



## The Endogenous Effect of Serum and Seminal Omega-3 Fatty Acids on the Sperm Indices of Infertile Males

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### Abstract

Infertility, defined as the inability to achieve pregnancy, affects 10-15% of couples worldwide and presents a significant health challenge. Essential polyunsaturated fatty acids (PUFAs), specifically omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are critical for cellular function, but their roles in male infertility are not well defined. This study investigated serum and seminal EPA and DHA levels and their association with sperm quality in infertile males. A total of 184 men (21–45 years) were recruited and categorized into fertile (n=61) and infertile (n=123) groups. Anthropometric and sexual history data were collected via questionnaires. After three days of sexual abstinence, 3 mL venous blood and semen samples were obtained. Semen analysis complied with WHO guidelines. Serum and seminal EPA and DHA concentrations were quantified using ELISA. Data analysis was performed in SPSS v22 with  $p < 0.05$  as the significance threshold. Infertile men exhibited significantly lower serum EPA ( $142.33 \pm 18.30 \mu\text{g/mL}$ ) and DHA ( $10.74 \pm 4.90 \mu\text{g/mL}$ ) compared to fertile controls (EPA:  $157.69 \pm 35.17 \mu\text{g/mL}$ ; DHA:  $11.90 \pm 3.24 \mu\text{g/mL}$ ;  $p < 0.05$ ). Seminal EPA and DHA were also reduced in infertile males (EPA:  $142.18 \pm 10.81$  vs.  $160.31 \pm 26.78 \mu\text{g/mL}$ ; DHA:  $10.97 \pm 1.15$  vs.  $13.13 \pm 2.03 \mu\text{g/mL}$ ;  $p < 0.05$ ). Sperm immotility was elevated in infertile men ( $p < 0.01$ ). Serum EPA strongly correlated with serum DHA ( $r = 0.871$ ,  $p < 0.001$ ) and inversely with sperm immotility ( $r = -0.309$ ,  $p < 0.049$ ). Seminal DHA correlated positively with seminal EPA ( $r = 0.374$ ,  $p < 0.01$ ) and inversely with systolic blood pressure ( $r = -0.458$ ,  $p < 0.032$ ). Blood pressure measures also associated inversely with sperm immotility. These findings suggest that reduced EPA and DHA levels may impair sperm function, contributing to male infertility. Routine assessment and supplementation of these fatty acids could enhance semen quality and reproductive outcomes.

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### Introduction

The inability to achieve a successful pregnancy after 12 months or more of regular, unprotected sexual intercourse, known as infertility, impacts about one in seven couples (Nsabimana *et al.*, 2024). Male factors contribute to approximately 40% of infertility cases, with diminished semen quality being a primary cause (Eisenberg *et al.*, 2023). A decline in human semen quality and overall fertility rates over recent decades suggests a future increase in demand for fertility treatments (Skakkebaek *et al.*, 2022). There is a widespread belief that increased consumption of polyunsaturated fatty acids (PUFAs) could enhance various indicators of male fertility, with research, such as findings by Rodak and Kratz (2023), highlighting their potential benefits in reproductive health. Polyunsaturated fatty acids (PUFAs) are classified as essential fatty acids (EFAs), meaning they are vital for

human health but cannot be synthesized by the body and must, therefore, be obtained through dietary sources. Among these important fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These specific PUFAs play crucial roles in various physiological functions, including maintaining cellular membrane flexibility (Mukerjee *et al.*, 2023). However, it has become increasingly recognized that specific long-chain omega-3 fatty acids (3FAs), particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), may exert their effects through more structured and organized pathways. DHA, a notable long-chain omega-3 fatty acid, is found in high concentrations in certain marine fishlike salmon and mackerel, as well as in various green plants, seeds, herbs, nuts, and oils. Fish synthesize very little EPA from dietary ALA (Hrebien-Filisińska, 2021). Humans require ALA, an

essential fatty acid, and convert some to EPA, but this conversion is much less efficient than direct EPA absorption (Wang *et al.*, 2024). Ensuring sufficient EPA is harder on diets lacking preformed EPA/DHA due to extra metabolic work, and conditions like diabetes or allergies can limit EPA metabolism from ALA (Baker *et al.*, 2025).

