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A STUDY OF INFLAMMATORY MARKERS (CRP, ADA & ESR) IN HYPOTHYROIDISM

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ABSTRACT

Background: Hypothyroidism slows down the metabolic activities producing various causes weight gain, poor appetite, shortness of breath constipation etc. These are associated with the immune deregulation which ultimately produces the inflammation. Inflammatory markers can be helpful assessment in diagnosis of hypothyroidism is not very well studied in the past. So, the goal of the study is to investigate role of these inflammatory (CRP, ADA &ESR) in hypothyroidism. **Material and Methods:** The study consists of 30 patients diagnosed with hypothyroidism and 30 healthy controls. The serum Total TSH, T3 &T4 were estimated by enzyme immunoassay competition method with ELFA technique by using automated VIDAS for the conformation of hypothyroidism. The concentration of CRP and ADA activity were determined on semi auto analyzer by quantitative turbidimetric methods. Similarly, ESR level were estimated by westergren tube method. **Results**: In the study, the mean CRP value (10.66±7.81) mg/dl, ADA (24.47±6.47) U/L & ESR (16.57±5.68) mm/hr were found significantly higher in hypothyroid patients in comparison to healthy controls. Similarly, there was no correlation obtained between TSH, T3 &T4 and CRP, ADA & ESR. **Conclusion:** The study has shown that there is significant increase in mean CRP, ADA &ESR level in hypothyroid patients in comparison to healthy controls.

KEYWORDS: ADA, CRP, ESR, Hypothyroidism.

INTRODUCTION

Hypothyroidism is a clinical syndrome that results from the insufficient production of thyroid hormones leading to slow down the metabolic activities.[1] Thyroid hormone regulates almost all the metabolic process in the body and their deficiency in the tissues can develop several pathological conditions presenting with different signs and symptoms.[2,3]

Hypothyroidisms is alarming as chief health problem in developed as well as in developing nation are 4-5% of the people are found to be associated with hypothyroidism in well developed nations.[4,5] The occurrence of the diseases has been observed more in female in comparison to male and affects mostly advanced age group people.[6] Iodine deficiency is the most common cause for the hypothyroidism and endemic goiter worldwide.[7]

Hypothyroidism is initiated with various symptoms like fatigueness, intolerance to cold, constipation, weight gain, poor appetite, shortness of breath. In females, heavy menstrual periods, abnormal sensation, poor hearing etc and signs like Dry, coarse skin, hair loss, myxedema, swelling of limbs, slow pulse rate etc causes immune deregulation which leads to inflammation.[8,9] Several studies have reported that various type of inflammatory marker have increased during hypothyroidism inflammation.

C-reactive protein (CRP)

The prime source of CRP is hepatic cell which is released in the circulation in response to inflammatory cytokines like interleukine-6(IL-6), Tumour necrosis factor alpha etc.[10] The higher concentration of inflammatory cytokines in the blood prevent the conversion of thyroxine into active tri-iodothyronine which is important for the maintenance of metabolism within the cell, leading to hypothyroidism.[11]

Adenosine Deaminase (ADA)
Adenosine Deaminase (ADA) is an important purine catabolic enzyme that promotes the deamination of adenosine to inosine supporting the regulation of adenosine cellular proportion.[12] The enzyme ADA have shown strong association with T-lymphocytes and B-lymphocytic function.[13,14] The auto immune diseases, Hashimoto's thyroiditis is linked with destruction of natural killer cell activity of blood lymphocyte.[15] Therefore, Serum ADA activity might be a useful marker in the prediction of hypothyroidism.

Erythrocyte sedimentation Rate (ESR)
Erythrocytes sedimentation rate is a simple and highly applicable test in medical practice for the detection of the inflammatory diseases.[16] The equilibrium between pro sedimentation factor especially fibrinogen charge of the erythrocytes regulates the erythrocytes sedimentation rate. The increased concentration of fibrinogen in the blood causes aggregation and promotes increased ESR level during the inflammatory process.[17]

The activity of these inflammatory markers CRP, ADA & ESR have been found involved in different inflammatory and autoimmune disorder.[18,19,20] The alterations in the level of these markers in thyroiditis are of interest and may have possible role in the development of the hypothyroidism. Till now, there are few studies which suggest the role of inflammation in hypothyroidism. However, other studies have disputed the role of inflammation in pathogenesis of hypothyroidism. In views of these controversies investigated to correlate the relation between inflammatory markers (CRP, ADA&ESR) and hypothyroidism, the present study was undertaken to investigate the role of inflammation in pathogenesis of hypothyroidism.

