoteratozoospermia (OATS) were 36(0.2 %), 33(2.8%) and 33(3.0%) using 1999, 2010 and 2021 WHO SFA reference values respectively. Fig 2 shows the trends of the percentage of the SFA samples that were abnormal considering each parameter i.e motility, morphology, azoospermia and sperm concentration based 1999, 2010 and 2021 WHO SFA reference values. Inferential statistical analysis done comparing effect of each WHO SFA criteria with other shows statistically significant results (p =0.00) when WHO 1999 criteria was compared to 2010 and 2021 SFA criteria but no statistically significant result when WHO 2010 criteria was compared to 2021 SFA criteria (Table 4).

DISCUSSION

This study analyzed the findings of semen analysis parameters at the University College Hospital, Ibadan between 2011 and 2020 using three sequential criteria set by WHO (World Health organization). There was a significant increase in the proportion of abnormal results (82.5%) using the 1999 WHO criteria in this study compared to an earlier study in the our facility which was 27.3% using the same criteria.[22] This proportion was also higher than findings from Sagamu in 2012 (49.5%), Benin city in 2017(66.5%) and Nnewi in 2010(68.0%).[3,8,23] The findings from Ife in 2013(31.8%) and Birnin-Kebbi in 2015 (47.6%) that used 2010 WHO criteria (criteria-matched studies) were much lower than 53.7% from our study corroborating the fact that there is an increase in the prevalence of abnormal semen parameters over the time.[7,24]

Among men with abnormal results, the proportion of those with azoospermia has remained relatively constant over the years at 6.2% as it was in

earlier study in the same institution.[22] Owolabi et al in Ile-Ife, South western, Nigeria similarly reported a prevalence of 6.2%.[24] However, the incidence of azoospermia was significantly higher as reported by Ugwa et al and Omo-Aghoja et al in North-western and south-south Nigeria respectively. [7,8] Ugboaja et al in south-eastern, Nigeria reported lower prevalence (1.4%) of azoospermia in their study.[23] There may be regional variation in the incidence of azoospermia, which may require further evaluation. It should also be noted that male partners with azoospermia will need sperm donors and assisted conception to have children.[8,15,16]

The proportion of participants with abnormal sperm motility was highest with the use of the strict 1999 WHO criteria (76.0%) but lowest with the 2010 criteria (48.8%) which obviously has the least stringent criteria in this regard. Therefore, participants who would have been declared as having abnormal semen quality were re-classified with the 2010 criteria. This further buttresses the assertion by some authors that the presence of some semen abnormalities does not exclusively determine male factor infertility.[3,24] The incidence of abnormal sperm motility was significantly lower in Sagamu (58.6%) and Nnewi (16.7%) using the 1999 criteria.[3,23] Similarly lower in Ile-Ife(11.5%) using the 2010 criteria.[24]

The incidence of abnormal morphology was significantly higher (7.3%) using the 1999 criteria due to the earlier stated stringent criteria used. However, the 2010 and 2021 criteria are more liberal in this regard but require further investigations to determine the lowest possible cut-off values for fertility. The reports from Ile-Ife(18.5%), and Birnin Kudu(33.3%) using the 2010 criteria were significantly higher than the findings from our study.[7,24] Similarly, findings from Benin-city(11.5%) using the 1999 criteria were significantly higher than findings from our study.[8]

The proportion of participants with abnormal sperm count was obviously highest using the 1999 criteria (40.4%). This is significantly higher than the findings by Omo-Aghoja et al in Benin-city (22.8%)[8] and Ugboaja et al in Nnewi(8.9%).[23] Astheno-oligozoospermia was the commonest combined abnormalities reported by our finding. This is consistent with findings from the earlier study in our institution despite higher proportion of these parameters. Although this is not in-keeping with findings by other authors.[5,7,8,23] The proportion of the semen samples with OAT abnormalities in this study were considerable small across all the WHO SFA criteria unlike the findings in a similar study by Boeri et al[25] where higher proportion of the semen samples analyzed had OAT and this has a significant implication on the fertility measures available for the infertile couple.

Comparing the overall findings using the three WHO criteria; it was shown that the findings using the 1999 criteria were significantly different from the findings using the 2010 and 2022 criteria. A significant limitation of this study is its retrospective nature. More so, since the clinical significance of these findings is important, a multi-center and cohort study might be necessary to determine the clinical relevance of these findings especially as it affects fertility outcomes of these men.

CONCLUSION

The incidence of seminal fluid abnormalities was noted to have increased over the years, when compared to earlier study done in our institution which is a source of concern as further studies are required to determine the possible factors responsible for this rise. Also, the WHO 1999 criteria were noted to be significantly different in the interpretation of a SFA result compared to the 2010 and 2021 criteria and further evaluation on the clinical significance of this finding might be necessary.

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