One of DHA's key attributes is its powerful antioxidant properties. These properties are essential for counteracting oxidative stress, a condition that can damage sperm cells and negatively impact male fertility. DHA enhances the body's antioxidant defenses, thereby providing protection against oxidative stress and ultimately supporting improved reproductive outcomes (Borgonovi *et al.*, 2023).

One of the primary ways in which omega-3 and omega-6 PUFAs influence spermatogenesis the process of sperm production and development, is through their incorporation into the cell membranes of spermatozoa. These PUFAs serve as crucial structural components of the cell membranes, contributing to their integrity and overall function (Islam *et al.*, 2023). The lipid bilayer structure of cell membranes relies heavily on the presence of these polyunsaturated fatty acids, as they provide flexibility and fluidity, enabling the membrane to function effectively (Harayama and Antonny, 2023). The significance of lipids in the sperm membrane cannot be overstated, as they are integral to the successful fertilization process. The interactivity of sperm with the oocyte, for instance, is facilitated by the properties of the sperm membrane lipids (Suhaiman and Belmonte, 2024). Additionally, the specific omega-3 fatty acid ratio within the membrane of sperm cells is crucial for preserving normal sperm integrity, viability, and overall functionality (Yuan *et al.*, 2023). Despite increasing understanding, little is known about comparing serum and seminal omega-3 fatty acid levels and their potential role in male infertility. Hence, this study will compare the levels and the impact of serum and seminal omega-3 fatty acids on the sperm quality of males with infertility.

## Materials and Methods

### Study Design

The fertility clinic at Osun State Teaching Hospital in Osogbo, Osun State, Nigeria, was selected as the site for this cross-sectional study on male infertility due to its high patient volume and accessibility for recruiting participants. The study aimed to investigate factors associated with male infertility

### Ethical Approval

Prior to the commencement of this study, comprehensive ethical clearance was obtained from the University of Osun Teaching Hospital (UNIOSUN

Teaching Hospital) Ethical Review Committee. This crucial approval, vital for all research involving human participants, confirms that the study protocol adheres to rigorous national and international ethical guidelines, including the principles of the Declaration of Helsinki. It specifically ensures the safeguarding of participant rights, welfare, and confidentiality. The official protocol identification number assigned to this ethical approval is UTH/REC/2024/06/967, issued in June 2024.

### Study Population

The study included two groups of male participants: infertile males (cases), diagnosed with infertility according to World Health Organization (WHO) criteria [19] via semen analysis and clinical evaluation at the Osun State Teaching Hospital fertility clinic; and age-matched fertile males (controls), whose fertility was proven by having fathered a child within the past two years.

## Inclusion and Exclusion Criteria

### Inclusion Criteria

Patients included in this study were married men aged 21 - 45 years with regular unprotected sex without conception, oligospermic and azoospermic infertile males with absence of any surgical history regarding the reproductive system and body mass index (BMI) in between 19 and 26 kg/m<sup>2</sup>.

### Exclusion Criteria

The study excluded those with a history of radiotherapy, chemotherapy, chronic illness or medication, injectable hormonal contraception, apparent abnormality in the reproductive system revealed by their medical history, clinical examinations, as well as those whose testis have been surgically removed and those who are not married according to the questionnaire administered.

### Sample Size Calculation

The study recruited a total of 184 participants, consisting of 121 infertile men (cases) and 63 age-matched fertile men (controls). This cohort size significantly exceeded the initial minimum of 72, which was determined using Leslie Fischer's sample size formula with a 5% infertility prevalence and an additional 10% calculated for attrition.

### Data Collection

Participant selection involved screening based on pre-defined inclusion and exclusion criteria. Eligible individuals were thoroughly informed about the study's purpose, procedures, potential risks, and benefits in both English and Yoruba. Before enrollment, all participants provided written informed consent. Data were subsequently collected via a structured questionnaire and semen analysis.

**Specimen Collection, Preparation and Storage**

Three milliliters (3 mL) of venous blood were obtained from the subjects. Blood was collected into plain bottles. The blood samples were allowed to clot, on centrifugation at 3000 revolutions per minute (rpm) for 10 minutes, the serum was separated and stored at  $-20^{\circ}\text{C}$ . Aliquots of the samples were analyzed for EPA and DHA fatty acids, follicle-stimulating hormone, luteinizing hormone, prolactin and testosterone.

