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Research Article

Immunomodulation, Hormonal Imbalance related to Bisphenol A induced Male Infertility

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Abstract

Background: Male infertility has several etiologies, including immunological diseases. Environmental factors affect the immune system and fertility conditions. Idiopathic male infertility is defined by altered semen parameters without a cause and no female factor infertility. Growing evidence suggests the immune system may independently contribute to male infertility.

Methods: Blood and seminal fluid samples were obtained from 90 men, including 30 healthy controls and 60 infertile male patients with no reported gynecological abnormalities in their partners. The Enzyme-Linked Immunosorbent Assay (ELISA) technique was used to estimate the concentration of serum total Bisphenol A (BPA), interleukin-1 beta (IL-1β), anti-sperm antibodies-immunoglobulin A (ASA-IgA), and F2-isoprostanes (F2-IsoPs). Hormone levels were analyzed using Cobas e-411.

Results: Significant differences ($p < 0.05$) were observed in BPA, IL-1β, ASA-IgA, F2-IsoPs, and estradiol (E2) levels, with higher mean values in infertile males, while testosterone levels were reduced. Semen parameters showed significantly lower mean values among patients compared to controls. A strong positive correlation was found between BPA and testosterone levels. IL-1β demonstrated significant positive correlations with E2, F2-IsoPs, and the LH/FSH ratio, and a negative correlation with testosterone. Luteinizing hormone (LH) showed a significant positive relationship with follicle-stimulating hormone (FSH). ASA-IgA was positively correlated with F2-IsoPs and IL-1β, but negatively correlated with testosterone. Receiver Operating Characteristic (ROC) analysis revealed high diagnostic accuracy for IL-1β and F2-IsoPs (AUC ≈ 0.74).

Conclusions: BPA exposure may induce autoimmune and oxidative mechanisms leading to male infertility via endocrine-immune crosstalk.

Keywords: Anti-sperm antibody, Bisphenol A, Interlukine-1β, Hormones, Infertility, Oxidative stress.

Introduction

Male infertility has multiple causes, including autoimmune diseases, environmental factors, and infections [1]. Exposure to Bisphenol A (BPA) has been associated with adverse effects on male fertility and reproductive health. Previous research has demonstrated that BPA interferes with hormonal balance, disrupting testicular function and sperm dynamics, and may induce the formation of anti-sperm antibodies (ASA), thereby reducing male fertility. The impact of serum BPA on oxidative stress (OS) and ASA-IgA levels can influence sperm concentration and motility [2-4].

Sperm cells act as both autoantigens and an alloantigen that is found in the human begins. Therefore, it is essential to have effective immunotolerance mechanisms when exposed to the immune system to maintain its fertility potential [4]. The presence of BPA in serum and ASA-IgA in the seminal plasma can activate the immune system, causing sperm agglutination and lysis [5]. BPA exposure may chemically modify sperm antigens-proteins located on the sperm cell surface-making them appear foreign to the immune system and triggering ASA formation [5]. Moreover, BPA has been shown to damage the blood-testis barrier (BTB) by increasing OS and modifying tight junction proteins. This damage

exposes previously hidden sperm antigens to immune recognition, initiating autoimmune reactions and ASA production [6].

Sperm immunotolerance is maintained through complex regulatory mechanisms, primarily governed by cytokines and endocrine interactions [7]. Elevated cytokine levels, particularly IL-1β, have been linked to testicular inflammation and impaired spermatogenesis. Abnormally high IL-1β levels, such as in inflammatory conditions, can negatively affect sperm development and function [8].

Furthermore, inflammation is closely associated with OS, which is well documented to impair sperm function [9]. F2-IsoPs are regarded as the most reliable biomarkers of lipid peroxidation and are widely used to assess oxidative state in various clinical conditions. The detection of F2-IsoPs in seminal plasma and sperm membranes reflects the extent of lipid peroxidation in male infertility. Oxidative stress and inflammation are interlinked, and elevated F2-IsoPs indicate enhanced lipid peroxidation, which can damage the sperm nucleus and trigger apoptosis, ultimately compromising fertility [10].

Sex hormones, such as testosterone, estradiol (E2), luteinizing hormone (LH), and follicle-stimulating hormone (FSH), play a crucial role in male reproductive health. Testosterone governs spermatogenesis and reproductive function, whereas E2, LH, and FSH orchestrate testicular activity and sperm generation. Environmental variables, like BPA, oxidative stress, or immune-mediated influences, might disrupt these hormones, hence diminishing sperm quality and contributing to male infertility. Understanding these hormonal interactions is crucial for elucidating the pathways that contribute to idiopathic infertility in males [11].

In this study, our objective is to identify BPA-associated factors that contribute to autoimmune male infertility and associated risk factors. This study hypothesized that chronic BPA exposure disrupts male fertility by modulating immune cytokines, enhancing oxidative stress, and disturbing gonadal hormonal balance.

