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Correlation of Bisphenol A in Blood serum with Male Reproductive Hormone in Iraqi infertile men.

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ABSTRACT

Bisphenol A (BPA) is one of the world's greatest produced chemicals. BPA is present in various consumer goods that are commonly used in daily life. It was considered an endocrine disruptor and effects on spermatogenesis and male fertility. To assessment the impact of BPA on male reproductive via evaluation the correlation the concentrations of BPA in blood serum with male reproductive hormone. The study was conducted on 28 men recorded at the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies /Al-Nahrain University, private clinic (AL-Zahawi) and Babel Teaching Hospital for Women and Children from January 2022 to April 2022. The blood serum was collected from men. The blood serum samples were assayed the FSH, LH, testosterone and prolactin hormones by mini VIDAS. The residual samples of blood serum were examined BPA concentrations. The measuring of BPA concentration in blood serum by using ELASA Kits. The result of hormones revealed that the correlation between concentrations of BPA and prolactin hormone was slightly positive in blood serum (r = 0.225). There is not detected relationship between BPA and FSH. The BPA concentrations were correlated a negative with testosterone in blood serum (r = - 0.599). Whereas, the LH was correlated slightly positive with blood serum BPA. This study indicated that the BPA in blood serum were highly concentration and there was proof that BPA could effect on male reproductive hormone.

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KEYWORD

Blood Serum, Male Reproductive Hormone, Bisphenol A.

1. Introduction

A number of ecological elements that affect male infertility. Male fertility and subfertility are highly dependent on lifestyle and environmental factors **(Esteves and Agarwal, 2011 [1])**. The standard definition of infertility is the failure to become pregnant after one year of unprotected sexual activity **(ASRM, 2017 [2])**. Infertility which affects approximately 10% to 15% of couples. A male factor is extant in nearby half of all infertility cases **(Massart et al., 2012 [3])**. There are a number of causes of male factor infertility, and both environmental and genetic factors could be affected **(Wong et al., 2000 [4])**. Some of the most frequent environmental exposures have been linked to alterations in male fertility, such as pesticides and herbicides and endocrine disruptors, including BPA **(Krzastek et al., 2020 [5])**. BPA is a plasticizer and monomer for plastics **(Vandenberg et al., 2007 [6])**. BPA may be found in a variety of substances, including water, individual care items, beverages, air, and dust **(Gallo et al., 2017 [7]; Hines et al., 2018 [8]; Liu et al., 2019 [9]; Fan et al., 2019 [10])**. One of the most broadly manufactured compounds in the world is BPA, whose total global production was assessed at 77 × 105 metric tons in 2015 and is predicted to hit 106 × 105 metric tons in 2022 **(Danielsson, 2020 [11])**. Due to its endocrine-disrupting chemicals, it is linked to a wide range of illnesses and conditions, including cardiovascular, obesity, and chronic respiratory diseases **(Iyigündodu et al., 2020 [12])**. Endocrine-disrupting chemicals (EDC) interfere with the functions of hormones **(Philippa and Darbre, 2019 [13])**. EDC are environmental contaminants that have the ability to disrupt the body's normal hormone levels and have a negative impact on a person's health **(Knez, 2013 [14])**. Therefore, the current study targeted to assessment of the impact of BPA on male reproductive hormones.

2. Patients and Methods

The study was included 28 men at the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies /Al-Nahrain University, private clinics (AL-Zahawi), and Babel Teaching Hospital for Women and Children from January 2022 to April 2022. This study had been accepted by the Committee of Local Ethicals (High Institute for Infertility Diagnosis). Detailed questionnaire was formatted depending on history and physical analysis. Markedly, cases were assorted depending to certain exclusion and inclusion criteria. The exclusion criteria included varicocele, chronic smoker, chemotherapy, genital infection, diabetes, history of drug abuse, genetic infertility (e.g., Y-chromosome microdeletions and Klinefelter's syndrome), and tumor syndrome that. All were excluded. The inclusion standards were signed to collect samples from patients (from 20 to 42 years) that were a good mental and physical health.

