



Salivary High Sensitive C-Reactive Protein and Gingival Health Status among a Group of Women with Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting women in their reproductive years. It is a complex disorder affects not only general health but also show a reciprocal link with the oral health. C-reactive protein is an acute phase protein which increase their concentration during certain inflammatory disorders and used as a biomarker of inflammation in the body. The aims of this study were to assess the gingival health status among a group of women with polycystic ovary syndrome as well as to estimate the levels of salivary high sensitive c-reactive protein in unstimulated saliva in relation to gingival health condition.

Materials and methods: Sixty two females with an age range 20-25 years old and with a body mass index range 18.5-24.9 (normal weight) were included in this study. They were divided into two groups; the study group which included thirty one females with polycystic ovary syndrome, those females attended Babylon Teaching Hospital/ Infertility Center with regular cycles, without clinical or biochemical features of hyperandrogenism and ultrasound exclusion of polycystic ovary (without polycystic ovary syndrome). Collection of unstimulated salivary samples was carried out under standardized conditions, salivary high sensitive c-reactive protein levels were estimated. Plaque index of Silness and Løe (1964) was used to assess dental plaque. While gingival index of Løe and Silness (1963) was used to assess gingival inflammation.

Results: Results showed that the mean value of plaque index was found to be higher in the control group (1.18 ± 0.03) than that in the study group (1.00 ± 0.08) with statistically highly significant difference ($p < 0.01$). While the mean value of gingival index was higher among the study group (1.52 ± 0.06) than that in the control group (1.31 ± 0.05) with statistically highly significant difference ($p < 0.01$). salivary levels of high sensitive c-reactive protein among women with polycystic ovary syndrome (1061.68 ± 75.41 pg/ml) were found to be higher than that of control (930.51 ± 94.65) with statistically highly significant difference ($p < 0.01$). The results in this study showed that the correlations between salivary high sensitive c-reactive protein with gingival index were statistically highly significant ($p < 0.01$) in women with polycystic ovary syndrome. While statistically no significant correlation between plaque index and high sensitive C-reactive protein ($p > 0.05$).

In order to assess the specificity and sensitivity of the use of salivary high sensitive c-reactive protein as a diagnostic tool, statistical analysis of Receiver

Operative Characteristics Curve (ROC) was used and predictive Value Measurements were done in this study. The results showed that the area under the curve for salivary high sensitive c-reactive protein test was (0.869) with highly significant p-value ($p < 0.01$). The best optimal cut off point for salivary high sensitive c-reactive protein was (1009) with (71%) sensitivity and (96.8%) specificity, indicating a very good predictive capacity for using salivary high sensitive c-reactive protein as a marker for the diagnosis of polycystic ovary syndrome.

Conclusions: It was concluded that gingival inflammation was high among women with polycystic ovary syndrome. Furthermore, salivary levels of high sensitive c-reactive protein were found to be high among women with polycystic ovary syndrome. It was suggested that the measurement of salivary high sensitive c-reactive protein may be helpful in diagnosis of women with polycystic ovary syndrome.

Key words: polycystic ovary syndrome, salivary high sensitive c-reactive protein, plaque index, gingival index.

Introduction

Polycystic ovary syndrome (PCOS) is now recognized as a common, heterogenous, heritable disorder affecting women throughout lifetime⁽¹⁾ and it is the leading cause of female anovulatory infertility⁽²⁾. The exact cause of PCOS is unknown, however, it results from a combination of genetic and environmental factors⁽³⁾. The precise prevalence of PCOS is unknown as the syndrome depends on the diagnostic criteria used, however, World Health Organization (WHO) estimates that it affected 116 millions women worldwide in 2012 (3.4% of women)⁽⁴⁾. It is a diagnosis of exclusion⁽⁵⁾. PCOS is chronic condition of anovulation or oligovulation with clinical or biochemical hyperandrogenism which occurs in the absence of other underlying condition⁽⁶⁾.

C-reactive protein (CRP) is "an acute phase protein produced by liver". Serum CRP measurements are widely used as a bio-marker of inflammation in the body⁽⁷⁾. It is demonstrated that levels of CRP are elevated in PCOS, it was concluded that C-reactive protein is considered as a marker of

inflammation among normal weight women with PCOS⁽⁸⁾.