Materials and Methods

Study Design

The specimens for the current case-control study were collected from infertile men from Erbil City at the Center for *In Vitro* Fertilization (IVF) from August 2024 to March 2025. The current study randomly recruited a total of 105 participants and assessed them using a questionnaire. Fifteen patients were excluded from the analysis at the beginning because they had a history of diseases that could potentially affect the results, semen quality, and quantity. Sixty idiopathic infertile men from urban areas were selected, and fasting men participated in the control group. The demographic characteristics of the 60 idiopathic infertile men, with a range of ages from 21 to 46 years. There were no reported gynecological abnormalities in their partners. Thirty people from rural areas, who had been previously warned to fast for 8 hours, were less exposed to plastic and had better environmental conditions, and participated in the control group. The participants had an age range of 21 to 46 (Table 1).

Sample Collection and Laboratory Assays

During sample collection, to avoid contamination with plastic and BPA, the collected blood was used in a Vanishpoint tube for blood collection and then transferred directly into glass tubes, without using any plastic tools. For centrifugation, glass gel tubes were used, and all samples were kept in specialized glass tubes at temperatures ≤−24 °C. Additionally, for seminal fluid collected by masturbation, the abstinence rate of sexual intercourse was between 2 and 7 days, and the WHO (2021) manual seminal fluid examination reference values were used for the following procedures, handling, and analysis parameters: semen volume, sperm concentration, motility, and morphology [12].

The serum total BPA concentration was measured using a BPA ELISA kit (ELK Biotechnology, China) in accordance with the manufacturer's instructions (ELK8383). The assay range for serum total BPA is 1.25-80 ng/mL. This kit includes a pre-coated microtiter plate with an antibody specific to BPA [13]. Following the instructions that came with ELISA kits from SunLong Biotech Co. Ltd. (China) [14]. Semen plasma was stored and processed according to the plasma sperm ASA-IgA (SL4475Hu) ELISA kit. The assay range for ASA-IgA is 44.8-4000 pg/mL, the assay range for cytokine serum IL-1β (SLD001Hu) is 3.9-250 pg/mL, and the assay range for serum F2-isoprostanes (SL3468Hu) is 10-420 ng/L [14]. Roche Diagnostics used an automatic immunochemistry analyzer (Cobas e-411, Roche, Germany) to measure hormone levels. The assay range for testosterone is 2.49 to 8.35 ng/mL, the assay range for E2 is 10-40 pg/mL, the assay range for LH is 1.3 to 8.0 mIU/mL, and the assay range for FSH is 1.5-12.4 mIU/mL [15].

Ethical Approval

It was determined by the medical ethics committee of Erbil Polytechnic University, Iraq, that the technique of the study was appropriate (the authorization number for the study was 24/0045 HR in 23 December 2024). In addition, verbal consent was collected from every participant.

Data Analysis

The data were analysed using GraphPad Prism Software Version 9.5.1, USA. For the ROC curve, normality of data was tested using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Both tests indicated non-normal distribution ($p < 0.05$) in both infertile and fertile groups; therefore, the Mann–Whitney U test was applied for group comparisons. Spearman's correlation was employed to assess the differences among the variant groups. A p-value ($p < 0.05$) was considered statistically significant, and all data are presented as mean ± standard deviation (SD) for the compared biomarkers. The chi-square test was used to test categorical variables such as the LH/FSH ratio.

Results

Comparisons of the Parameter Levels between the Patients and the Control Groups

Most patients (60%) and controls (66.7%) had a healthy body mass index (BMI) (18.5–24.9), while overweight and obesity were less common. The majority of patients and controls were middle-aged adults (31–45 years). Among patients, 56.7% had primary and 43.3% had secondary infertility, with longer marriage duration observed in secondary cases. Most patients (60%) and controls (70%) were non-smokers; cigarette use was higher among patients, and shisha use occurred only in this group. None reported alcohol consumption (Table 1).

The study's comparison of serum total BPA levels with those of the control groups revealed a statistically significant difference. The levels in infertile males exceed those in fertile males (mean ± SD for patients is 13.05 ng/mL ± 12.58 and mean ± SD for controls is 10.07 ± 8.557; $p = 0.0293$). Serum IL-1β levels were significantly higher in the patients, with a (mean ± SD of patients 198.2 Pg/mL ± 117.0 compared to 162.7 ± 45.27 in the control group ($p = 0.0001$)). Sperm plasma ASA-IgA levels in patients significantly increased compared to the control group (mean ± SD for patients: 2789 Pg/mL ± 399.3; for control: 2513.0 ± 436.2; $p = 0.0021$). Blood F2-IsoP levels are indicative of OS compared to the control group (mean ± SD for patients: 284.5 ng/L ± 78.84; for controls: 228.3 ± 75.85; $p = 0.0005$) (Figure 1).