**Semen Collection**

Subjects and controls were requested to observe a three (3) day period of abstinence. The collection of the semen was done by coitus or masturbation. The semen was sent to the laboratory for analysis.

**Semen Analysis**

Microscopic analyses for seminal fluid analysis (SFA) were carried out within 30 minutes of collection to ensure the accurate analysis of the semen. The semen was separated by centrifugation at 3000 revolutions per minute (rpm) for 10 minutes the plasma was separated and stored at  $-20^{\circ}\text{C}$ . The seminal plasma was separated and stored at  $-20^{\circ}\text{C}$  before biochemical analysis. Seminal volume, total sperm cell count, motility, morphology, and viability were evaluated according to the methods and standards outlined by the WHO (2010).

**Biochemical Analysis****Serum and Seminal Human EPA and DHA Analysis**

Method: Enzyme-linked immunosorbent assay (ELISA)

Product Name: Human Eicosapentaenoic Acid (EPA) ELISA Kit (CAT. NO: EKHU-3104) and Docosahexaenoic Acid (DHA) ELISA Kit (CAT. NO: EKHU-3103). Melsin Medical Co., Limited, China.

**Principle of the Test**

The microtiter plate provided in this kit has been pre-coated with antibody. Add standard, samples and HRP-conjugated antibody to wells. After incubation and washing to remove the uncombined enzyme, add Chromogen solutions A and B. The colour of the

liquid will change to blue. At the presence of acid, the colour finally becomes yellow. The colour change is measured spectrophotometrically at a wavelength of 450nm. The concentration of the marker (TNF- $\alpha$  or IL-10) in the samples is then determined by comparing the optical density of the samples to the standard curve.

**Test Procedure**

Before commencing the assay procedure, all reagents were prepared. 50  $\mu\text{L}$  of standards were added to the standard wells, followed by the sequential addition of 10  $\mu\text{L}$  of the test sample and 40  $\mu\text{L}$  of sample diluent to the test sample wells. Subsequently, 100  $\mu\text{L}$  of HRP-conjugate reagent was introduced into each well, which was then covered with an adhesive strip and incubated for 60 minutes at  $37^{\circ}\text{C}$ . Following this incubation, the washing process, aspirating and washing a total of five times by filling with 400  $\mu\text{L}$  of Wash Solution using an auto washer. After the final wash, any remaining solution was removed by decanting, and the plate was inverted and blotted against clean paper towels to ensure dryness. Next, 50  $\mu\text{L}$  of chromogen A and B were added, respectively, to each well, gently mixed, and incubated for an additional 15 minutes at  $37^{\circ}\text{C}$ . Finally, 50  $\mu\text{L}$  of Stop Solution was added to each well before the optical density was read at 450 nm using a microtiter plate reader within 15 minutes.

**Results****Demographic Indices**

Table 3.1 shows the anthropometric values in infertile and fertile subjects. The mean age of infertile men ( $36.50 \pm 6.42$ ) and fertile males ( $36.24 \pm 10.98$ )  $p < 0.069$ . The mean value of systolic blood pressure in the infertile group ( $123.62 \pm 7.08$ ) and fertile men ( $123.44 \pm 9.51$ ) which falls within the WHO normal range (110-140mmHg), diastolic blood pressure in infertile men ( $77.15 \pm 5.25$ ) and fertile ( $76.06 \pm 5.78$ ) (70-90mmHg), body mass index of infertile men ( $23.92 \pm 2.86$ ) and fertile men ( $< 30$ ). However, the values in infertile and fertile controls were significantly different.

Table 3.1: The comparison of anthropometric indices of infertile and fertile male

Anthropometric Indices	Infertile Male Mean $\pm$ SD	Fertile Male Mean $\pm$ SD	P-Value
<b>AGE (yr)</b>	36.50 $\pm$ 6.42	36.24 $\pm$ 10.98	0.069
<b>Body Mass Index (BMI) (Kg/m<sup>2</sup>)</b>	28.49 $\pm$ 7.31	23.42 $\pm$ 2.76	1.000
<b>Systolic Blood Pressure (mmHg)</b>	123.62 $\pm$ 7.081	123.44 $\pm$ 9.513	0.133
<b>Diastolic Blood Pressure (mmHg)</b>	77.15 $\pm$ 5.25	76.06 $\pm$ 5.78	0.29

