Section A-Research paper
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Correlation between Chronic Inflammation and Oxidative Stress in hypothyroid females with Polycystic Ovary Syndrome.

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Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder that affects a significant number of women during their reproductive years, making it a topic of considerable research interest [1]. Additionally, PCOS is recognized as a leading cause of anovulatory infertility, further highlighting its clinical significance [1]. The phenomenon of ovarian morphology change was initially documented by Chereau in 1844 [2]. Subsequently, the diagnostic criteria for this condition were established by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) in 2003. These criteria, known as the Rotterdam Consensus Criteria, were developed based on comprehensive research conducted over several decades. Polycystic ovary syndrome (PCOS) is a complex and diverse medical condition characterized by a wide range of clinical manifestations. These manifestations primarily consist of menstrual irregularities, such as menstrual disorder and secondary amenorrhea, as well as abnormal levels of hormones in the bloodstream. Other common clinical features associated with PCOS include excessive hair growth (hirsutism), acne, obesity, and difficulties in conceiving (infertility) [3].

Oxidative stress is a phenomenon that arises from the disruption of the delicate equilibrium between oxidants and antioxidants within the human body. Cell membranes, known for their high content of polyunsaturated fatty acids (PUFA), are susceptible to oxidative damage

caused by free radicals. The process under consideration is commonly referred to as lipid peroxidation, which involves the oxidative degradation of lipids. One notable outcome of this process is the production of malondialdehyde (MDA), which holds significant importance in this context. The correlation between the extent of lipid peroxidation and its role as a commonly used biomarker for assessing oxidant status has been extensively studied [4]. Antioxidant enzymes play a crucial role in the preservation of cellular redox equilibrium in the face of oxidative stress. Superoxide dismutase (SOD) is considered to be a significant enzyme in the body's antioxidant defence system. It plays a crucial role in converting the superoxide anion radical into hydrogen peroxide, thereby safeguarding cells from reactive oxygen species (ROS). Various reactive oxygen species (ROS) have been found to target proteins, carbohydrates, nucleic acids, and lipids, resulting in their oxidation and the generation of a wide range of products [5].

C-reactive protein (CRP) is an acute-phase protein that is synthesized by the liver. It exists as a homo pentamer and exhibits specific binding affinity towards phosphorylcholine in a manner that is dependent on the presence of calcium ions (Ca2+). The levels of this substance exhibit a significant increase during instances of bodily inflammation. The observed increase in C-reactive protein (CRP) levels can be attributed to an elevation in the plasma concentration of interleukin-6 (IL-6), which is primarily produced by macrophages and adipocytes. During the acute phase response, it has been observed that C-reactive protein (CRP) levels exhibit a rapid increase within a span of 2 hours following an acute insult. Furthermore, these levels surpass the normal limits within 6 hours and reach their peak at approximately 48 hours. The resolution of the acute phase response is accompanied by a decline in C-reactive protein (CRP) levels, which follows a half-life of approximately 18 hours. In acute inflammation, such as during infection, it has been observed that C-reactive protein (CRP) levels can increase significantly, up to 50000-fold [6].

Thyroid disorders and polycystic ovary syndrome (PCOS) are widely recognized as prevalent endocrine disorders within the general population. While the etiopathogenesis, or the underlying causes, of hypothyroidism and polycystic ovary syndrome (PCOS) differ significantly, there are several shared features between these two conditions. The literature has documented that primary hypothyroidism is associated with an observed rise in ovarian volume and the presence of cystic changes within the ovaries. Recent research has shed light on the prevalence of thyroid disorders among women with polycystic ovary syndrome (PCOS) in comparison to the general population[7].

Aim and Objective of the study: To Study of Correlation between Chronic Inflammation and Oxidative Stress in hypothyroid females with PCOS.