Testosterone levels in patients were lower than in control groups (mean ± SD for patients is 3.417 ng/mL ± 1.313, and for controls it is 4.191 ± 1.174, which was highly significant ($p = 0.0014$)). The E2 levels in patients were higher than in the healthy groups and were significant (mean ± SD for patients is 26.36 pg/mL ± 10.61, and mean ± SD for controls is 20.76 ± 5.496, $p = 0.0397$). The LH, FSH, and LH/FSH ratio levels in patients were not significantly different from those in the control groups. LH levels (mean ± SD for patients: 5.768 mIU/mL ± 2.365; for controls: 5.803 ± 2.119; $p = 0.706$), FSH levels (mean ± SD for patients: 5.228 mIU/mL ± 3.996; versus controls: 4.310 ± 1.803; difference $p = 0.964$), and LH/FSH ratio levels (mean ± SD for patients: 1.410 mIU/mL ± 0.7068; versus controls: 1.489 ± 0.6075; $p = 0.376$). The results indicated that 88.3% of patients demonstrated an LH/FSH ratio ≤ 2 ($p = 0.0719$), which is non-significant for diagnosing infertility in males (Figure 2).

According to questionnaires, the results of comparisons between seminal analyses of infertile males exposed to plastics and fasting fertility health groups without plastics exposure were considered significant. The sperm concentration ($\times 10^6$/ml) (mean ± SD for patients: 51.97 ± 47.28, median = 39.20: for controls: 159.6 ± 83.15, median = 127.5: $p < 0.0001$), total motility percentage (mean ± SD for; patients: 41.08 ± 16.17, median = 45.0: for controls: 61.33 ± 7.063, median = 60.0: $p < 0.0001$), progressive motility percentage (mean ± SD; for patients: 33.92 ± 16.62, median = 35.0: for controls: 56.00 ± 7.812, median = 55.0; $p < 0.0001$), and morphology percentage (mean ± SD; for patients: 3.283 ± 3.211, median = 2.0: for controls: 14.90 ± 7.251, median = 13.30; $p < 0.0001$), and the compared seminal volume/ml in patients was not significantly different from those in the control groups (mean ± SD for patients: 2.712 ± 1.085, median = 2.90: for controls: 3.070 ± 1.176, median = 3.070; $p = 0.242$) (Table 2).

The semen plasma ASA-IgA among patients between the groups, non-agglutination and agglutination, were significant groups (n = 42, mean ± SD for non-agglutination: 2623.0 pg/mL ± 295.5; n = 18, mean ± SD for agglutination: 3171.5 ± 343.1; $p < 0.0001$) (Figure 3).

The levels of BPA in the blood showed a significant relationship with testosterone levels ($r = 0.257$; $p = 0.047$) but a weak relationship with E2 levels ($r = 0.10$; $p = 0.444$) and no relationship with IL-1β levels ($r = 0.03$; $p = 0.860$).

Table 1: The demographic characterization of patients who participated in the study and control group.

Characteristics	Categories	Patients (n=60) (%)	Control (n=30) (%)
Body mass index (BMI)	healthy range - 18.5-24.9	36 (60.0)	20 (66.67)
	Overweight - 25-29.9	21 (35.0)	9 (30.0)
	obesity - 30-39.9	3 (5.0)	1 (3.33)
Age	Young adults17-30 years	16 (26.67)	14 (46.67)
	Middle-aged adults 31-45 years	42 (70.83)	15 (50.0)
	Old-aged adults up to 45 years	2 (3.33)	1 (3.33)
Infertile types			30 (100)
Primary		34 (56.67)	
Primary duration of marital/34*100	1-5 years	18 (52.94)	
	6-10 years	13 (38.24)	
	up to 10 years	3 (8.82)	
Secondary		26 (43.33)	
Secondary, duration of marital/26*100	1-5 years	4 (15.38)	
	6-10 years	10 (38.46)	
	up to 10 years	12 (46.15)	
Smoking and shisha	No	36 (60.00)	21 (70.00)
	Cigarettes	16 (26.67)	6 (20.00)
	Shisha	5 (8.33)	0
	Both Cigarettes and Shisha	3 (5.00)	3 (10.00)
Alcoholism	Yes	0	0
	No	60 (100)	30 (100)
Using plastic tools (Bottles, Dish, Etc.)	Yes	52 (86.67)	3 (10.00)
	No/Protective	8 (13.33)	27 (90.00)