Significant difference ( $p < 0.05$ )

KEY: Kilogram per meter square (Kg/m<sup>2</sup>), Year (yr), Millimeter Mercury (mmHg)

**The Percentage of Sperm Immotility in Fertile and Infertile Males**

Table 3.2 illustrates a significant difference in sperm immotility between the study groups. The percentage or prevalence of immotile sperm was significantly elevated in infertile males in contrast with the fertile

group ( $p < 0.01$ ). This disparity indicates that a deficiency in sperm's ability to move is a key characteristic setting apart infertile men, pointing towards its profound impact on reproductive capacity

Table 3.2: The Percentage of Sperm Immotility in Fertile and Infertile Males

Sperm parameter	Infertile Male Mean $\pm$ SD	Fertile Male Mean $\pm$ SD	P-Value
Immotility	48.92 $\pm$ 2.79	35.39 $\pm$ 7.25	0.000 <sup>#</sup>

<sup>#</sup>Significant difference ( $p < 0.01$ )

**The levels of Serum and Seminal Omega-3 Fatty Acids in Fertile and Infertile Males**

Data presented in Table 3.3 indicate a significant difference in circulating fatty acid profiles between infertile and fertile male populations. Specifically, serum concentrations of eicosapentaenoic acid (EPA) were found to be significantly lower in the infertile male compared to the fertile control subjects ( $p <$

0.05). While a trend for decreased serum docosahexaenoic acid (DHA) was also observed in infertile males, this difference did not achieve statistical significance. Consistent with the systemic findings, analysis of seminal plasma demonstrated a significant reduction in the levels of both EPA and DHA in infertile males when compared to fertile controls ( $p < 0.05$ ).

Table 3.3: Mean  $\pm$  standard deviation of the levels of serum and seminal EPA and DHA in fertile and infertile males

Parameters	Fertile Male Mean $\pm$ SD N = 61	Infertile Male Mean $\pm$ SD N = 123	F-value	P-value
Serum DHA ( $\mu\text{g/mL}$ )	11.91 $\pm$ 3.24	10.74 $\pm$ 4.90	0.017	0.896
Serum EPA ( $\mu\text{g/mL}$ )	157.69 $\pm$ 35.17	142.33 $\pm$ 18.30	7.582	0.009*
Seminal DHA ( $\mu\text{g/mL}$ )	13.13 $\pm$ 2.03	10.99 $\pm$ 1.15	9.276	0.004*
Seminal EPA ( $\mu\text{g/mL}$ )	160.31 $\pm$ 26.78	142.18 $\pm$ 10.81	4.339	0.044*

\*Significant at the  $P < 0.05$  level.

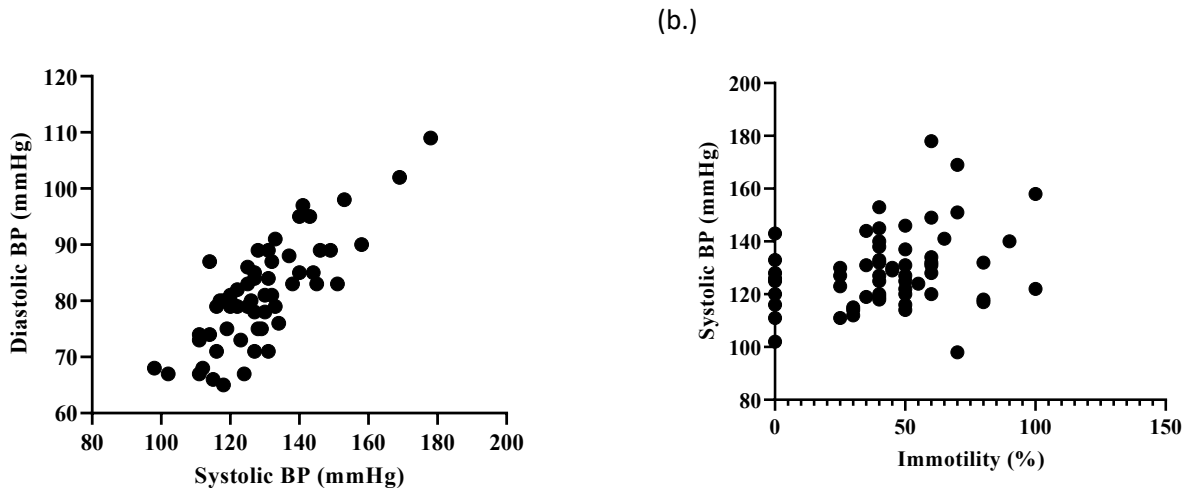
Key: EPA– Eicosapentaenoic Acid; DHA – Docosahexaenoic Acid