MATERIAL AND METHODS

Subject selection
In this hospital based study, a total 30 patients aged 20-50 were diagnosed as hypothyroidism, confirmed by the TSH,T3&T4(TSH>6.16µIU/ml) were selected from the medical OPD &IPD of Teerthanker Mahaveer Medical college & Reserch center, Moradabad and 30 healthy subjects were selected as controls.

Exclusion Criteria: The following individuals were excluded from the study.[21]

Diabetes mellitus, Hypertension, Pregnancy, smoking, Chronic kidney diseases, those suffering from chronic inflammatory diseases like Tuberculosis, leprosy etc.

Sample collection: 5ml of venous blood was drawn with aseptic precaution from anticubital vein of all the subjects after overnight fasting for 8 hours. The blood was collected in plain vial for the estimation of C-reactive protein (CRP) and Adenosine Deaminase (ADA) activity and was incubated for 37^0c for 30 minute. Similarly, EDTA Vial (2ml blood to 0.5ml sodium citrate) was used for the measurement of ESR (Erythrocyte sedimentation Rate).

Methods
The serum totals TSH, T3 & T4 for thyroid confirmation were estimated by enzyme immunoassay competition method with ELFA (Enzyme linked fluorescent assay) by using fully automated VIDAS. The concentration of CRP and ADA activity were estimated on semi auto analyzer. Similarly, ESR was measured on westergren tube.

Statistical analysis
All the parameters analysed (Serum TSH, T3, T4, CRP, ADA &ESR) were expressed in Mean± SD. To analyze the difference among the Parameters of hypothyroid patients group and controls, Student's t-test was used and association were analysed by calculation of correlation (r-value) using SPSS Program. The value considered significant was as follows:-
P<0.05-as significant.

RESULTS

Total 30 hypothyroid patients and 30 healthy controls having comparable age and sex was enrolled for the study. There was no significant difference between the groups. The mean ± SD value of TSH (11.30±3.6 Vs 3.27±1.27)µIU/ml was statistically higher and significant than that of control groups. Similarly, the mean ± SD value of T4 (7.125±3.48 Vs 8.15± 1.30) and T3 (2.96± 9.85 Vs1.07± 0.37) were also found higher but statistically insignificant in hypothyroid patients in comparison to healthy controls.

Table (1): Comparison of Serum TSH, T3 &T4, CRP, ADA & ESR in hypothyroid Patients with healthy controls.

Parameters	Hypothyroid Mean ± S.D (N=30)	Healthy controls Mean± S.D (N=30)	P-value
TSH (µIu/ml)	11.307 ± 3.596	3.266 ± 1.272	0.00
T3(ng/ml)	2.9555 ± 9.85	1.0733 ± 0.372	0.322
T4 (µg/dl)	7.125 3.489	8.157 ± 1.3057	0.135
CRP(mg/dl)	10.655 ± 7.817	5.449 ± 1.77	0.001
ADA (U/L)	33.87 ± 14.13	24.46 467 ± 6.468	0.002
ESR (mm/hr)	26.8 ± 8.659	16.566 ± 5.679	0.000

The mean±SD of CRP (10.65±7.8 Vs 5.44±1.77)mg/dl and ADA (33.87±14.13 Vs 24.46±6.46)U/L were observed significantly higher in hypothyroid patients in comparison to healthy controls. In the same way, on measuring the ESR level, mean± SD of ESR (26.8±8.6 Vs16.56 ±5.6) mm/h r was obtained significantly increased statistically.

There was no significant correlation found Between TSH, T3&T4 with markers CRP and ADA & ESR.

Table (2): Comparison of TSH, T3&T4 with CRP, and ADA & ESR in hypothyroid patients with healthy controls.