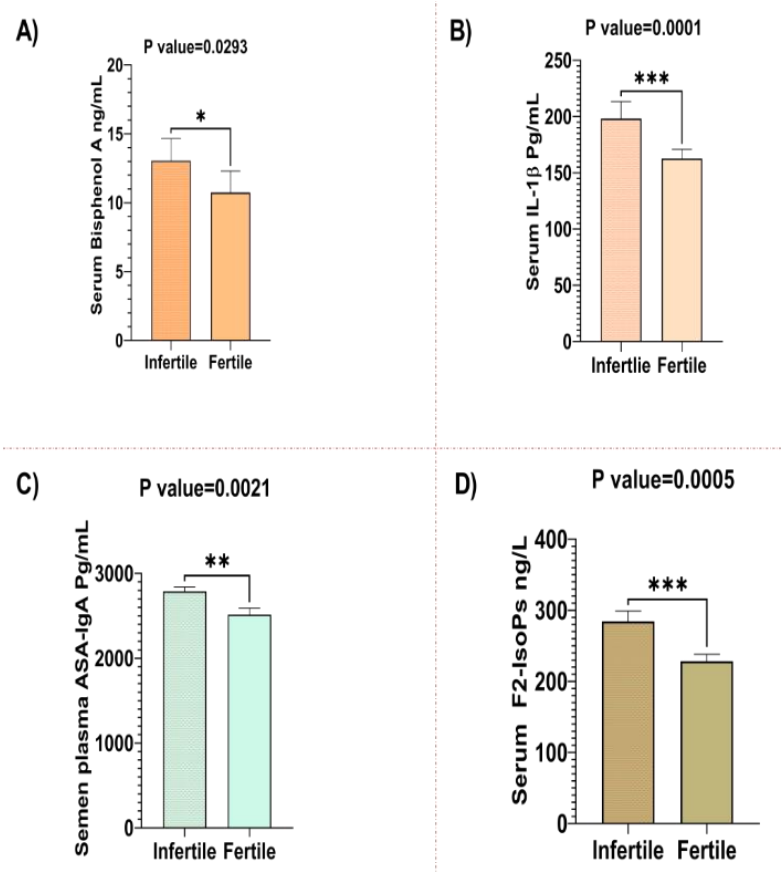

Figure 1: Comparison of serum and semen biomarkers between infertile and fertile men. (A) Serum total Bisphenol A and (B) IL-1β were significantly higher in infertile men. (C) Semen plasma ASA-IgA levels were elevated in infertile men, while (D) serum F2-Isoprostanes showed increased oxidative stress. Data are mean ± 95% CI; n = 90 (60 infertile, 30 fertile controls).

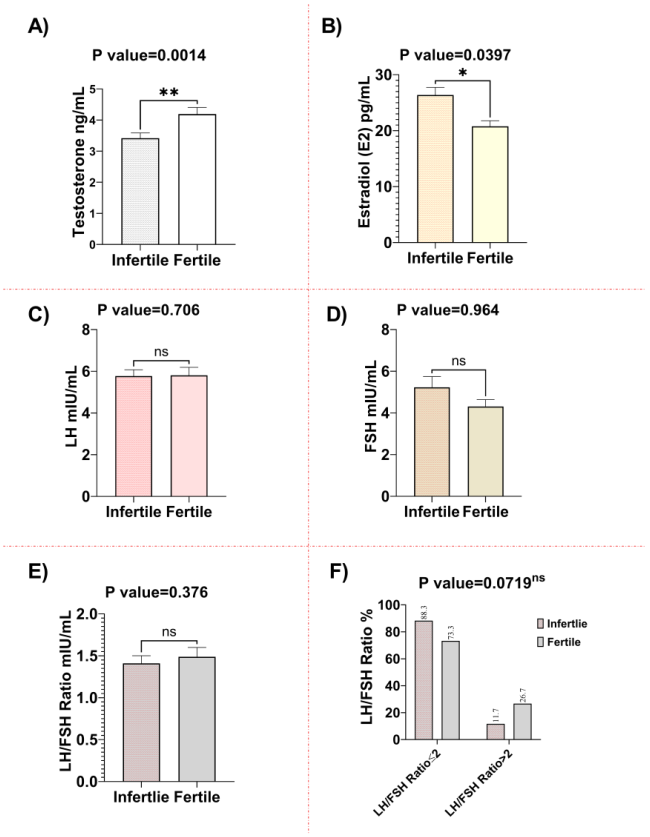

Figure 2: Hormonal profile differences between infertile and fertile men. Infertile men exhibited (A) lower testosterone and (B) higher estradiol (E2), with (C) LH elevated and (D) FSH decreased, leading to a (E) increased LH/FSH ratio. Data are mean ± 95% CI; n = 90. Chi-square test applied for categorical LH/FSH ratio.

Table 2: The Comparisons of the seminal parameters between the male infertility and the fertile men groups.