It has become evident over the past 30 years that PCOS is more than a reproductive disorder⁽⁹⁾. PCOS shows a link with oral health in addition to its effect on general health⁽¹⁰⁾. Periodontal diseases and PCOS are the most common disorders in women with significant public health impact⁽¹¹⁾. This syndrome have an impact on gingival inflammation or vice versa⁽¹⁰⁾. Previous study⁽¹²⁾ was found that the level of c-reactive protein was high in subjects with gingivitis.

Salivary diagnostic approaches have been developed to monitor oral diseases such as periodontal diseases^(13,14). Saliva is said to be a "mirror of the body" because it provides vital clues to systemic health⁽¹⁵⁾; therefore, saliva has become useful as an alternative for blood in medical diagnosis and research⁽¹⁶⁾. Besides, the development of new technologies may promote a wider use of salivary assay in the near future⁽¹⁷⁾.

As far as it is known, there was no previous Iraqi study concerning the

estimation of the salivary levels of high sensitive c-reactive protein and their relation with gingival health condition among women with PCOS. Furthermore, in order to gain knowledge regarding the gingival health status and salivary high sensitive c-reactive protein for this target group in which saliva may provide a simple, inexpensive and noninvasive measure, therefore, this study was designed and conducted.

Materials and methods

The total sample composed of sixty two females aged (20-25) years and with body mass index ranged 18.5-24.9 (normal weight). Those were divided into two groups: thirty one women newly diagnosed with PCOS who attended Babylon Teaching Hospital/ Infertility Clinic as a study group and thirty one women with regular menses, without clinical or biochemical features of PCOS and ultrasound exclusion of polycystic ovary syndrome from the relatives of those women as a control group. This study was carried out during the period from the end of December (2014) till the end of May (2015). The study group was diagnosed according to Rotterdam criteria. Exclusion criteria included: smoking, pregnancy, previous diagnosis of condition with hormonal disturbance, presence of systemic disease (diabetes, hypertension, cardiovascular disease), medication affecting periodontium, confounding medications (contraceptive pills, steroid hormone), use of antibiotic and /or inflammatory drugs within the last months, the presence of less than 20 natural teeth. Collection of unstimulated salivary samples was carried out under standardized conditions following the instruction cited by (Navazesh and Kumer, 2008)⁽¹⁸⁾, the salivary samples were

collected and stored in -20C until analysis, salivary high sensitive c-reactive protein level was measured by ELISA method using Salimetrics ELISA kit. Plaque index of Silness and Løe (1964)⁽¹⁹⁾ was used to assess dental plaque. While gingival inflammation was evaluated using gingival index of Løe and Silness (1963)⁽²⁰⁾. Data analysis was conducted through the application of the (SPSS version 18). The analysis of data included: Mean, Standard deviation, paired t-test, Pearson Correlation (r), Receiver Operative Characteristics Curve (ROC curve).

Results

Table (1) shows the mean values of plaque index and gingival index among the study and control groups. It was found that the mean value of plaque index was higher in the control group than that in the study group with statistically highly significant difference ($p < 0.01$). while the mean value of gingival index was higher among the study group than that in the control group with statistically highly significant difference ($p < 0.01$).

Table (2) shows the mean value and standard deviation of hs-CRP among the study and control groups. It was found that salivary hs-CRP concentration was higher in the study group when compared with that in the control group with statistically highly significant difference between two groups ($P < 0.01$).

Table (3) shows the correlation between salivary high sensitive c-reactive protein with oral variables (PII and GI). It was found that the correlation between salivary hs-CRP and GI was statistically highly significant ($p < 0.01$). While statistically not significant correlation was found between hs-CRP and PII in PCOS group.

Table (4) shows the best optimal cut off point for salivary hs-CRP as a diagnostic tool. It was found that the optimal cut off point for salivary hs-CRP was (1009) with (71%) sensitivity and (96.8%).

Figure(1) shows the Receiver Operative Characteristic Curve (ROC) curve for salivary hs-CRP that was used to assess the specificity and sensitivity of use of salivary hs-CRP as a diagnostic tool for PCOS.