MATERIALS AND METHODS

The current investigation examines a cohort of 268 females diagnosed with hypothyroidism and polycystic ovary syndrome (PCOS), ranging in age from 15 to 40 years. This cohort includes both obese and non-obese individuals. Additionally, a control group of 100 healthy individuals is included for comparison purposes. The research was conducted at the Department of Biochemistry and the Department of Obstetrics and Gynaecology, Index Medical College and Research Centre, Malwanchal University, Indore. The research study is conducted following the necessary approval from the Institutional Ethics Committee to ensure the ethical use of human subjects in the study. The collection of a comprehensive historical record and obtaining informed consent are essential components in the research process when working with human subjects. Fasting blood samples were collected from the participants. The collected samples were then subjected to centrifugation to separate the components. Following centrifugation, the resulting serum was carefully stored in a refrigerator to maintain its stability and integrity. The measurement of MDA (malondialdehyde) was conducted using the enzyme-linked immunosorbent assay (ELISA) technique, while the measurement of CRP (C-reactive protein) was performed using the ERBA 360, a fully automated biochemistry analyser.

EXCLUSION CRITEREA:

Surgical patients, Pregnant women, ICU admitted patients, Subjects sufferings from Respiratory disorders, Heart patients, Smokers, Alcoholic women.

Statistical analysis of the results: Data statistics was done by using SPSS version 21 and correlation was done by Karl Pearson coefficient of correlation. Data was expressed as Mean ± SD. A value of $P < 0.001$ was considered highly significant.

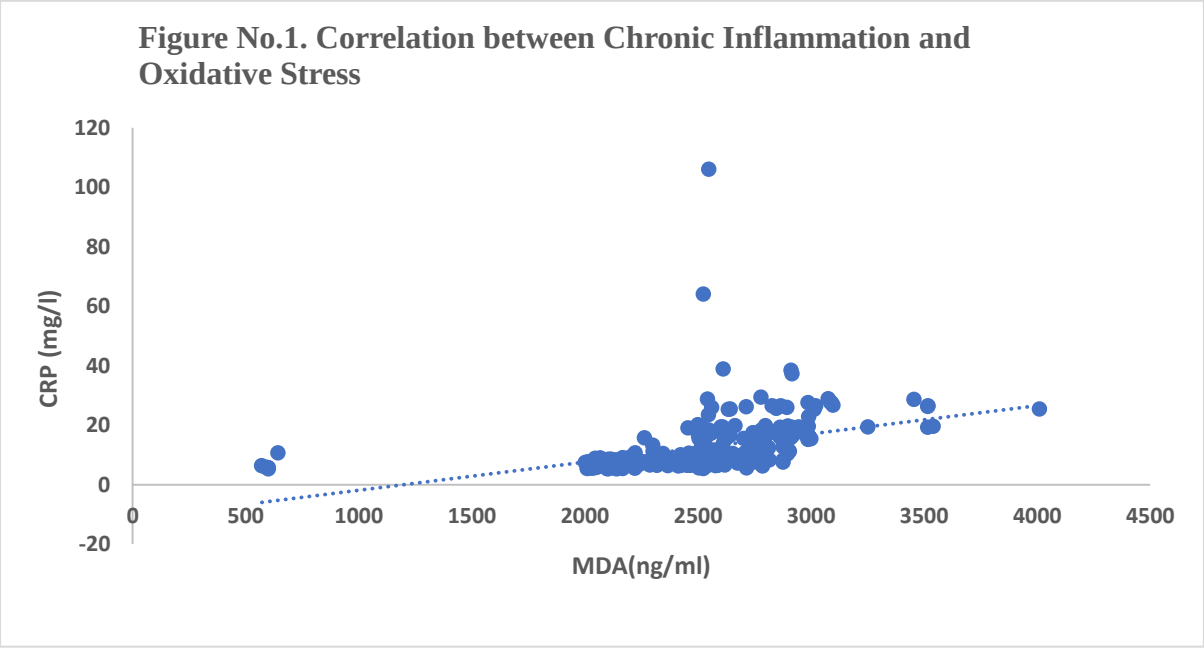
Observation and results:

The statistical analysis conducted in this study projected a significant increase in the levels of MDA (malondialdehyde) and CRP (C-reactive protein) among hypothyroid females with polycystic ovary syndrome (PCOS), as illustrated in Table 1. In the present study, it was noted that the average C-reactive protein (CRP) concentration was found to be 12.38±9.48, while the average malondialdehyde (MDA) concentration was observed to be 2505.5±421.3. The statistical analysis revealed a significant correlation between MDA and CRP in the

subjects ($p < 0.001$). The relationship between chronic inflammation and oxidative stress is further elucidated through the scatter diagram presented in Figure 1.