Seminal fluid parameters	Mean ± SD of Control Non-exposure to plastics	Mean ± SD of Patients primary and secondary infertile men	Median (control-patients)	P-value
Sperm concentration (×10^6/ml)	159.6 ± 83.15	51.97 ± 47.28	127.5-39.20	<0.0001****
Total motility (×10^6/ml)	61.33 ± 7.063	41.08 ± 16.17	60.0-45.0	<0.0001****
Progressive motility (Active + slow) (%)	56.00 ± 7.812	33.92 ± 16.62	55.0-35.0	<0.0001****
Morphology (%)	14.90 ± 7.251	3.283 ± 3.211	13.50-2.0	<0.0001****
Seminal volume (ml)	3.070 ± 1.176	2.712 ± 1.085	3.0-2.90	0.242^{ns}

SD: standard deviation, ns: non-significant.

The Spearman's correlation between serum BPA levels with LH and FSH levels showed that there was a weak negative relationship between the concentration of BPA and LH, FSH. The correlations were not significant between BPA with LH levels (r =−0.12; p = 0.355), BPA and FSH levels (r =− 0.07; p = 0.590) (Figure 4-A).

The levels of IL-1β are strongly linked to those of F2-IsoPs (r = 0.263; p = 0.042), E2 levels (r = 0.350; p = 0.006), and LH/FSH ratio (r = 0.258; p = 0.047), and there is either a weak negative or no correlation with testosterone levels (r =−0.194; p = 0.138) in patients (Figure 4-B).

There was a strong positive relationship between the levels of ASA-IgA in sperm plasma and the levels of F2-IsoPs (r = 0.468; p = 0.00016), and there was a strong positive association between the levels of ASA-IgA and IL-1β levels (r = 0.468; p = 0.003), which means increased OS and inflammation in the infertile men. The levels of ASA-IgA showed a significant negative correlation with testosterone levels (r =− 0.274; p = 0.034), which means a reduced level of concentration, which impacts the seminal parameters (Figure 4-C). The levels of LH were strongly positively correlated with FSH levels (r = 0.530; p < 0.00001*)* in patient groups (Figure 4-D). They would demonstrate robust positive correlations, underscoring the connections between inflammation, OS, and the immune system.

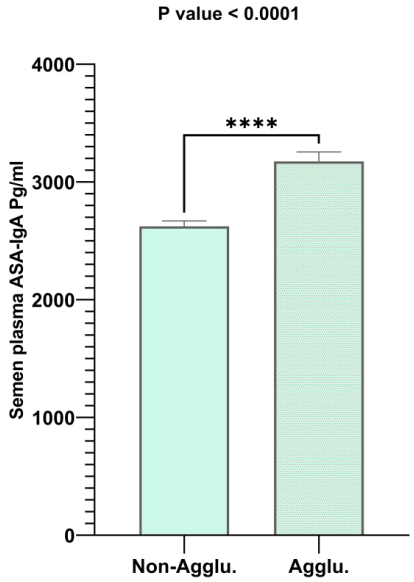

Figure 3: Effect of sperm agglutination on ASA-IgA levels. ASA-IgA concentrations were higher in samples showing sperm agglutination compared to non-agglutinated sperm, indicating an immunological contribution to infertility.

