

# Commentary

## Definition of Oligozoospermia- A Commentary

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Semen analysis is an important tool in male infertility investigation. Through its cellular and chemical components, human semen can provide information on the functional properties of the organs producing this fluid, i.e., the testes, epididymis and accessory glands<sup>1</sup>.

The history of semen analysis dates back to 1677 when Anton von Leeuwenhoek made a remarkable discovery of the spermatozoa, which he called animalcules or spermatozoon. In his letter to The Royal Society of London, he described the structure of spermatozoa so accurately that in retrospect, his illustrations with the help of such a primitive microscope seem incredible. Leeuwenhoek was also the first to discover the presence of spermatozoa in the fallopian tubes and uterus of an animal apart from demonstrating that the sperm are produced in the testicles<sup>2</sup>.

Upon discovery of the sperm, analysis of semen entered a more scientific realm. Semen analysis was developed by pioneers in the field like Lode, MacLeod Heim and Hotchkiss, not to forget Eliasson and Gold<sup>3</sup>. It was Edward Martin, in the year 1902, who first put forth the inclusion of semen analysis in male infertility investigation<sup>4</sup>. Even with all the efforts put in by such brilliant scientists to standardize semen analysis, it still is, as Christopher De Jonge rightly said, the subject of both commendation and condemnation<sup>5</sup>. Semen analysis remains a numbers game<sup>6</sup>.

In 1980, the WHO published its first manual on semen analysis thereby establishing standards internationally. It has been updated periodically; five manuals have been published over the last three decades. It has undergone numerous changes over the years, the initial ones being more consensus-based while the last one seems evidence-based, despite its discrepancies.

Oligozoospermia is the nomenclature given when the sperm concentration is less than 15 million/ml, according to the WHO manual 5th edition. However, the values for this nomenclature have varied quite significantly over the last few decades (Table-1). A normal sample, in the 1940's, was considered to have a sperm count of 60 mil/ml or more<sup>7</sup>. This, over the years, was lowered to 20 mil/ml based on a consensus by international andrologists of yesteryears. While nobody knows exactly as to why this value was chosen, it was published by the WHO in its' last 4 manuals and had become a gold standard (still is, in a few labs across

the world) for identifying the boundary between normal and oligozoospermic samples.

Semen parameters	WHO 1980	WHO 1987	WHO 1992	WHO 1999	WHO 2010
Volume (ml)	--	≥ 2	≥ 2	≥ 2	≥1.5
Sperm concentration (10 <sup>6</sup> /ml)	20 - 200	≥ 20	≥ 20	≥ 20	≥15
Total sperm concentration (10 <sup>6</sup> )	--	≥ 40	≥ 40	≥ 40	≥39
Total motility (% motile)	≥ 60	≥ 50	≥ 50	≥ 50	≥40
Progressive motility	≥ 25	≥ 25%	≥ 25% (grade A)	≥ 25% (grade A)	≥32% (A+B)
Vitality (% alive)	--	≥ 50	≥ 75	≥ 75	≥58
Morphology (% normal)	80.5	≥ 50	≥ 30	14	≥4

Table 1 - Variations in values of semen across the years

The current edition value of 15 mil/ml for sperm concentration also seems arbitrary though evidence-based. It's anybody's guess as to how this can result in 39 million/ejaculate with a volume of 1.5 ml<sup>8</sup>. The expression of sperm concentration per ml and not per ejaculate seems incorrect as it is the output of sperm in the semen that is of interest. A 2 ml sample of 30 million per ejaculate will have 15 million per ml but a 5 ml sample of 30 million per ejaculate will have only 6million per ml. So to report the former as 'normal' and the latter as 'subnormal' or 'abnormal' seems unjustified.

It is imperative to remember that reference ranges given by the WHO manual are not absolute and definitely not diagnostic cut-off values but only results obtained out of an observation of a fertile population, which reflects an 'approximate' probability that the fertility potential could be high<sup>9</sup>.

Also, the reference values for the latest edition of the WHO manual were based on a single sample from each participant<sup>10</sup>. The WHO contradicts itself with such an evidence when it has clearly mentioned in the very same manual that, "a man's semen quality cannot be characterized from a single semen sample"<sup>8</sup>. A semen sample shows high intra-individual variation and therefore categorizing a sample as oligozoospermic based on a single analysis is incorrect.

There are multiple factors which can result in a low sperm count. Loss of portion of sample during collection, days of abstinence, infection, partial obstruction of genital tract, drugs, environmental pollutants and other toxic factors due to unhealthy lifestyle. There are numerous papers stating that the use of cell phones, long periods of watching television and stress could result in decline of sperm count and motility<sup>11</sup>. It has also been reported that oligozoospermia and azoospermia are caused by micro-deletions in the AZF region in the long arm of the Y chromosome, which is related to spermatogenesis<sup>12</sup>.

A man's sperm count is determined by the number of Sertoli cells in his testes, whose number is ascertained early in development i.e. six months before and after birth. As the germ cells develop they depend on Sertoli cells for support, physically and metabolically. However, each Sertoli cell is restricted to support only a certain number of germ cells. So the number of Sertoli cells, which by itself cannot increase after puberty, in each testis determines the overall sperm output. If the testis is exposed to any adverse factors later in life, like toxins, pollutants, disease or drugs, it might result in a drop in the sperm count but nothing can increase it<sup>13</sup>.

Oligozoospermia is not an isolated condition; it is frequently associated with compromised sperm quality, including reduced motility and abnormal morphology, as in oligoasthenoteratozoospermia (OATS). The cause of this is still unknown thereby making the efficacy of any treatment for the same very doubtful.

Male infertility cannot be determined solely on the result of a semen analysis as there is no evidence stating what number and quality of sperm are required for a man to be considered fertile. Oligozoospermia also has to be seen in the context of female fertility as infertility involves the couple and not just the male or female. There is no definite number below which pregnancy is impossible nor is there a number above which pregnancy is certainly possible.

Oligozoospermia (except in extreme cases of occasional sperm in the ejaculate), even in 2014, remains undefined.

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