Table .1. Correlation between Chronic Inflammation and Oxidative Stress

Parameters	**N**	**Mean**	**Std. Deviation**	**Karl Pearsons's Coefficient of Correlation (r)**	**P Value**
CRP((mg/L)	268	12.385	9.4893	0.421	**<0.001***
MDA(ng/ml)	268	2505.748	421.3913		



Discussion: The findings of this study indicate that individuals with hypothyroidism and polycystic ovary syndrome (PCOS) may experience chronic low-grade inflammation, specifically characterized by elevated levels of C-reactive protein (CRP) and an increase in oxidative stress. In a study examining the relationship between polycystic ovary syndrome (PCOS), hypothyroidism, and certain biomarkers, it was found that women with both PCOS and hypothyroidism displayed significantly elevated levels of C-reactive protein (CRP) and malondialdehyde (MDA) compared to their counterparts who had normal ovulation, were no hyperandrogenic, and were matched in terms of age and body mass index (BMI). These

findings suggest a potential association between PCOS, hypothyroidism, and increased concentrations of CRP and MDA.

According to a study conducted by Kumar Sumit et al, it was observed that patients in Group A experienced a notable increase in FT4 levels following treatment, accompanied by a decrease in TSH values. The results of the study indicated a significant reduction in MDA levels following the treatment intervention ($P < 0.001$). Following treatment in Group B patients, there was a significant increase in FT4 levels, accompanied by a decrease in TSH values ($P < 0.05$). Following the administration of treatment, a significant reduction in the estimated level of MDA was observed ($P < 0.001$). The results of the study indicate that there was a notable decrease in MDA levels observed in both experimental groups following the administration of the treatment. Within Group B, a noticeable decrease in the percentage of MDA was observed; however, it did not reach a level of statistical significance. The analysis conducted involved the use of repeated measure MANOVA to investigate any potential differences in the levels of MDA between the two groups. The results of this analysis indicated that no statistically significant difference was observed in the MDA levels between the two groups. The reduction of MDA, expressed as a percentage, was observed to be 39.5% in patients belonging to Group A. In a similar vein, it was observed that patients belonging to Group B exhibited a notable reduction of 45.4% in their respective percentages. The relationship between oxidative stress and hypothyroidism has been investigated in various studies. Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS) and the body's ability to detoxify Hypothyroidism has been associated with an elevated level of oxidative stress. The objective of this investigation was to assess the levels of the biomarker, malondialdehyde (MDA), in individuals diagnosed with treatment-naive primary hypothyroidism. Following administration of L-thyroxine, a notable decrease in the stress marker is observed, indicating a significant reduction in stress levels. The utilization of MDA as a potential biomarker for the quantification and surveillance of oxidative stress has been extensively investigated in various research studies. The current body of research has not yet reached a definitive conclusion regarding the impact of adding selenium as an antioxidant. In this study, we aim to investigate the effects of a specific intervention on a particular outcome.

In a study conducted by **Kazım Uckan et al.,** a comprehensive analysis was performed to investigate the demographic characteristics and basic clinical features of the study population. The study examined the mean age of participants in three different groups: the control group, the nonobese PCOS group, and the obese PCOS group. The mean age for the control group