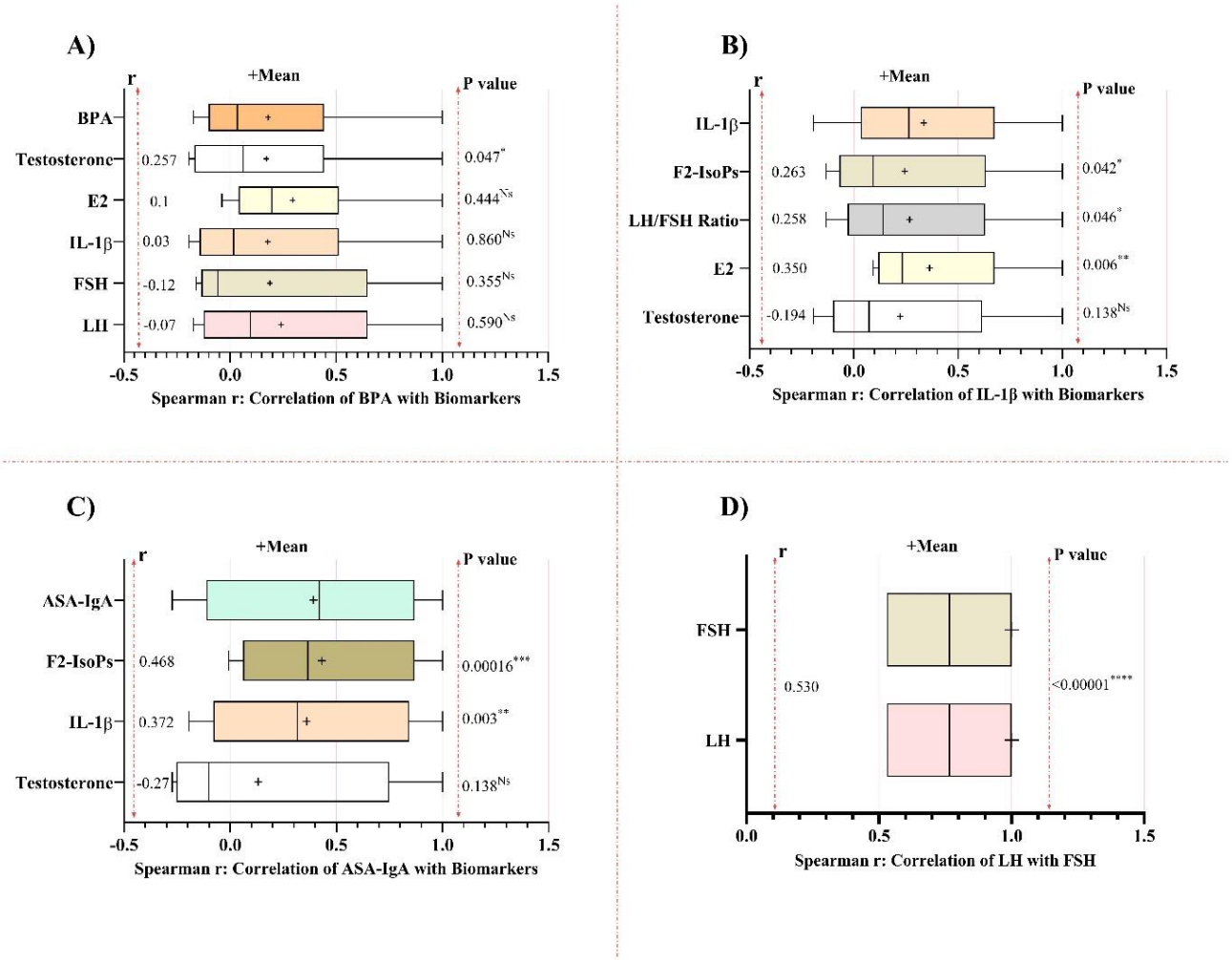

Figure 4: Spearman's correlation matrix among clinical, hormonal, and biochemical parameters in infertile men. Positive and negative correlations are visualized, highlighting strong associations between oxidative stress markers, ASA-IgA, and hormonal imbalances.

Figure 5 shows the receiver-operating characteristic (ROC) curve and standard error (SE) presented biomarkers. BPA has low or moderate discriminative ability, AUC = 0.641, SE = 0.069, and the optimal cut-off value, determined by the maximum Youden index, was 6.875, giving 81.7 % sensitivity (95% CI 70.1–89.4) and 50.0 % specificity (95%

CI 33.2–66.9) (Figure 5-A). Seminal plasma ASA-IgA, AUC = 0.696, SE = 0.0614, and the optimal cut-off value was 2.608, giving 58.3% sensitivity (95% CI 44.9–70.9) and 73.3% specificity (95% CI 54.1–87.7) (Figure 5 -B). At this threshold, the positive likelihood ratio was 2.19, considered moderate discriminative ability. Serum IL-1β presented a greater AUC = 0.7422, SE = 0.0621, and the optimal cut-off value was 140.7, giving 100.0% sensitivity (95% CI 93.98–100.0) and 33.3% specificity (95% CI 19.2–51.2) (Figure 5-C). At this threshold, the positive likelihood ratio was 1.50, which means exact discriminative ability. Serum F2-IsoPs has a greater AUC = 0.7421, SE = 0.0622, and the optimal cut-off value was 320.7, which provided a sensitivity of 93.3% (95% CI 84.1–97.4) and a specificity of 43.3% (95% CI 27.4–60.8) (Figure 5-D). At this threshold, the positive likelihood ratio was 1.647, which presented greater discriminative ability.

Discussion

The statistically substantial age disparity between the fertile and infertile cohorts in this study substantiates the notion that age is a crucial determinant of male fertility, but other underlying reasons for infertility must not be disregarded. In the cohort, most infertile men were middle-aged (31–45 years), whereas fertile controls were more evenly distributed between young and middle-aged adults. Similarly, while the majority of both groups had a healthy BMI (60% of patients and 66.7% of controls), a considerable proportion of infertile men were overweight or obese, suggesting that BMI alone cannot fully explain fertility differences. Lifestyle factors such as smoking were also more prevalent among infertile men. These findings indicate that additional variables, including environmental exposures, lifestyle choices, and genetics, may affect male fertility in ways not entirely elucidated by BMI or age alone. Prior research has underscored the influence of stress, tobacco use, and exposure to environmental pollutants as significant factors affecting fertility [16].