1- Assessment of Male Reproductive Hormone and BPA Concentrations in Blood serum

The samples of blood serum were drawn from each man (5 ml). Blood sampling for hormonal assays was carry out using a mini VIDAS apparatus and using an enzyme-linked fluorescent assay method was done to assay prolactin, testosterone FSH, and LH, and the kits were purchased from BioMerieux. The normal value of male hormones was involved in this study (FSH 1.7-12.0 mlU/ml, LH 1.1-7.0 mlU/ml, Testosterone 3.0-10.6 ng/ml, and Prolactin 3.0-25.0 ng/ml). The residual samples of blood serum were keeping by freezing at -20°C. The blood serum is measuring the concentration of bisphenol A. The measuring of BPA concentrations was performed using ELISA (Enzyme-Linked Immunosorbent Assay kit) manufacture by My-Bio-Source

Corporation (Catalog No: MBS167621)-USA .

ELISA is the sensitivity level of BPA, which was 0.23 ng/ml. Estimated the optical density value set to 450 nm through 10 min after adding the solution of stop. The BPA concentrations standard curve by ELISA was between 0.5 to 200 ng/ml and done at duplicate.

2- Statistical analysis

The correlation of the BPA in blood serum with FSH, LH, Prolactin, and Testosterone hormone were estimated by applying the coefficient of correlation (r) at the following equation:

$$\text{Correlation Coefficient } (X,Y) = \frac{\sum(x-\bar{x})(y-\bar{y})}{\sqrt{\sum(x-\bar{x})^2\sum(y-\bar{y})^2}}$$

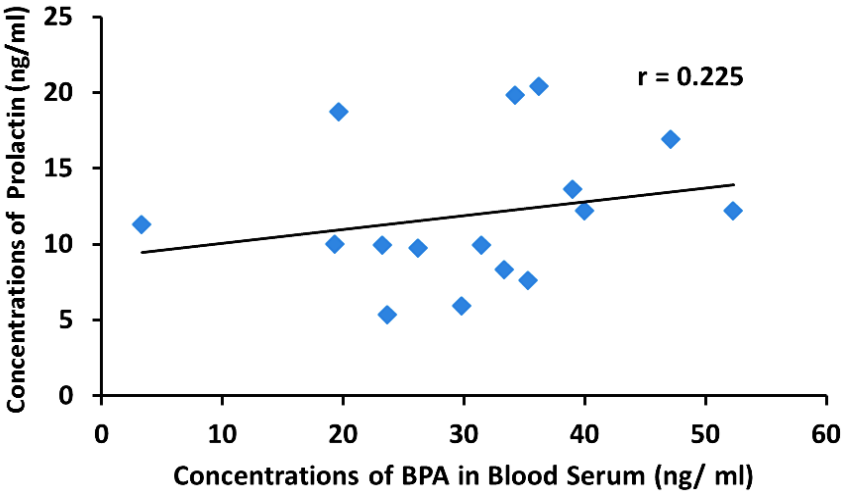
3. Results

The study included 28 men included the age that ranged between 20- and 42 years. The body mass index ranged from 21.09 to 31.55 Kg/m2. The correlation of BPA concentrations in blood serum with male hormones assay are shown in **(Table 1)**. The mean concentration of serum prolactin level was 12.02 ±4.90 ng/ml, and it was ranged from 5.3 to 20.4 ng/ml. **(Figure 1)** shows the correlation of concentrations of BPA with prolactin hormone was slight positive in blood serum (r = 0.225). There are not detected obvious relationship about the BPA effect on prolactin. The mean concentration of serum testosterone level was 4.51 ±2.14 ng/ml, and it ranged from 0.83 to 8.58 ng/ml. A negative correlation between BPA concentration in blood serum with testosterone were r = - 0.599, as shown in **(Figure 2)**. The mean of concentration serum FSH level was 4.64 ±3.48 mlU/ml, whereas the maximum and minimum of level FSH serum were 0.76 and 17.8 mlU/ml, respectively. The correlation of FSH with concentrations of BPA is shown in **(Figure 3)**. It was not observed the correlation between FSH and concentration of BPA in blood serum (r = 0.002). The mean, maximum, and minimum serum LH levels were 5.02

