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INTEGRATED DIAGNOSTIC VALUE OF SEMINAL FRUCTOSE, CITRATE, AND PH IN THE EVALUATION OF MALE INFERTILITY

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Abstract: This narrative review evaluates the diagnostic utility of key biochemical markers in semen analysis—fructose, citrate, and pH—in the assessment of male infertility. Seminal fructose reflects seminal vesicle function, citrate represents prostatic secretory activity, and pH integrates the relative contributions of accessory sex glands while remaining sensitive to inflammatory and preanalytical factors. Through a structured literature review and laboratory-oriented methodological synthesis, we demonstrate that absent or markedly reduced fructose strongly suggests ejaculatory duct obstruction or seminal vesicle agenesis; acidic seminal pH indicates diminished seminal vesicle contribution; and reduced citrate is consistent with prostatic inflammation or secretory hypofunction. Rather than addressing these parameters in isolation, this review highlights their combined diagnostic value in differentiating obstructive azoospermia, low-volume ejaculation, and inflammatory conditions. Analytical variability, preanalytical pitfalls, and the need for harmonization according to the World Health Organization (WHO) laboratory manual are discussed. We conclude that integrated interpretation of fructose, citrate, and pH alongside conventional semen parameters enhances diagnostic accuracy, clinical decision-making, and cost-effectiveness in the evaluation of male infertility.

Keywords: semen analysis, fructose, citrate, pH, seminal plasma, prostate, seminal vesicles, azoospermia, inflammation

Introduction

Male infertility constitutes a major global reproductive health concern, with male-related factors contributing to approximately 40–50% of infertility cases. Although routine semen analysis remains the cornerstone of andrological assessment, conventional parameters—ejaculate volume, sperm concentration, motility, and morphology—often fail to elucidate the underlying etiology. In this context, biochemical markers of seminal plasma provide essential functional information regarding the accessory sex glands, particularly the seminal vesicles and prostate.

Among these markers, seminal fructose, citrate, and pH are the most widely applied in clinical practice. Fructose is synthesized predominantly by the seminal vesicles and serves as a critical energy substrate for spermatozoa. Citrate is secreted by the prostate and reflects its metabolic and secretory function, while seminal pH represents the balance between alkaline seminal vesicle fluid and acidic prostatic secretion. Since the seminal work of T. Mann, fructose has been recognized as a characteristic constituent of seminal plasma, a concept that remains fundamental in modern andrology. This review systematizes the physiological basis, analytical

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considerations, and clinical interpretation of fructose, citrate, and pH, emphasizing their integrated diagnostic significance in male infertility.

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Materials and Methods

Study Design

This study is a narrative review employing a structured methodological approach, focusing on diagnostic interpretation, analytical variability, and clinical integration of seminal fructose, citrate, and pH.

Search Strategy

A comprehensive literature search was performed using PubMed, Scopus, and Google Scholar, covering publications from January 2000 to December 2024. Search terms included combinations of *semen fructose*, *seminal citrate*, *semen pH*, *azoospermia*, *ejaculatory duct obstruction*, *seminal vesicle function*, and *prostatitis biomarkers*.

Inclusion and Exclusion Criteria

Original clinical studies, narrative and systematic reviews, and international guideline documents addressing biochemical semen analysis in adult men were included. Animal studies, isolated case reports, and publications lacking biochemical semen data were excluded.

Analytical Synthesis

Data were synthesized qualitatively using a thematic framework based on gland-specific physiology, reproducible diagnostic patterns, and analytical and preanalytical variability. As the objective was a clinically oriented narrative synthesis rather than a quantitative meta-analysis, PRISMA guidelines were not applied.

Results

Seminal Fructose

The reviewed literature consistently demonstrates that seminal fructose is produced by the seminal vesicles and plays a key role in sperm energy metabolism and seminal alkalinity. Markedly reduced or absent fructose strongly suggests ejaculatory duct obstruction, seminal vesicle agenesis, or severe secretory dysfunction. This finding is classically associated with low ejaculate volume, acidic pH, and azoospermia or severe oligozoospermia. However, incomplete sample collection and other preanalytical errors may mimic this pattern and must be carefully excluded.

Apparent reduction in seminal fructose may also result from continued sperm metabolic activity, particularly glycolysis, during delayed sample processing or prolonged incubation at

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room temperature. This highlights the importance of timely analysis and standardized preanalytical handling to avoid false interpretation of seminal vesicle dysfunction.