Serum BPA level is associated with infertility, reproductive tract diseases, and pregnancy harm. In the current study, the comparison illustrates the result: statistics indicate BPA levels rose in infertile males. In humans, endocrine-disrupting chemicals (EDCs) affect various parts of the endocrine system, especially the testis and prostate in males. EDCs with distinct hormone-like activities have varying influences on endocrine establishments [17-19]. BPA significantly increases the release of cytokines, including IL-1β, which contributes to the development of inflammation. Yanzhen Liu *et al.* (2014) studied and reported the impact of BPA on the cytokine responses of human macrophages. It also found effects on pro-inflammatory and anti-inflammatory cytokines. BPA altered the production of cytokines by utilizing a process that relies on estrogen receptors α and β (ERα and ERβ). They discovered that BPA's impact on cytokine levels was linked to the activation of the ERK/NF-κB signalling pathway [19].

This study showed that BPA enhanced IL-1β production compared with control groups, while higher concentrations showed a complex dose-response relationship [20-21] and are significantly positively correlated with endocrine hormones like E2 and the LH/FSH ratio [22]. As in the outlet discussion conducted by Leal et al. (2006) it was reported that there was an association between inflammatory markers, such as IL-1β with LH and FSH [23]. Moreover, IL-1β had a negative association with testosterone levels, which inhibits function and reduces spermatogenesis. Moreover, a previous study suggested that testosterone may be regulated by IL-1β. In this study IL-1β had a negative association with testosterone levels, which inhibits proper function and reduces spermatogenesis [24]. IL-1β was significantly correlated with the OS marker F2-IsoPs, suggesting that increased IL-1β, a pro-inflammatory cytokine, promotes the generation of reactive oxygen species (ROS), which in turn induces lipid peroxidation and elevates F2-IsoPs levels. This relationship indicates that higher IL-1β levels are associated with increased OS, whereas in healthy individuals, lower IL-1β corresponds to reduced ROS activity and consequently lower F2-IsoPs, reflecting balanced redox status [25]. The relationships between F2-IsoPs and low ROS levels, which are associated with health, are important for sperm function because they control activation, capacitation, and the acrosome response. This may affect sperm motility, morphology, and fertilisation capability, while diminished levels of F2-IsoPs correlate with ROS activity that facilitates proper sperm signalling and function. This clarifies why infertile males had a significantly higher rate in this study compared with healthy men [26].

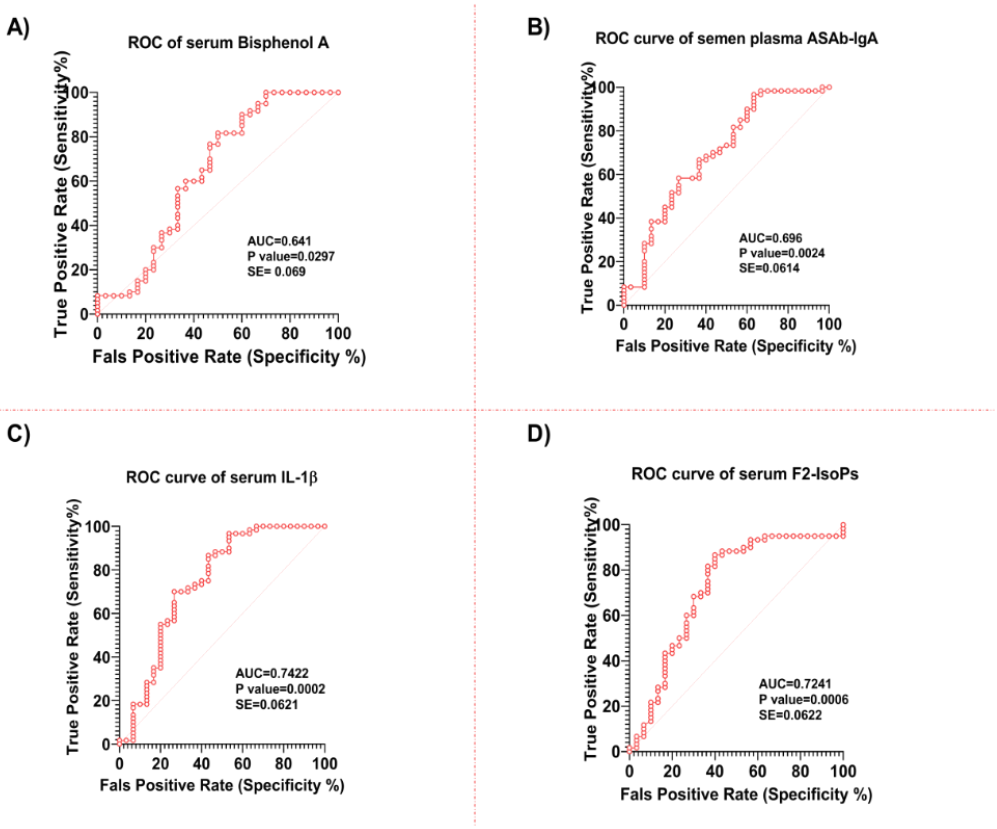

Figure 5: The ROC curve presented the diagnostic accuracy of A- serum total Bisphenol A, B- Semen plasma ASA-IgA, C- serum IL-1β, and D- serum F2-IsoPs for male infertility.