was 23.68 ± 2.21, while the nonobese PCOS group had a mean age of 24.12 ± 3.25. The obese PCOS group had a slightly lower mean age of 23.11 ± 2.88. There were no statistically significant differences observed among the three groups in terms of age ($p > 0.001$). The study groups exhibited a statistically significant disparity in various parameters, including waist-hip ratio (cm), weight (kg), height (cm), BMI (kg/m2), menstrual cycle (day), Ferriman–Gallwey score, systolic blood pressure (SBP), and diastolic blood pressure (DBP) ($p < 0.001$). In the PCOS patient group, a positive correlation was found between MDA and various factors including BMI, triglyceride levels, LDL cholesterol levels, waist-hip ratio, total cholesterol levels, and insulin levels. A negative correlation was observed between systolic blood pressure (SBP), diastolic blood pressure (DBP), superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and glutathione peroxidase (GPx). The study examines the positive correlation between MDA levels and various parameters associated with metabolic syndromes, including dyslipidaemia, hypertension, and hyperinsulinemia. This correlation suggests that heightened oxidative stress observed in patients with polycystic ovary syndrome (PCOS) is linked to oxidative stress in cardiovascular diseases, such as cardiovascular disease and metabolic syndrome (MS). Previous studies have reported a significant negative correlation between the levels of glutathione (GSH), glutathione peroxidase (GPx), catalase (CAT), superoxide dismutase (SOD), waist-hip ratio (WHR), and total cholesterol. The present study aims to investigate the potential relationship between glutathione (GSH), glutathione peroxidase (GPx), catalase (CAT), superoxide dismutase (SOD), and high-density lipoprotein (HDL) levels. The objective is to determine if there exists a positive correlation among these variables. In a recent study conducted by researchers, the topic of interest was explored in depth. The study

In a study conducted by **Xiajie Hu et al**, a comprehensive analysis was performed on a total of 20 studies. These studies consisted of 7 case-control studies and 13 cross-sectional studies. The study encompassed a comprehensive sample size of 7857 participants from a diverse range of 13 countries. Multiple studies have provided evidence suggesting that individuals diagnosed with polycystic ovary syndrome (PCOS) exhibit a higher susceptibility to developing hypertension (HT). Conversely, it has been observed that individuals with HT also face an elevated risk of developing PCOS when compared to control groups. The study examined the prevalence of hypertension (HT) in patients with polycystic ovary syndrome (PCOS) across different countries, specifically focusing on India, Turkey, South America, Asia, and Europe. The findings revealed that the prevalence of HT in PCOS patients was

higher in India and Turkey compared to other countries. Additionally, the study observed a higher prevalence of HT in PCOS patients in South America compared to Asia and Europe. The present study provides evidence supporting a correlation between Polycystic Ovary Syndrome (PCOS) and Hypothyroidism (HT). However, further investigation is warranted to elucidate the underlying mechanisms linking PCOS and HT. Simultaneously, it is imperative to conduct regular screenings for hypertensive (HT) risk in patients with polycystic ovary syndrome (PCOS), as well as screenings for PCOS risk in patients with hypertension (HT).According to recent research, it has been found that [10]. This finding is significant as it Phelan et al. also arrived at similar conclusions in their research. In a comprehensive investigation, the researcher examined the relationship between hsCRP and various cytokines in relation to insulin resistance. Notably, the findings revealed a significant correlation between these factors. Additionally, the study observed that women with polycystic ovary syndrome (PCOS) exhibited elevated white blood cell (WBC) counts, even when compared to women who were equally obese and insulin-resistant. This observation highlights a distinct characteristic of PCOS in relation to WBC levels. There is a possibility that hyperandrogenaemia, either on its own or in conjunction with central adiposity and insulin resistance (IR), could potentially provide an explanation for the occurrence of leucocytosis. The precise mechanism underlying this phenomenon remains to be fully understood. This study aims to explore the potential role of androgen in the development and activation of leukocytes and low-grade inflammation. In conducting our research, we analysed various sources of information to gain a comprehensive understanding of the topic.

Conclusion:- In this study, a positive correlation was observed between the levels of C-reactive protein (CRP) and malondialdehyde (MDA). The correlation coefficient (r value) was found to be 0.421, indicating a moderate positive relationship between CRP and MDA. The observed correlation exhibited a high level of statistical significance, as indicated by a p-value of less than 0.001.

The observed positive correlation between C-reactive protein (CRP) and malondialdehyde (MDA) suggests a significant association between chronic inflammation and oxidative stress in individuals with hypothyroidism and polycystic ovary syndrome (PCOS).

The present findings suggest that there is an observed elevation in chronic inflammation and oxidative stress in individuals diagnosed with hypothyroidism and polycystic ovary syndrome (PCOS).

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