Evaluation of Presepsin as a Predictive Marker in Women Undergoing ICSI

Bushra Rasheed Al-Azawea, Hayder A. L. Mossa, Liqaa R. Altamimi, and Lubna Amer Al-Anbary

ABSTRACT

Presepsin is an original biomarker with 13 kDa molecular weight for identifying general inflammation and sepsis. The receptor for lipopolysaccharide/lipopolysaccharide binding protein (LPS/LBP) complexes -CD14 (cluster of differentiation) is uttered on the cell membranes of macrophage, monocyte, and granulocyte cells. The LPS/LBP-CD14 complex is freed into circulation by detaching CD14 from the cell membrane, generating a soluble-CD14. (s-CD14), that is triggered by the plasma proteases, producing sCD14- subtype, Presepsin. The assessment of the implication of Presepsin levels in women with infertility lacks in publications. Furthermore, in the present ART’s drill, a precise examination to forecast ovarian response, that may have both amplified the effectiveness and condensed the prices of ART’s, is still missing and there is a necessity for information on the expectedness of ovarian response in controlled ovarian stimulation .The goal of this study was to determine the ability of using Presepsin as a biomarker to evaluate the clinical pregnancy rate in a cohort of couples undergoing ICSI in a sample of Iraqi population.

Patients and Methods: Sixty infertile women selected for undergoing intracytoplasmic sperm injection, the patient’s ovarian stimulation was by antagonist protocol accordingly to their clinical findings.

Results: The results of the study shows there was no significant difference in the serum Presepsin between pregnant and non-pregnant ladies, 421.57 (1534.65) versus 0.00 484.15 (1322.23), respectively (P = 0.875), Furthermore, there was no significant difference in follicular fluid Presepsin between pregnant and non-pregnant ladies, 1286.73 (1232.00) versus 0.00 484.15 (1467.00), respectively (P = 0.296).

Conclusions: It concluded that serum or follicular fluid Presepsin as a biomarker is a poor predictor of fertility outcome with no significant difference between pregnant and non-pregnant ladies.

Keywords: Presepsin, Clinical Pregnancy Outcome, Iraqi Women, ICSI.

I. INTRODUCTION

Infertility is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse [1].

Twenty to thirty percent of infertility cases are caused by male infertility, while 20-35% is due to female infertility, 25-40% is due to combined problems and, and in 10-20% of cases, the cause is unknown. The most common expressed of female infertility is ovulatory problems which are generally manifested by sparse or absent menstrual periods [2].

For a woman to conceive, certain things should take place: intercourse must be around the time when the ovum is released from the ovary; has to be working at optimum levels; and her hormones must be well balanced. Fertilization problems occur mainly due to either structural problem in the Fallopian tubes or uterus or problems in releasing follicles. Infertility may be attributed to hypothalamic pituitary factors which are hypogonadotrophic hypogonadism, also called hypothalamic pituitary failure (low follicular stimulating hormone FSH and low estrogen), normogonadotrophic hypogonadism (normal FSH and estrogen) which is due to hypothalamic -pituitary ovarian axis defect, hyper gonadotrophic hypogonadism (high FSH and low estrogen), also called ovarian failure [3].

Presepsin is a novel, 13 kDa molecular weight biomarker for diagnosing systemic inflammation and sepsis. The circulating soluble form of CD14, a cluster of differentiation (CD) marker protein expressed on the surface of various cells including monocytes, macrophages, neutrophils, and B cells, is activated by plasma proteases, generating a 64 aminoacid-residue fragment named sCD14-subtype (sCD14-ST) [4], [5].

While the biological role of Presepsin has not been completely elucidated, it is considered to be a regulatory
factor capable of modulating cellular and humoral immune responses by interacting directly with T and B cells [6].

The clinical significance of the acute phase reactant, CRP, in the infertility population has been evaluated by some previous published reports [7], [8].

Even though diagnostic value of Presepsin in sepsis cases has been accepted, scarce publications assessing the significance of this peptide in infertility population, and to the best of knowledge, is evaluating the presence of Presepsin in both plasma and follicular fluid (FF) and its effect on the reproductive performance of infertile couples by the present study.

II. PATIENTS, MATERIALS AND METHODS

Sixty infertile female patients aged range 18–41 years, BMI range (20-28.5) were recruited from the infertility clinic in High Institute for Infertility Diagnosis and Assisted Reproductive Technologies at Al- Nahrain University and from private fertility center (Baghdad Specialist Center) all undergoing controlled ovarian stimulation for IVF /ICSI treatment were by antagonist protocol accordingly to their clinical findings.

Hormonal analysis was performed at day two of the menstrual cycle, included serum FSH, LH, Estradiol (E₂), Prolactin, Testosterone, and Thyroid stimulating hormone.

All ultrasound scanning in assisted conception was performed transvaginally, while the Hysterosalpingography (HSG) was performed to exclude tubal blockage and to check for hydrosalpinges as it has a negative impact on the success rate, also to assess the integrity of the uterine cavity [9].

While a full history and physical examination for male partner were done by the urologist, a comprehensive semen analysis was performed for all males referred for assisted conception to ascertain the most appropriate technique suitable for the patient after (3-5) day of abstinence.