Researchers also found that high levels of BPA in serum can change the BTB proteins that are important for spermatogenesis [27]. Elevated serum BPA concentrations can compromise the blood–testis barrier (BTB) by modifying the expression and positioning of tight junction and adherens junction proteins, including claudin, occludin, and N-cadherin. The blood-testis barrier is crucial for establishing a specialized milieu for spermatogenesis and safeguarding germ cells from toxins and immunological assaults. BPA-induced disruption enhances BTB permeability, exposing germ cells to oxidative stress and immunological stimuli, hence impairing spermatogenesis and eventually diminishing sperm quality and fertility [28].

When comparing semen plasma ASA-IgA levels in individuals from healthy groups with infertile males, this variation suggests that BPA may increase semen plasma ASA-IgA levels in infertile male sperm. Antigenic proteins interact with immune cells to generate ASA-IgA. ASA-IgA is produced against the head, neck, and tail of sperm cells, resulting in agglutination causing reduced sperm function [29-30]. We also observed that in a group of patients with agglutination in semen analysis, the concentration of semen plasma ASA-IgA was significantly elevated. The current study has yielded these results, leading to decreased sperm motility and concentration.

ASA may directly or indirectly affect numerous processes of human fertilization, including capacitation, implantation, fertilization, and acrosome response. Multiple studies showed that couples with ASA had a lower conception rate. Our result reflected a similar outcome [4, 27, 31]. In this study, there were strong positive connections between semen plasma ASA-IgA and F2-IsoPs and IL-1β in infertile men. Additionally, a modest negative association exists with the testosterone hormone. Elevated levels of ASA-IgA are associated with increased oxidative stress, inflammation, and hormonal dysfunction in the genital tract, which diminishes both the quantity and quality of sperm production.

This study compares E2 levels in infertile men exposed to BPA with those in a control group. The findings indicate elevated E2 levels in the BPA-exposed group, suggesting potential endocrine disruption. Furthermore, a significant positive correlation between BPA and testosterone levels was observed, implying that BPA exposure may suppress testosterone secretion. This hormonal imbalance could adversely affect spermatogenesis and sperm morphology, leading to reduced fertility [32]. The present investigation demonstrated that LH and FSH are essential regulators of

spermatogenesis, acting through testosterone production and Sertoli cell function, respectively, and found that BPA levels correlated strongly with testosterone levels and negatively with LH and FSH hormones, causing endocrine abnormalities and lower sperm quality and quantity. Matuszczak E. et al. (2019) also observed the same phenomenon [33].

In this study, the amounts of LH, FSH, and the LH/FSH ratio were normal and did not show any significant differences. In a previous study, it was found that exposure to BPA significantly increased FSH and LH hormone levels, but smoking and BMI had an impact on the patients. Because of this, the effect of BPA may be less pronounced on LH and FSH levels. The effects of BPA on reproductive health are complex and require further research [34].

The ROC curve evaluated the diagnostic potential of combining biomarkers such as BPA, ASA-IgA, IL-1β, and F2-IsoPs for male infertility. Male infertility patients exhibited higher levels of these markers compared to control groups, indicating a significant relationship. BPA is considered a moderately specific or dependable biomarker. IL-1β, semen plasma ASA-IgA, and F2-IsoPs are considered specific or dependable biomarkers for diagnosing or detecting male infertility.

This study is limited by its single-center sample and the restricted availability of prior data, which may impact the generalizability of the results. The cross-sectional design limits the ability to draw causal conclusions, and self-reported lifestyle data may be susceptible to bias. Furthermore, additional environmental or genetic variables affecting male fertility were not entirely regulated. Consequently, further and comprehensive research is necessary to validate the results of the current study and to thoroughly elucidate the involvement of BPA, ASA-IgA, cytokine IL-1β, and F2-IsoPs in male infertility. Environmental conditions lead to impaired immune systems and spermatogenesis. Future studies are required to identify the unknown factors causing "idiopathic" male infertility.

Conclusions

The present study demonstrates that Bisphenol A exposure contributes to male infertility through immune-mediated inflammation, oxidative stress, and disruption of hormonal homeostasis. The interplay among IL-1β, F2-isoprostanes, and ASA-IgA suggests an immuno-endocrine pathway underlying sperm dysfunction. Preventive measures to reduce BPA exposure are essential for preserving male reproductive health. By understanding that environmental contaminants lead to impaired immunity and spermatogenesis, the study recommends better public health policy to decrease BPA exposure.

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