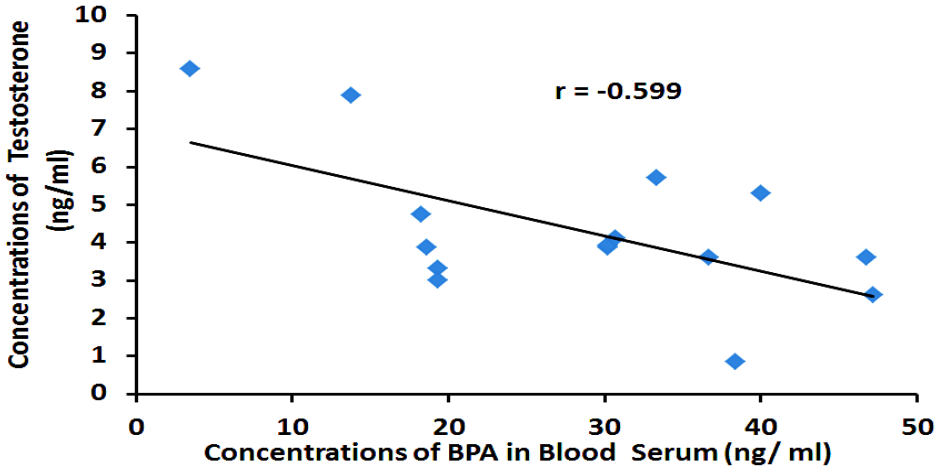
±2.15, 9.17, and 1.8 mlU/ml. The correlation of BPA concentrations with LH is shown in **(Figure 4)**. The results of the correlation of BPA in blood serum was slightly positive (r = 0.286)

Table (1): Correlation of BPA concentrations in blood serum with males' hormones

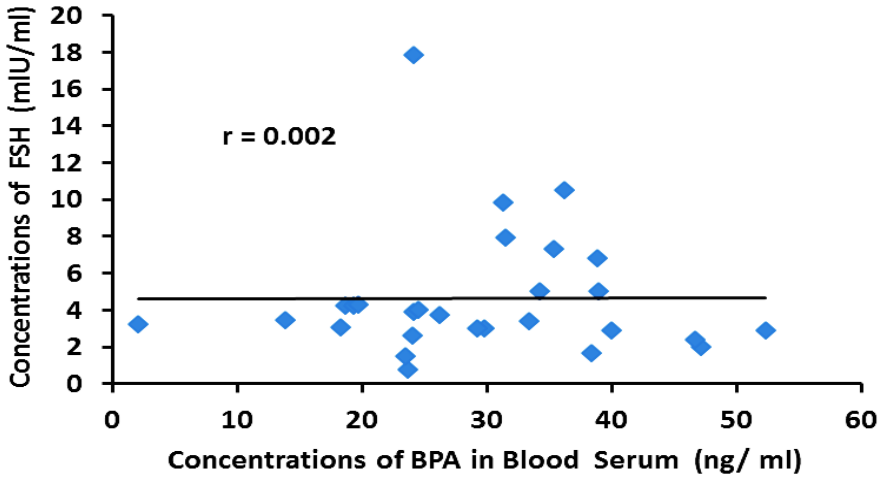
Blood serum			
	Mean ±SD	**Ranged**	**r**
FSH	4.64 ± 3.48	0.76- 17.8	0.002
LH	5.02 ± 2.15	1.8- 9.17	0.286
Testosterone	4.51± 2.14	0.83- 8.58	-0.599
Prolactin	12.02 ± 4.90	5.3- 20.4	0.225



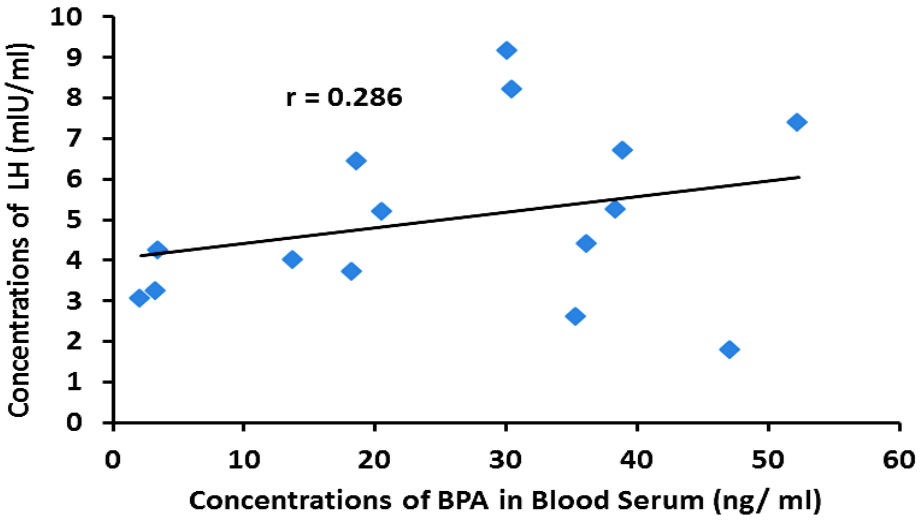
(Figure 1): The correlation of BPA concentration in blood serum with Prolactin hormone