Parameters	TSH		T3		T4	
	r-value	P-value	r-value	P-value	r-value	p-value
CRP(mm/dl)	0.056	0.769	-0.131	0.490	0.316	0.089
ADA(U/L)	0.021	0.911	-0.159	0.400	0.33	0.72
ESR(mm/hr)	0.025	0.896	-0.73	0.702	0.428	0.18

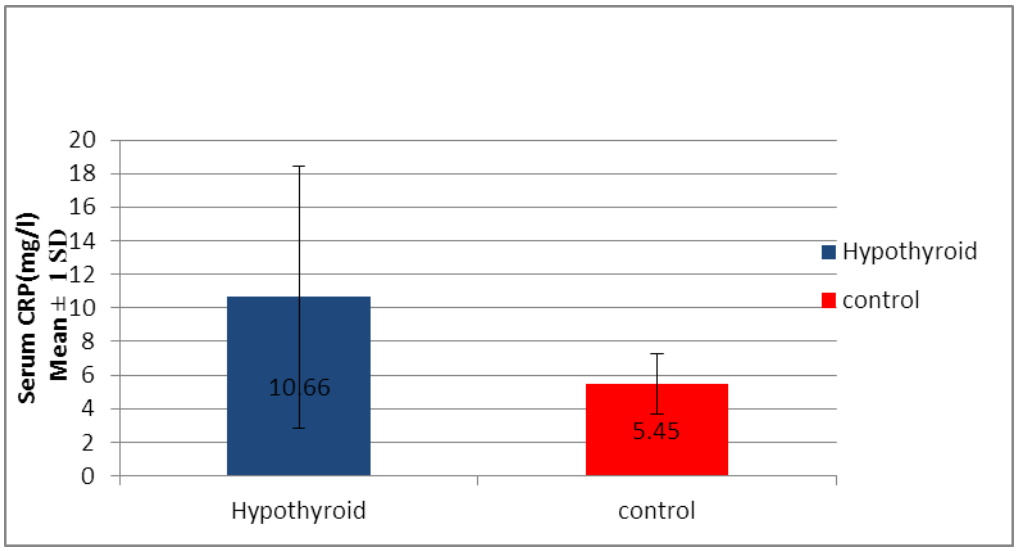


Figure (1.1): Comparison of Serum CRP between hypothyroid patients and healthy Controls.

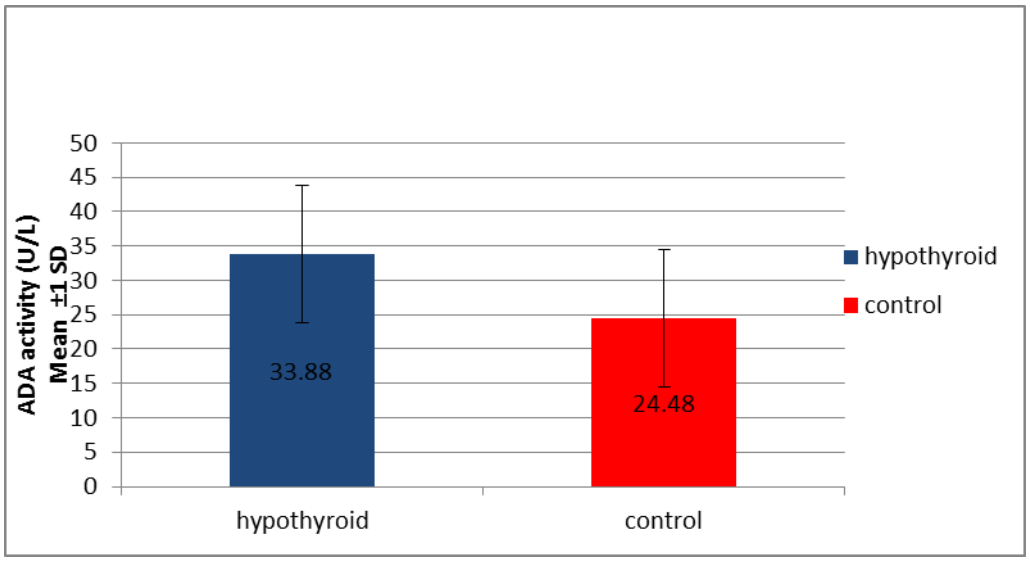
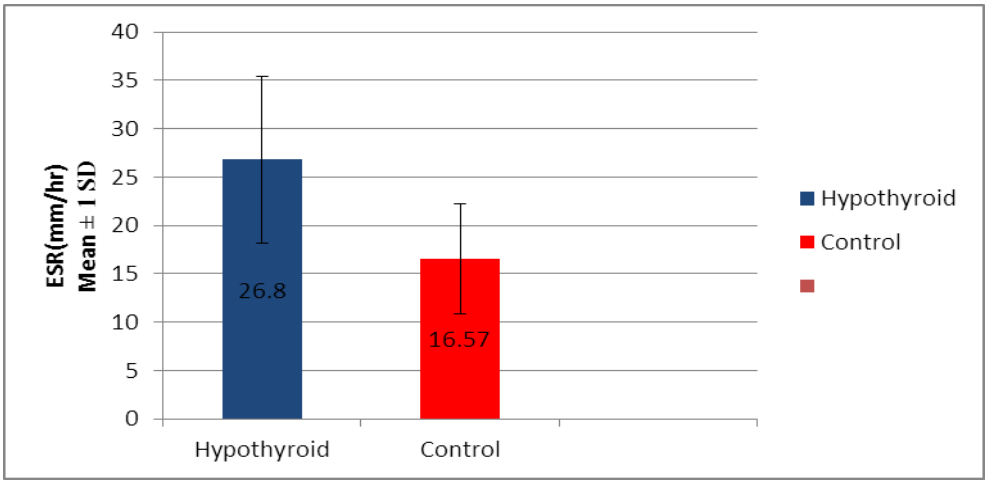