Seminal Citrate

Seminal citrate reflects the biosynthetic and secretory activity of the prostate gland. Reduced citrate concentrations are associated with prostatic inflammation, impaired secretory capacity, and increased oxidative stress. Inflammatory processes within the prostate disrupt zinc-dependent mitochondrial enzymes involved in citrate synthesis, leading to reduced citrate secretion into seminal plasma. Preservation of fructose with reduced citrate suggests isolated prostatic pathology, whereas concurrent reduction of both markers indicates more extensive accessory gland dysfunction.

Seminal pH

Seminal pH is an integrative parameter determined by the relative contributions of alkaline seminal vesicle fluid and acidic prostatic secretion. According to WHO guidelines, normal seminal pH ranges from 7.2 to 8.0. Values below 7.2 suggest seminal vesicle dysfunction or ejaculatory duct obstruction, while pH values exceeding 8.0 are commonly associated with inflammatory conditions such as prostatitis or vesiculitis.

Integrated Diagnostic Patterns

Interpretation of fructose, citrate, and pH in combination reveals consistent diagnostic patterns across studies. A characteristic diagnostic triad for ejaculatory duct obstruction consists of low ejaculate volume (<1.5 mL, according to WHO criteria), acidic seminal pH (<7.2), and absent or markedly reduced seminal fructose. When present together in azoospermic or severely oligozoospermic patients, this constellation strongly suggests impaired seminal vesicle emptying due to distal obstruction. These findings should be confirmed after exclusion of preanalytical errors and supported by imaging modalities such as transrectal ultrasound.

Table 1. Integrated interpretation of seminal biochemical markers

Volume	pH	Fructose	Citrate	Likely diagnosis
Low (<1.5 mL)	Acidic (<7.2)	Absent/low	Normal or low	Ejaculatory duct obstruction / seminal vesicle dysfunction
Normal	Normal	Normal	Low	Prostatic inflammation or hypofunction
Normal	Alkaline (>8.0)	Normal	Low	Prostatitis / vesiculitis
Low	Normal	Normal	Normal	Incomplete collection /

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				functional disorder

Discussion

Fructose, citrate, and pH are physiologically interconnected markers that provide complementary insights into accessory gland function. While each parameter has established diagnostic relevance, isolated interpretation may result in diagnostic error. Integrated evaluation improves diagnostic precision, supports targeted investigation, and enhances cost-effective clinical decision-making.

Analytical methodology significantly influences result interpretation. Colorimetric fructose assays remain widely used but are more susceptible to interference and calibration variability than enzymatic methods. Citrate measurements likewise exhibit substantial inter-laboratory variability due to methodological differences, reporting units, and reference ranges. Preanalytical factors—including incomplete ejaculation, delayed analysis, and prolonged exposure to air—further affect results, particularly seminal pH and fructose concentration.

Although the classical triad of low ejaculate volume, acidic pH, and absent fructose remains a valuable indicator of ejaculatory duct obstruction, confirmatory investigations such as transrectal ultrasound are essential to exclude preanalytical artifacts and overlapping inflammatory conditions. Therefore, biochemical semen analysis should always be interpreted in conjunction with clinical findings, imaging studies, and hormonal evaluation.

Limitations

This review has inherent limitations. As a narrative synthesis, it does not provide quantitative estimates of diagnostic accuracy. The included studies demonstrate considerable heterogeneity in analytical methods, reference ranges, and patient populations, limiting direct comparison. Inter-laboratory variability and differences in preanalytical handling further constrain the generalizability of specific cut-off values.

Conclusions

Fructose, citrate, and pH are essential biochemical markers in semen analysis for evaluating accessory gland function. Absence or marked reduction of fructose supports seminal vesicle dysfunction or ejaculatory duct obstruction, acidic pH reflects diminished seminal vesicle contribution, and reduced citrate indicates prostatic hypofunction or inflammation. Integrated interpretation of these parameters improves differential diagnosis of low ejaculate volume and azoospermia, enhances diagnostic efficiency, and supports cost-effective clinical decision-making. Strict adherence to WHO-recommended methodologies and careful control of preanalytical variables are crucial for clinical accuracy. Future research should prioritize analytical harmonization and explore integration of classical seminal plasma biomarkers with emerging approaches such as metabolomics, oxidative stress profiling, and sperm DNA fragmentation indices.

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