**The Correlation between Systolic, Diastolic Blood Pressure and Sperm Immotility**

In the context of blood pressure dynamics, Figure 3.3a-b graphically illustrates a compelling relationship: Figure 3.3a systolic blood pressure (SBP) and diastolic blood pressure (DBP) show a linear relationship with a strong positive correlation ( $r = 0.79$ ,  $p < 0.0001$ ). The correlation coefficient ( $r$ ) of 0.790 indicates that approximately 62.4% of the variability in one measure can be explained by the variability in the other, highlighting a very close relationship. The exceptionally low  $p$ -value ( $p < 0.0001$ ) reveals that this observed association is highly statistically reliable. This correlation underscores the pathophysiological mechanisms of arterial pressure

regulation, suggesting that this strong interdependence between SBP and DBP is critical for understanding cardiovascular health and disease progression, implying that factors affecting one often influence the other.

As detailed in Figure 3.3b, a statistically significant inverse correlation was observed between systolic blood pressure and sperm immotility. The Pearson product-moment correlation coefficient ( $r = -0.293$ ) indicates a weak-to-moderate negative linear association. The statistical significance of this relationship ( $p < 0.022$ ) suggests that the likelihood of observing such a correlation is less than 2.2%.



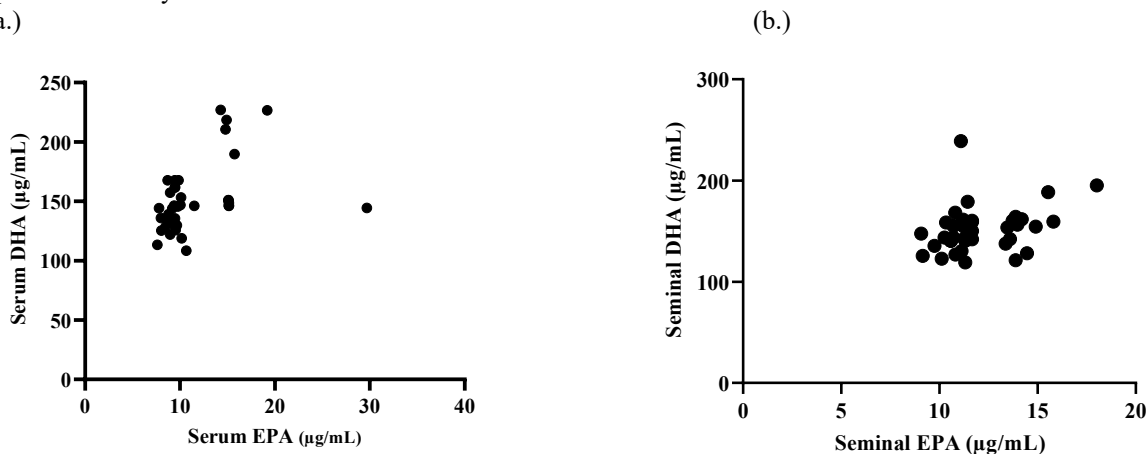
Figures 3.1a and b: A scattered dot shows the correlation between (a.) the systolic blood pressure and diastolic blood pressure (b.) the systolic blood pressure and sperm immotility

