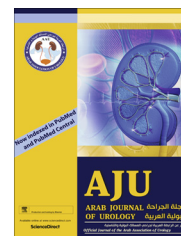




## Arab Journal of Urology

(Official Journal of the Arab Association of Urology)

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### REVIEW

# Prediction of male infertility by the World Health Organization laboratory manual for assessment of semen analysis: A systematic review

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Received 26 September 2017, Received in revised form 18 October 2017, Accepted 21 October 2017

#### KEYWORDS

Semen analysis;  
WHO;  
Fifth edition  
guidelines;  
Laboratory manual;  
Male infertility;  
Prediction

#### ABBREVIATIONS

ASA, anti-sperm  
antibodies;  
PRISMA, Preferred  
Reporting Items for  
Systematic Reviews  
and Meta-Analyse

**Abstract Objective:** To discuss the role, reliability and limitations of the semen analysis in the evaluation of fertility with reference to the World Health Organization (WHO) fifth edition guidelines, with semen analysis reference values published in 2010. We also discuss the limitations of using a single threshold value to distinguish ‘abnormal’ and ‘normal’ parameters.

**Methods:** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to search the MEDLINE, EMBASE, and the Cochrane electronic database for articles discussing the effectiveness of semen analysis.

**Results:** Limitations affecting the reliability of semen analysis as a predictor of fertility were found. These include: the lack of consideration of the female factor, the vaguely defined threshold values, and the intra-individual variation in semen parameters.

**Conclusions:** Impaired semen parameters alone cannot be used to predict fertility as these men still have a chance of being fertile, except when a man has azoospermia, necrozoospermia or globozoospermia.

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Peer review under responsibility of Arab Association of Urology.



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<https://doi.org/10.1016/j.aju.2017.10.005>

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Please cite this article in press as: Patel AS et al. Prediction of male infertility by the World Health Organization laboratory manual for assessment of semen analysis: A systematic review. *Arab J Urol* (2017), <https://doi.org/10.1016/j.aju.2017.10.005>

## Introduction

Semen analyses have been the test of choice for assessing the male partner in an infertile couple. Studies linking quality of the ejaculate and fertility have been around since the 1930s [1]. In 1980, the WHO recruited a team of physicians and scientists to publish a manual describing in detail what the normal semen parameters of a fertile man should be and how to analyse semen in the laboratory. Since then, they have updated the manual four times, with the latest being in 2010 [2]. Although analysing semen samples can provide valuable information about the fertility of the male in certain situations, it does have several limitations [3]. The goal of the present review is to discuss the role, reliability and limitations of semen analyses in the evaluation of infertility, as well as the disadvantages of using a single threshold value to distinguish abnormal and normal parameters.

### What is a semen analysis?

Semen consists of two components: the spermatozoa made by the seminiferous tubules of the testis, and the seminal fluid produced by the accessory glands that nourishes sperm and has a role in interacting with the female reproductive tract to influence fertility [4]. These components are reflected in the semen analysis by the sperm count, which reflects the number of spermatozoa in the semen sample; and the volume of the semen, which reflects the amount of seminal fluid produced [2]. Sperm motility is defined as the percentage of sperm that show signs of movement, whilst the sperm morphology is the percentage of sperm that appears to have a normal cellular structure. Sperm vitality is defined as the percentage of sperm that are viable in the sample.

A semen sample is collected by masturbation after an abstinence period of 2–7 days, preferably near the laboratory to limit the time between collection and analysis. The physical characteristics of the semen sample, such as the volume, pH, colour, liquefaction and viscosity is measured, and the sample is then evaluated under a microscope to determine the motility, vitality, concentration, and morphology [5]. The values obtained are compared to the reference values determined by the WHO manual. The reference ranges for semen characteristics are given in Table 1.

Studies have shown that the total motile sperm count (volume  $\times$  concentration  $\times$  motility) has been the most predictive factor in determining fertility compared to volume, concentration, and motility individually [6].

### Determining normal semen parameters

The reference values for the semen parameters established in the 2010 WHO manual were described in a report by Cooper et al. [7] in 2010. The study analysed

**Table 1** Semen analyses lower reference limits defined by the WHO laboratory manual for the examination and processing of human semen in 2010.

Semen characteristic	Lower reference limit
Volume, mL	1.5
Sperm concentration, $10^6$ /mL	39
Total sperm number, $10^6$	15
Total motility (PR + NP), %	40
Progressive motility (PR), %	32
Vitality (live spermatozoa), %	58
Sperm morphology (normal forms), %	4
pH	$\geq 7.2$
Seminal fructose, $\mu\text{mol}/\text{ejaculate}$	$\geq 13$

PR, progressive motility; NP, non-progressive motility.

the semen analysis data from 1953 men from five studies across three continents. The 1953 men included in the study had got their partner pregnant in  $\leq 12$  months ensuring that all these men were fertile. After the semen analysis the data were analysed, the 5th centile was calculated and it was used as the lower reference limit in the fifth edition manual published by the WHO. The 5th centile for reference ranges was used to match what is widely accepted in clinical chemistry, which states that 95% of the data should be included in the reference interval.

There are many limitations with the study, some of which were discussed by the authors themselves. The lack of an equal population distribution means that some areas of the world are over-represented, whilst others are under-represented [7]. For example, only 10% of the population involved in the study was from the southern hemisphere, and most of the included population was from Europe [5].

Another limitation is that only fertile couples were included in the evaluation of normal values. Whilst the WHO study did account for this by comparing it to a normal ‘unscreened’ group that represents the general population, they never compared their values to that of infertile men. Because of this, it is difficult to accurately predict fertility with the WHO reference values [7].

### Methods

We reviewed the databases of MEDLINE, EMBASE, and the Cochrane Library as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines on 15 August, 2017 (Fig. 1) [8]. The search was conducted with the following keywords: ‘semen analysis’, ‘World Health Organization’ and ‘infertility’. Articles were evaluated based on their title or abstract and were included if they discussed the reliability or the limitations of semen analysis. Articles were excluded if they were not written in English.

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