Transvaginal ultrasound guided oocyte retrieval was done 34-36 hours following the hCG injection under general anesthesia.

Blood samples were collected from each woman enrolled in ICSI procedure. The blood was allowed to coagulate for 30 minutes then centrifuged at 1500 rpm for 15 minutes to separate the serum. The serum was quickly frozen and stored at -20 °C until hormonal assays were performed [10].

III. RESULTS

Statistical analysis in the current study was based on the inclusion of 60 subfertile women and at the end of the study, positive clinical pregnancy was achieved in 28 ladies accounting for a rate of 46.7 %, as shown in Fig. 1. From now and then, results will be outlined according to pregnancy outcome so that characteristics of pregnant women will be contrasted with those women who failed to get clinical pregnancy.

Serum and follicular fluid marker, Presepsin, of subfertile women participating in the current study was described as median and inter-quartile range (IQR) due to non-normality distribution of these quantitative variables following performance of Kolmogorov-Smirnov test.

Results shows there was no significant difference in the serum Presepsin between pregnant and non-pregnant ladies, 421.57 (1534.65) versus 878.64 (1322.23), respectively (P = 0.875). Furthermore, there was no significant difference in follicular fluid Presepsin between pregnant and non-pregnant ladies, 1286.73 (1232.00) versus 0.00 484.15 (1467.00), respectively (P = 0.296) (Table 1, Fig. 2).

The serum and follicular fluid Presepsin were further analyzed aiming at finding the best cutoff value that can predict positive clinical pregnancy outcome. The cutoff value of serum Presepsin was ≤ 421.574 with poor accuracy of 51.4 %, poor sensitivity of 52.6 % and fair specificity of 68.2 %. The cutoff value of follicular fluid Presepsin was > 469.88 with poor accuracy of 59.6 %, good sensitivity of 73.7% and poor specificity of 50 % (Table 2, Fig. 3).
TABLE 2: CHARACTERISTICS OF ROC CURVE CONCERNING SERUM AND FOLLICULAR FLUID PRESEPSIN

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Serum</th>
<th>Follicular fluid</th>
</tr>
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<tbody>
<tr>
<td>Cutoff</td>
<td>≤421.57</td>
<td>&gt;469.88</td>
</tr>
<tr>
<td>AUC CI</td>
<td>0.514</td>
<td>0.596</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.353 - 0.673</td>
<td>0.431 - 0.746</td>
</tr>
<tr>
<td>Accuracy</td>
<td>51.4</td>
<td>59.6</td>
</tr>
<tr>
<td>P</td>
<td>0.881</td>
<td>0.300</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>52.6</td>
<td>73.7</td>
</tr>
<tr>
<td>Specificity</td>
<td>68.2</td>
<td>50.0</td>
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</tbody>
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Fig. 3. Receiver operator characteristic (ROC) curve analysis to find the best serum and follicular fluid Presepsin cutoff values that predict positive clinical pregnancy outcome.

IV. DISCUSSION

In the present study, positive clinical pregnancy was achieved in 19 ladies accounting for a rate of 46.3 %. In one Iraqi study carried out at Fertility Center in An-Najaf governorate at Al-Sadr Medical City, the successful clinical pregnancy rate following ICSI was 28.9 % (11), which is less than that of the present study. In another Iraqi study included 54 couples and conducted in Baghdad IVF infertility center, the clinical pregnancy outcome following ICSI was 20.4 % (12) which is lower than that achieved in the current study.

However, a pregnancy rate of 51 % was recorded by some Iraqi authors in a study carried out at the High institute for infertility diagnosis and Treatment / AL-Nahrain University and Specialist Fertility Department/ Al-Bonook hospital [13]. In nearby countries, the successful clinical pregnancy rate following ART has ranged from 21.5 to 33.9 % [14], [15], indicating that the rate of positive clinical pregnancy in the current study is one of the best achieved rates.

However, in a number of fertility centers in the United States, the rate of positive clinical pregnancy has reached relatively high figures between 43.9 % and 54.2 % [16]. Therefore, the conductance of the current study and other studies in fertility center is aiming an increasing the rate of successful clinical pregnancy following ART procedures.

In this study, moreover, there was no significant difference in the serum Presepsin between pregnant and non-pregnant ladies. Furthermore, there was no significant difference in follicular fluid Presepsin between pregnant and non-pregnant ladies. The finding is in line Ovayolu et al., who found no significant association serum and follicular fluid Presepsin and clinical pregnancy outcome in sub fertile women undergoing ART [17].

The results are also consistent with the finding of another study carried out by Ovayolu et al. who described that follicular fluid Presepsin is a poor predictor of fertility outcome in poor and normal responders [18].

The clinical significance of the acute phase reactant, CRP, in the infertility population has been evaluated by some previous published reports [19], [20].

It has been accepted that not only the levels but also the trend of the inflammatory markers at the different stages of reproductive processes are of pivotal clinical significance. Indeed, literature assessment demonstrated that the variation pattern of plasma CRP levels on different days in women undergoing IVF has been investigated by several studies [21], [22]. However, we found that the inflammatory marker Presepsin is of no value with this regard.

REFERENCES