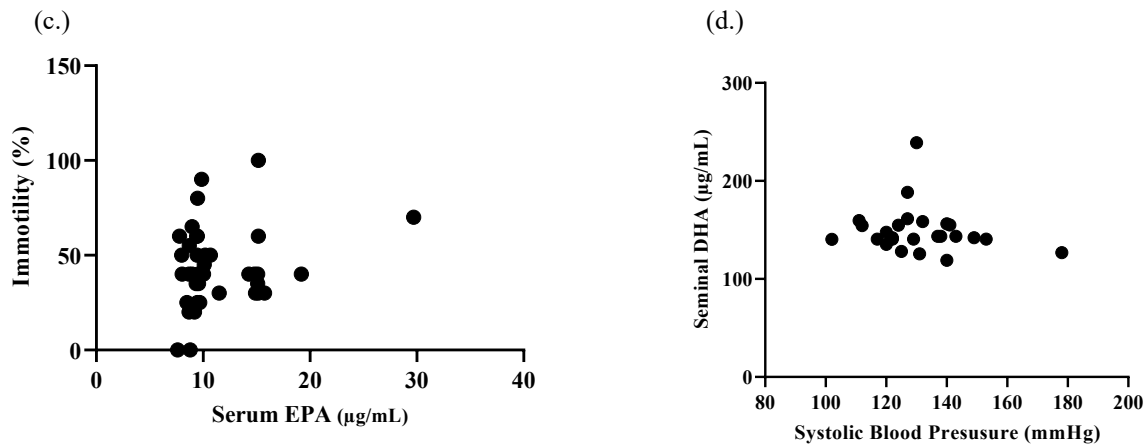
**The Correlation of Omega 3 FA (EPA & DHA), Systolic Blood Pressure and Immotility**

Figure 3.2a-d provides insights into the relationships between key fatty acids in different biological samples. Figure 3.4a illustrates a significant positive linear correlation between serum EPA and serum DHA concentrations, with a moderate association strength quantified by a Pearson correlation coefficient ( $r$ ) of 0.429 and a high statistical significance ( $p < 0.006$ ). Complementing this, Figure 3.2b further demonstrates a positive linear correlation between seminal EPA and seminal DHA levels, suggesting a similar interconnectedness within seminal fluid, although with a slightly weaker correlation coefficient of  $r = 0.322$ , which is still statistically significant ( $< 0.040$ ).

Figure 3.2c represents a statistically significant inverse correlation between blood levels of Eicosapentaenoic Acid (EPA), an essential omega-3 fatty acid, and sperm immotility. This means that individuals with

higher serum concentrations of EPA tend to exhibit a lower percentage of non-motile sperm. The observed correlation coefficient ( $r = 0.309$ ) quantifies this moderate association, and its  $p < 0.049$  confirms that this relationship is statistically significant, suggesting a beneficial role for EPA in supporting male reproductive health. Figure 3.2d illustrates a statistically significant inverse correlation between the presence of seminal docosahexaenoic acid (DHA) and systolic blood pressure. The correlation coefficient ( $r = 0.458$ ) represents a moderately strong negative relationship, and the  $p$ -value ( $p < 0.032$ ) confirms that this observed association is statistically significant and unlikely to be due to random chance, suggesting a potential physiological link between seminal DHA levels and cardiovascular health.





Figures 3.2a and: A scattered plot of the correlation: (a.) serum DHA and EPA, (b.) the seminal DHA and EPA, (c.) serum EPA and sperm immotility, and (d.) seminal DHA and systolic blood pressure  
Key: EPA– Eicosapentanoic Acid; DHA – Docosahexaenoic Acid

### Discussion

The steady decline in human semen quality and overall fertility rates seen over recent decades indicates a growing demand for fertility treatments. Most common issues are related to sperm production, maturation, transport, or function (Sengupta *et al.*, 2023). Polyunsaturated fatty acids (PUFAs) attract significant interest due to their vital role in human health. Since the body cannot produce them, they must be obtained through diet for physiological processes, especially in maintaining the flexibility of cell membranes (Ali and Szabó, 2023). The potential role of essential polyunsaturated fatty acids (PUFAs) in addressing the observed decline in human semen quality and overall fertility was extensively addressed in this study.

In this study, we observed that the percentage of immotile sperm was significantly elevated in infertile males in contrast with the fertile group. The present finding directly implicates sperm immotility as a primary contributor to male infertility. This is consistent with a vast body of existing literature, meta-analyses, and clinical guidelines that have consistently demonstrated a strong negative correlation between immotility/poor motility and infertility (Dcunha *et al.*, 2022; Chakraborty and Saha, 2022). Certain conditions, such as varicocele (Agarwal *et al.*, 2022), excessive seminal oxidative stress (Takeshima *et al.*, 2021), and certain genetic mutations affecting flagellar development (Pereira and Sousa, 2023) compromise sperm motility, leading to an increased percentage of immotile or non-progressively motile sperm. This

aligns perfectly with the current finding, suggesting that the infertile male in this study likely suffered from one or more of these underlying conditions contributing to their elevated sperm immotility.