Discussion

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women in their reproductive years⁽²¹⁾. It affects general health as well as oral health⁽¹⁰⁾. PCOS and periodontal diseases are the commonest disorders in women with a significant public health impact⁽¹¹⁾.

The results of the current study showed that the mean value of the plaque index was found to be higher in the control group compared to that in the study group with statistically highly significant difference ($p < 0.01$). This may be due to oral health negligence in the control group and this could be attributed to lack of motivation about dental plaque control. This result was inconsistent with the result reported by previous studies^(11,22,10) which found that the mean value of dental plaque was lower in the control group.

The result of present study showed a highly significant increased gingival inflammation represented by higher gingival index among PCOS group. This result was also reported by other researchers^(9, 22) who found that gingivitis was higher in the PCOS group than that in the control group. This could be explained by the fact that gingival inflammation may be linked to systemic inflammation⁽²³⁾. It was reported that PCOS is considered as a

state of a low grade chronic inflammation⁽²⁴⁾. Furthermore, PCOS is one of the endocrine disorder characterized by hormonal imbalance and among these, steroid hormones⁽²⁵⁾ which have been mostly linked with periodontal pathogenesis⁽²⁶⁾. It was found that the gingival tissue is one of the targets for steroid hormones which can exacerbate gingivitis during period of hormonal fluctuation⁽²⁷⁾. A previous study reported an increase in the level of estrogen hormone among women with PCOS⁽²⁵⁾, the gingival tissue respond to increased level of estrogen hormone by undergoing vasodilatation and increased capillary permeability also there is increased migration of fluid and white blood cells out of blood vessels. Cyclic increase in the production of sex steroid hormones often alter the biology of gingival tissue and vasculature, and recognition by effector cells of the local immune system^(28,29).

Regarding C-RP, hs-CRP was used in current study, as it was more specific and precise, furthermore, it was possible to detect even the low level of CRP⁽³⁰⁾. The result revealed that there was a statistically highly significant difference ($p < 0.001$) in the concentration of hs-CRP between the study and control groups. The level of hs-CRP in saliva was higher in PCOS group than that in the control group. This result was also reported by previous study⁽²²⁾ which found that there was a significant increase in the level of salivary CRP among women with PCOS compared to control group.

The high level of circulating CRP among women with PCOS may be due to the reflection of the chronic low-grade inflammation present in the disorder⁽³⁰⁾ or it may be of a genetic origin since it was found that single nucleotide polymorphism (SNPs) in CRP genes are associated with increased plasma level of CRP⁽³¹⁾

.Furthermore, high level of CRP could be due to other confounding factors such as sleep disturbances, hidden bacterial infection and depression⁽³²⁾. It was reported that circulating CRP can reach saliva through GCF or by salivary glands and high level of CRP in saliva may reflect an abnormal high infiltration from blood due to tissue damage and inflammation⁽³³⁾. Previous studies^(34,8) which found that women with PCOS had high level of CRP and had carrying at least one marker of low grade inflammation which is CRP. According to the result of this study, the Receiver Operative Characteristics Curve (ROC) curve test, which was also used to assess the specificity and sensitivity of the use of salivary hs-CRP a biomarker for PCOS. In medicine, the ROC analysis had been extensively used in the evaluation of diagnostic tests⁽³⁵⁾. It was found that the area under the curve for hs-CRP was (0.8) and positive predictive value measurements at (71%) sensitivity and (96.8%) specificity with cutoff point of (1009) indicating good predictive capacity for salivary hs-CRP as a biomarker for the diagnosis of PCOS.

From the results of this study, it was concluded that women with PCOS had high gingival inflammation, thus, an organized, comprehensive oral health preventive and educational programs in addition to the intense oral hygiene programs are essential to improve the gingival health condition of women with polycystic ovary syndrome.

An interesting result in this study that high sensitive C-reactive protein can be used as a marker for diagnosis of women with polycystic ovary syndrome.

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Table (1): Plaque index, gingival index(mean±SD) among the study and control groups.