Figure (1.2): comparison of ADA activity between hypothyroid patients and healthy controls.



Figure(1.3): Comparison of ESR between hypothyroid and healthy controls.

DISCUSSION

In several studies, increased level of C-reactive (CRP), Adenosine Deaminase (ADA) and erythrocytes sedimentation Rate (ESR) have been observed in hypothyroidism. The increased level of these inflammatory markers may be due inflammation in hypothyroidism. Therefore, the study was planned to investigate the possible role of inflammation in hypothyroid patients.

In the study, inflammatory markers VIZ, CRP, ADA&ESR levels were compared between the hypothyroid patients and healthy controls. On comparing Serum CRP level, the hypothyroid subjects were found to be significantly higher in comparison to that of healthy controls (0.001). Similarly, serum ADA activity and ESR level were also found to be significantly higher in hypothyroid patients in compared to healthy controls, (P=0.002) and (P=0.000) respectively.

Numerous other studies conducted to predict the role of inflammatory markers in hypothyroidism has shown similar findings which supports the observation of this study revealing that the level of inflammatory markers are found to be significantly raised in hypothyroidism.

Czarnywojtek et al have demonstrated the elevated CRP level in hypothyroidism showing a close match with the current study.[22] **Taddei et al.** have demonstrated the significant elevation in serum CRP and ESR level in hypothyroid patients in comparison to healthy controls.[23,19]

Similar nature of result was reported by **ESen Savas et.al** in their study. They carried out their study on 86 hypothyroid patients (82 female and 4 male) who were admitted to outpatient clinic of Gaziantep University School of Medicine. They found significantly higher erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in comparison to the non thyroid control group (P=0.001) & (P=0.007).[24]

The insufficient thyroid hormones in hypothyroidism state cannot fulfil the requirement of the body which causes impairment in normal metabolic activities.[1] The impaired metabolic state develop several abnormalities, like weight gain, reduction in the resting energy expenditure, reduced lipolysis and increased cholesterol level etc.[25] These conditions produce the immune dysregulation which ultimately leads to inflammation.[8,9] In response of the inflammation or tissues injuries, several types of markers and cytokines including CRP are released into circulation.

In this study, mean serum ESR level was found significantly higher in hypothyroidism and the results were comparable with the results reported in several studies conducted in the past. The exact mechanism explaining how ESR is associated with other diseases have not been explained clearly. It may be possible that inflammation play role in reducing erythrocyte survival rate. Inflammation may also affect erythropoesis, erythrocyte circulatory half life promoting anisocytosis and thus increases ESR level.[26,27]

Several studies were conducted in regards to serum Adenosine deaminase (ADA) activity as an inflammatory marker in hypothyroidism. The results obtained were significant and higher in hypothyroid individuals in comparison to healthy controls which match with current finding of the study.

In a study conducted by **Vishnu madhuri et.al,** mean serum ADA(U/L) activity in the hypothyroid group (27.82±6.64) mg/L was found higher as compared to healthy controls(12.19±2.22) U/L and the result was significant($p<0.0001$).[28]

In another similar type of study carried out by Litvinenko, he has reported increased activity of serum ADA in 72% of the hypothyroid patients.[29]

CONCLUSION

On the basis of observed data in this study, it can be suggested that hypothyroidism is associated with

significantly increased of inflammatory markers C - reactive protein (CRP), adenosine deaminase (ADA) & Erythrocytes sedimentation rate (ESR). By the outcome of the study, we can give torch to the clinician working in their general practice for the diagnosis of hypothyroid. As the study has some limitation like sample size, so further study with large sample size required to establish these inflammatory markers as a better diagnostic tools.

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