A significant and strong correlation between SBP and DBP observed in this study corresponds with well-established findings in cardiovascular physiology that systolic blood pressure (SBP) is significantly and strongly correlated with diastolic blood pressure (DBP) (Perman *et al.*, 2024). This strong positive correlation is physiologically intuitive given that both measures are dynamic components of the same cardiac cycle and arterial pressure within the circulatory system. Both SBP and DBP are influenced by cardiac output and systemic vascular resistance (Sinha and Chowienczyk, 2023; Lu *et al.*, 2022). Changes in arterial elasticity, a common feature of aging and conditions like atherosclerosis, also profoundly affect both pressures, often leading to a wider pulse pressure (Day, 2021; Cunha and Olsen, 2024).

Our finding of a statistically significant inverse correlation between systolic blood pressure and sperm immotility presents an intriguing link between cardiovascular health and male reproductive function. This suggests that higher SBP (within a healthy range) is associated with better sperm motility. This is consistent with Alawamlh *et al.* (2020), who reported that adequate systemic blood pressure is essential for optimal perfusion of all organs, including the testes and epididymis, which are critical sites for spermatogenesis and sperm maturation, respectively. Optimal blood flow ensures the delivery of necessary

nutrients, oxygen, and hormones, while facilitating the removal of metabolic waste products, all of which are crucial for healthy sperm development and function (Rotimi *et al.*, 2024; Chen *et al.*, 2025; Kumar *et al.*, 2025). Lower SBP, indicating reduced systemic perfusion or underlying cardiovascular compromise, might lead to suboptimal conditions in the male reproductive organs, potentially impairing sperm motility (Akinloye *et al.*, 2014; Salvio *et al.*, 2022). Common underlying factors that influence both blood pressure regulation and reproductive health, such as lifestyle choices (diet, exercise, smoking, alcohol consumption) and hormonal profiles, could serve as mediating or confounding variables (Rotimi and Singh, 2024; Tesarik, J., 2025).

The findings of this study showed that both serum and seminal levels of EPA and DHA are significantly lower in infertile males compared to fertile controls. This aligns with Abdollahzadeh *et al.* (2023); Chen *et al.* (2023); Amirjannati *et al.* (2025), and Henkel *et al.* (2025), who reported that DHA concentrations were significantly reduced in the sperm and seminal plasma of oligoasthenoteratozoospermic (infertile) men compared to normozoospermic controls. Similarly, Almujaaydil, M. S. (2023) demonstrated that infertile men had lower seminal and sperm fatty acid content, including EPA and DHA, compared to fertile men. EPA and DHA are integral components of cell membranes, particularly those of spermatozoa, crucial for maintaining optimal membrane fluidity, which is essential for key sperm functions such as motility, capacitation, and the acrosome reaction (Naz *et al.*, 2022). The deficiency suggests a compromised overall fatty acid profile that may directly impair spermatogenesis and sperm function.

Adequate systemic EPA levels could be a protective factor against male infertility associated with poor sperm motility (Rodriguez-Martinez *et al.*, 2021). Consistent with our findings that showed an inverse correlation between seminal EPA and sperm immotility, this highlighting a crucial link between systemic omega-3 status and male reproductive health. This finding aligns with growing evidence supporting the beneficial role of n-3 PUFAs in male reproductive health and sperm quality (Safarinejad M. R. 2011; Yuan *et al.*, 2023; Abdollahzadeh *et al.*, 2023; Hosseini *et al.*, 2021). A systematic review by Haeri *et al.* (2023) and Ghewade *et al.* (2024) collectively reported that PUFA improves sperm parameters (sperm motility and morphology). Spermatozoa membranes are exceptionally rich in polyunsaturated fatty acids (PUFAs), particularly DHA, which are critical for maintaining membrane fluidity, integrity, and the subsequent processes of sperm motility, capacitation, and fertilization (Moretti and Collodel,

2025). While DHA is more directly incorporated into sperm phospholipids and plays a predominant structural role, systemic EPA levels may influence the overall fatty acid composition, reduce oxidative stress, and modulate inflammatory pathways within the epididymal and testicular environments, thereby indirectly supporting optimal sperm function and reducing the proportion of non-motile sperm (Wang *et al.*, 2025; Naz *et al.*, 2022). These observations and review findings indicate that the presence of adequate EPA within seminal plasma is beneficial, directly contributing to enhanced sperm kinematic characteristics and a desirable reduction in the proportion of immotile spermatozoa, ultimately underscoring its pivotal role in male reproductive competence.

