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PREDICTIVE LIMITS OF WHO SEMEN ANALYSIS FOR REAL FERTILITY OUTCOMES: A CRITICAL APPRAISAL OF DIAGNOSTIC UTILITY IN MALE REPRODUCTIVE MEDICINE

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Abstract

The World Health Organization (WHO) semen analysis remains the cornerstone of male fertility assessment, providing standardized reference values for sperm concentration, motility, and morphology. However, its ability to predict real-world fertility outcomes remains contest. This paper critically evaluates the predictive capacity and limitations of WHO semen analysis in relation to natural conception, assisted reproductive outcomes, and live birth rates. This narrative review synthesizes evidence from epidemiological studies, cohort analyses, meta-analyses, and guideline reports examining correlations between semen parameters and reproductive outcomes. Emphasis is placed on predictive validity, diagnostic thresholds, and clinical applicability. While abnormal semen parameters are associated with reduced fertility, normal WHO-defined values do not reliably predict fertility potential. Significant overlap exists between fertile and infertile populations. Semen analysis demonstrates limited sensitivity and specificity for predicting natural conception and ART success. Functional sperm defects, including DNA fragmentation and oxidative stress, are not captured by routine analysis. WHO semen analysis provides valuable baseline information but has limited predictive power for real fertility outcomes. Its utility lies in screening rather than prognostication. Integration with functional biomarkers and clinical context is necessary to improve diagnostic accuracy and patient management.

Introduction

Semen analysis is used to assess sperm concentration, motility, morphology and volume, and the diagnostic judgmental approach to infertility in women is central to modern reproductive medicine. Semen analysis is widely practiced, but clinicians recognize a fundamental barrier: sperm analysis does not directly impact sperm density. Instead, it provides surrogate markers of reproductive potential. The contrast in laboratory parameters and real

world outcomes, whether it be natural conception, time to pregnancies, or live birth, demonstrates important questions of its predictive validity. The WHO's second manuals, which is currently in its sixth edition, has refined reference limits based on fertile populations. These thresholds are statistical distributions, rather than biologically insignificant. Thus, men known as "normal" may still infertility, and abnormal parameters can provide conception. This review investigates the predictive limitations of WHO semen analysis, the extent to which the analysis offers insights, strengths, weaknesses, and role in modern reproductive medicine.

Conceptual Framework: What Does Semen Analysis Measure?

Parameters and Reference Values

WHO Semen Analysis Evaluates Several Key Parameters:

- Sperm concentration
- Total sperm count
- Progressive motility
- Morphology
- Semen volume

Reference values are derived from men whose partners achieved pregnancy within 12 months, typically representing the 5th percentile of this population.

Statistical Versus Biological Thresholds

A critical distinction must be made between statistical normality and biological fertility. WHO reference limits define the lower boundary of a fertile population, not a threshold for infertility. Thus, these values are inherently probabilistic rather than deterministic.

Predictive Value for Natural Conception
Correlation with Time-to-Pregnancy

Epidemiological studies demonstrate modest correlations between semen parameters and time-to-pregnancy. Higher sperm concentration and motility are generally associated with shorter conception times. However, the relationship is nonlinear and influenced by female factors, coital frequency, and environmental variables.

Overlap Between Fertile and Infertile Populations

A consistent finding across cohort studies is the substantial overlap in semen parameters between fertile and infertile men. Many men with values below WHO thresholds achieve natural conception, while others with normal parameters remain infertile.

This overlap limits the discriminatory power of semen analysis and undermines its predictive precision.

Predictive Value in Assisted Reproduction
Intrauterine Insemination (IUI)

Semen parameters have greater predictive value in IUI than in natural conception. Total motile sperm count is often used to determine eligibility and predict success rates. Nonetheless, even in this context, predictive accuracy remains moderate.

In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI)

In IVF, poor semen parameters may reduce fertilization rates. However, ICSI largely bypasses these limitations by directly injecting a single sperm into the oocyte. As a result, conventional semen parameters have limited predictive value for ICSI outcomes.

Importantly, neither IVF nor ICSI outcomes are reliably predicted by semen analysis alone, particularly with respect to embryo quality and live birth.

Biological Limitations of Semen Analysis
Absence of Functional Assessment

Semen analysis evaluates structural and kinetic properties but does not assess functional competence. Critical processes such as capacitation, acrosome reaction, and sperm–oocyte interaction are not captured.

DNA Integrity and Oxidative Stress

Sperm DNA fragmentation and oxidative stress are key determinants of reproductive success. These factors influence fertilization, embryo development, and miscarriage risk but are not reflected in standard semen parameters.

Heterogeneity of Sperm Population

Ejaculates contain heterogeneous sperm populations with varying functional capacity. Semen analysis provides averaged values, potentially masking subpopulations of dysfunctional sperm.

Clinical Implications

Diagnostic Utility

Semen analysis remains essential as an initial screening tool. It identifies severe abnormalities such as azoospermia, oligospermia, and asthenozoospermia, which have clear clinical implications.

Limitations in Prognostication

For most patients, semen analysis cannot reliably predict fertility outcomes. Clinical decisions based solely on these parameters risk both over-treatment and under-treatment.

Need for Integrated Assessment

Optimal evaluation requires integration of semen analysis with:

- Clinical history and examination
- Hormonal profiling
- Genetic testing
- Advanced sperm function tests

Emerging Alternatives and Adjuncts

Advances in reproductive biology have introduced new diagnostic tools aimed at addressing the limitations of semen analysis. These include:

- Sperm DNA fragmentation assays
- Oxidative stress testing
- Proteomic and metabolomic profiling
- Artificial intelligence–based sperm analysis

While promising, these technologies require further validation before widespread adoption.

Limitations of Recent Evidence

There are some limitations, which impede the use of semen analysis in the literature:

There is heterogeneity of study design; laboratory practices vary; the female factor leads to some of the findings. The result has been that results of these experiments don't yield clear, consistent results that provide us hope to explore semen analysis as a subset of traditional human-beef and other sexual roles.

Future Directions

Future research should focus on:

- Developing composite fertility indices integrating multiple biomarkers
- Longitudinal studies linking semen parameters to live birth outcomes
- Standardization of advanced diagnostic tests
- Incorporation of machine learning for predictive modeling

Such approaches may enhance the predictive accuracy of male fertility assessment.

Conclusion

WHO semen analysis remains a vital model for evaluation of male infertility but it cannot be accurately and effectively predict fertility effects in practice. It is effectively used as a screening instrument but lacks the precision and sensitivity required for accurate prediction. The future of male

fertility evaluation depends on an analysis that integrates conventional variables and functional and molecular biomarkers. In order to validate such concepts, clinicians will have to critically explore semen analysis as a larger clinical domain and understand both its utility and limitations.

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