Statistical Difference		Group				Variable
		Control		Study		
p-value	t-test	±SD	Mean	±SD	Mean	
0.00**	12.30	0.03	1.18	0.08	1.00	PII
0.00**	15.09	0.05	1.31	0.06	1.52	GI

**=Highly significant at P<0.01 df=60

Table (2): Salivary high sensitive C-reactive protein (mean±SD)among study and control groups.

Statistical Difference		Group				Variable
p-value	t-test	Control		Study		
		±SD	Mean	±SD	Mean	
0.00**	6.59	94.65	930.51	75.41	1061.68	Salivary high sensitive C-reactive protein (pg/ml)

**=Highly significant at P<0.01 df=60

Table (3): Correlation coefficient between salivary hs-CRP with plaque index, gingival index among the study and control groups.

Control				Study				Variable
GI		PII		GI		PII		
P	r	P	r	P	r	P	r	
0.00**	0.69	0.01*	0.45	0.00**	0.76	0.53 [#]	-0.12	hs-CRP (pg/ml)

** = Highly significant at P<0.01.

= not significant at P>0.05.

*= significant at P<0.05.

Table (4): Cutoff point ,sensitivity, specificity and area under curve of salivary hs-CRP

P-value	Area under curve	Specificity %	Sensitivity %	Cut off	Test Result Variable	Variable
0.000**	0.869	96.8	71	1009	Optimal	Salivary hs-CRP

**=Highly significant at P<0.01

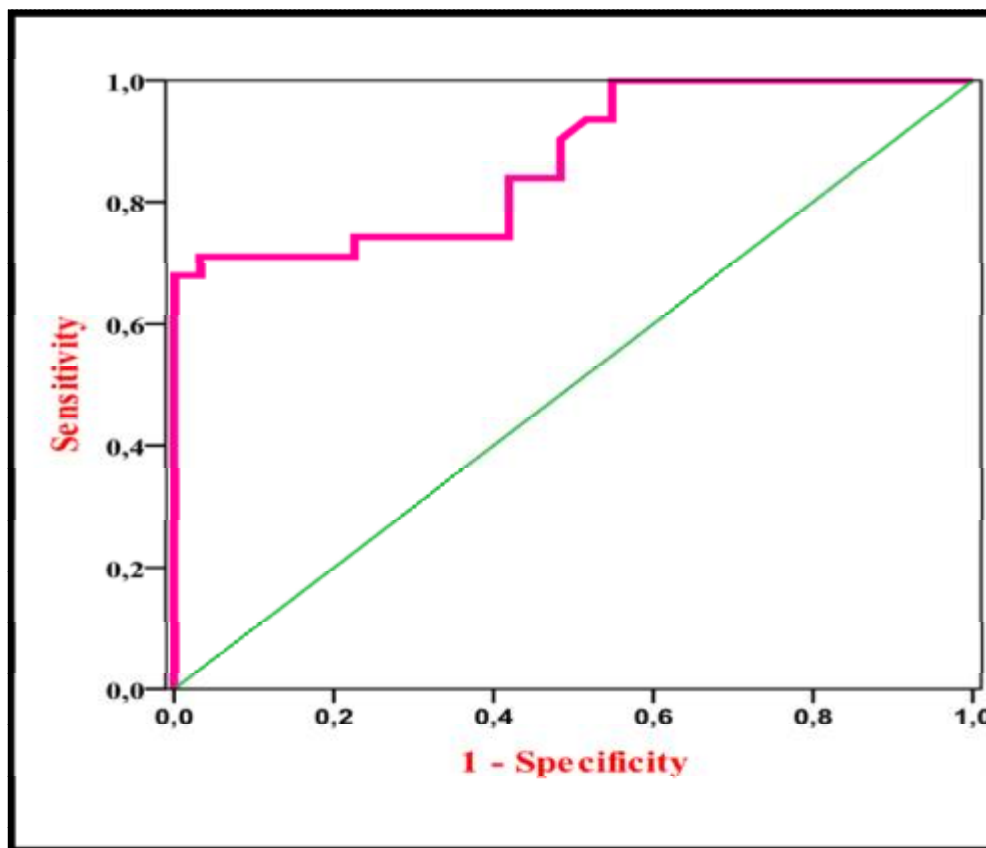


Figure (1): The ROC curve for salivary c-reactive protein.