In this study, seminal DHA inversely correlates with systolic blood pressure. This finding aligns with an extensive body of literature demonstrating the cardioprotective effects of n-3 PUFAs, including their established role in blood pressure regulation (Zec *et al.*, 2019; Zhang *et al.*, 2022; Zhou and Wei, 2023). Although this correlation is observed with seminal DHA, it likely reflects a broader systemic benefit. Individuals with higher dietary intake and circulating levels of DHA, who typically exhibit lower blood pressure, also have these beneficial fatty acids present in their seminal fluid (Ferramosca and Zara, 2022). This highlights the systemic impact of n-3 PUFAs on overall physiological health, which extends beyond specific organ systems and reflects a holistic state of well-being.

A significantly positive correlation between serum eicosapentaenoic acid (EPA) and serum docosahexaenoic acid (DHA) ( $p < 0.01$ ) was observed in this study, which is consistent with prior findings of Hosseini *et al.* (2019). Both are key long-chain omega-3 fatty acids, primarily derived from dietary sources like fatty fish or supplements, and share common metabolic pathways, notably through desaturation and elongation processes, and contribute synergistically to anti-inflammatory and cardiovascular benefits (Glencross *et al.*, 2025). This strong relationship suggests that interventions aimed at increasing one are highly likely to simultaneously elevate levels of the other in systemic circulation, reinforcing their combined beneficial effects on overall lipid profiles and cellular membrane fluidity (Patted *et al.*, 2024). Seminal EPA/DHA levels directly impact sperm quality. In spermatogenesis, seminal EPA/DHA aids the function of Sertoli cells, which support germ cells, and Leydig cells, which produce testosterone (Ri *et al.*, 2022; Yuan *et al.*, 2023). Its levels provide the immediate, direct environment for spermatozoa membrane composition and metabolic processes

(Rodriguez *et al.*, 2021). It was also observed in this study, a significant positive correlation exists between seminal docosahexaenoic acid (DHA) and seminal eicosapentaenoic acid (EPA) within the seminal compartment. These localized concentrations of the fatty acids are vital for protecting spermatozoa from oxidative stress, as sperm possess a high polyunsaturated fatty acid (PUFA) content and limited intrinsic defence mechanisms (Aitken *et al.*, 2022; Wang *et al.*, 2025; Rodak and Kratz, 2023). This observation aligns with several studies that demonstrate inherent associations among various n-3 PUFAs across different physiological compartments and reproductive fluids, indicating a systemic integration of their metabolism and functional roles (Chen *et al.*, 2023). The body converts EPA into DHA through elongation and desaturation steps, or retroconverts DHA to EPA (Mensah, M. A., 2024; Moustafa, A., 2021). This bidirectional metabolic pathway establishes a continuous interplay and equilibrium between EPA and DHA, directly explaining why their concentrations within the seminal fluid exhibit a significant positive correlation (Vashisht and Gahlay, 2024; Chen *et al.*, 2025). Adequate levels of n-3 PUFAs are essential for maintaining the integrity of the blood-testis barrier, which prevents systemic DHA/EPA (from serum) from accurately reflecting the specific concentrations available locally (Abdollahzadeh *et al.*, 2023; Moretti and Collodel, 2025). This finding suggests a coordinated presence and potential interdependency of these two crucial omega-3 polyunsaturated fatty acids (n-3 PUFAs) within male reproductive fluids.

### Conclusion

This study conclusively demonstrates that infertile males have significantly lower systemic and seminal levels of EPA and DHA, essential polyunsaturated fatty acids critical for optimal sperm function and cellular integrity. These deficiencies directly correlate with impaired sperm motility and overall male reproductive health, while also reflecting broader systemic benefits like blood pressure regulation. Therefore, integrating dietary interventions or supplementation with EPA and DHA should be considered a viable and beneficial strategy to enhance semen quality and support fertility in men. Further clinical investigations are recommended to establish optimal dosage and long-term efficacy of n-3 PUFA supplementation in male infertility management.

### Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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