(Figure 2): The correlation of BPA concentration in blood serum with Testosterone hormone



(Figure 3): Correlation of concentration BPA in blood serum with FSH hormone



(Figure 4): Correlation of concentration BPA in blood serum with Luteinizing (LH) hormone

4. Discussion

A numerous of chemicals with endocrine-disrupting significant are existing in environmental and occupational locations **(Ten et al., 2008 [15])**. The primary chemical groups linked to male infertility risk phthalates, bisphenols, and pesticides **(Marić et al., 2021 [16])**. Male sex hormone levels may be impacted by exposure to a high level of BPA **(Zhou et al., 2013 [17])**.

By performing quantitative assessment of serum hormonal levels (Prolactin, Testosterone, FSH, and LH) and correlated with BPA concentration in blood serum. The results of prolactin hormone showed BPA concentrations in blood serum was weakly positive **(Figure 1** and **Table 1).** In studies done by **Shokry et al. (2020) [18]** and **Meeker et al. (2010) [19]**, there was no significant correlation between prolactin and BPA. It was observed from this study the testosterone level

was negatively correlation with BPA concentration in blood serum, illustrated in **(Figure 2)** and **(Table 1)**. These results agreed with **Zang et al. (2016) [20],** who discovered that BPA can lower mice's testosterone levels and prevent them from engaging in sexual behavior. Also, **Scinicariello and Buser (2016) [21]** found similar results, the negative relationships between boys' testosterone levels and BPA concentration. Furthermore, BPA causes benign testicular tumors, lowers testosterone levels in men, and degrades sperm quality **(Czarnywojtek et al., 2021 [22])**. In addition, testicular testosterone levels were lowered by the BPA, and plasma luteinizing hormone was associated with the testosterone levels **(Nakamura et al., 2010 [23])**. BPA often prevents spermatogenesis by affecting the Sertoli cells' activity directly and indirectly by lowering testosterone synthesis **(Ye et al., 2021 [24])** .In the current study, it was appeared to be no correlation of FSH in blood serum with BPA concentrations as shown in **(Table 1)** and **(Figure 3)**. **Hao et al. (2011) [25]** indicated that no effect of BPA on FSH level. The data revealed that the concentrations of BPA in blood serum were correlated with LH slightly positive (r = 0.286), as shown in **(Table 1)** and **(Figure 4). Nakamura et al. (2010) [23]** reported that BPA has a direct impact on the pituitary gland in addition to the Leydig cells. These findings are in agreement with studies done by **Cha et al. (2008) [26]** and **Liang et al. (2017) [27]** which they found serum testosterone levels were substantially lower than controls, although LH levels was significantly greater. **Matuszczak et al. (2019) [28]** who indicated to diminish the effects of BPA on human fertility, its use needs to be reduced.

6- Conclusion

According to the obtained results, the negative correlation was between BPA concentration and testosterone in blood serum. Hence, biomonitoring

seems to be the best approach of a valuation of BPA total input from different sources. It is recommended that advance investigations be perform regarding the impact of BPA mechanisms on male reproductive hormones.

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Author Contribution

Noor Dhafiri performed the study. Rana R. Al Saadi, Raed G. Reshan, Mahammed E Al-Defiery, and Ali A. Bedair supervised the work .

Conflict of Interest

The authors declare no conflict of interest .

Ethical Clearance

The study was approved by the Ethical Approval Committee.

Financial Disclosure

There is no financial disclosure.

Ethical Clearance

The study was approved by the Ethical Approval Committee

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