Research Article

Assessment of The Role of High Sensitivity C- Reactive Protein in Prediction of Immune Thrombocytopenia Response to Treatment by Steroids

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Abstract

Background: Nowadays, Primary Immune Thrombocytopenia diagnosis (ITP) is based on identifying a platelet count < 100×10^9/L and exclusion of other causes of thrombocytopenia. Currently , there are no standard tests or biomarkers to diagnose primary ITP or predict its prognosis and response to treatment. **Objectives :**Our study aims at assessing the role of High sensitivity C- Reactive Protein in ITP pathogenesis and in the prediction of the disease behavior and response to treatment. **Methods:** Our study was done on four groups: **Group I** consisted of 28 newly diagnosed ITP patients in whom data were recorded before and after treatment with corticosteroids, **Group II** had 10 corticosteroid responder ITP patients, **Group III** contained 10 corticosteroid resistant ITP patients , while Group IV had 18 age and sex matched healthy control subjects to whom the previous three groups were compared. **Results**: Newly diagnosed ITP patients in our study were found to have significantly higher levels of High sensitivity CRP before treatment with corticosteroids compared to the same patients levels after treatment with corticosteroids, p value <0.001. Also, Comparing High sensitivity C- Reactive Protein levels in the four studied groups showed that they were higher in Corticosteroid resistant ITP patients (Group III) compared to the other three groups. p value <0.001. **Conclusion**: High sensitivity CRP level was found to be associated with ITP resistance to corticosteroid treatment, and it was found to decrease in the newly diagnosed patients after starting treatment by corticosteroids.

Key Words: Autoimmune - Immune thrombocytopenia - HSCRP - Resistant ITP - Corticosteroids .

Introduction

Primary immune thrombocytopenia (ITP) is an acquired immune mediated disorder characterized by isolated thrombocytopenia, defined as a peripheral blood platelet count less than 100×10^9/L, and the absence of any obvious initiating and/or underlying cause of the thrombocytopenia (Rodeghiero F et al., 2009). Concepts surrounding the mechanisms of thrombocytopenia in ITP have shifted from the traditional view of increased platelet destruction mediated by autoantibodies to more complex mechanisms in which both impaired platelet production and T cell–mediated effects play a role (Zhang et al., 2006).

On the other hand, CRP is increasingly being recognised as an important prognostic marker in many cardiovascular and auto-immune diseases. CRP is a non-specific marker of inflammation and has some favourable properties and also some limitations. The dynamic response of CRP to therapy that aims to modify the inflammatory process and the clinical context of a patient are of pivotal importance when CRP concentrations are interpreted (Ho et al., 2009) .

Material and Methods

Patients:

Group I consisted of 28 newly diagnosed ITP patients in whom data were recorded before and after treatment with corticosteroids, Group II had 10 corticosteroid responder ITP patients, Group III contained 10 corticosteroid resistant ITP patients, while Group IV had 18 age and sex matched healthy control subjects to whom the previous three groups were compared.

1- Routine laboratory Investigations: Using the commertially available kits, all patients underwent full laboratory investigation including complete blood count, INR, complete liver, renal function tests and viral markers .

***2*- High Sensitivity C-Reactive Protein:** using (HS-CRP) ELISA Kit, United States Of America.

3- Anti nuclear antibodies (ANA) level: by using Human ANA ELISA kit , Biorbyt , Units States.

4- Anti double stranded DNA antibodies (Anti-ds DNA) level: by using Human Anti-ds DNA ELISA kit, Biorbyt, Units States.

5 - Bone marrow examination: (was done in special conditions) .

6- Imaging studies: Abdominal ultrasound with Doppler analysis was performed by the ultrasound machine, **Toshiba Xario 100, Japan with 3-5MHz tranceducer**.

7- Statistical analysis: Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS software version 25).

Results

Table (1) represents a comparison of the laboratory data between the studied groups. Hemoglobin (Hb) level was nearly equal in the four groups (Mean + SD = 11.5 +1.1, 11.1 + 1, 11.9 +0.8, 12.9 +1.2). Also, there is statistically significant results as regards ESR in both first and second hours . In the first hour Median (IQR) was highest at Group II (Median IQR = 11.5 (10-13) compared to 6 (5-10), 6 (5-7.8), and 7.5 (6-10) in Group I, II, IV respectively), P = 0.002. Median ESR $^{\text{second hour}}$ was also higher at Group II (17 (14.8 - 19.3) compared to 10 (8-12), 10 (8-15.5), 12(10 - 15.8) in Group I, II, IV respectively), p= 0.005.

Comparing CRP level in the four groups, It was found to be higher at group III compared to the other groups (Median IQR 8875.5 (5397.8-12858) in Group III compared to 7781 (3683-10381), 7417 (5883.5-10529.8), 4476 (2779.3-6048.3) in Group I, II, IV respectively, p = 0.005.

Table (1): Laboratory data of the studied groups

	Group I	Group II	Group III	Group IV	P value
	Newly diagnosed	CS responder	CS resistant	Control	
	N=27	N=10	N=10	N=18	
Hb *Range* *Mean ± SD*	(9-14) [a] 11.5±1.1	(10.5-13) 11.9±0.8	(10-13) [a] 11.1±1	(11-15) [b] 12.9±1.2	***<0.001****
TLC *Median* *IQR*	6 (4.6-8)	5.5 (4.2-6.6)	6.1 (4.3-10.3)	6.4 (5-7.7)	*0.458*
Platelets *Median* *IQR*	9 [a] (8-11)	113 [c] (90-127.5)	19.5 [b] (16-22.3)	307 [d] (225.3-346.3)	***<0.001****
ESR 1st hour *Median* *IQR*	6 [a] (5-10)	11.5 [b] (10-13)	6 [a] (5-7.8)	7.5 [a] (6-10)	***0.002****
ESR 2nd hour *Median* *IQR*	10 [a] (8-12)	17 [b] (14.8-19.3)	10 [a] (8-15.5)	12 [a] (10-15.8)	***0.005****
CRP *Median* *IQR*	7781 [a] (3683-10381)	7417 [a] (5883.5-10529.8)	8875.5 [a] (5397.8-12858)	4476 [b] (2779.3-6048.3)	***0.005****

- One-way ANOVA test for parametric quantitative data between the four groups followed by post hoc analysis between each two groups
- Kruskal Wallis test for non-parametric quantitative data (expressed as median) between the four groups followed by Mann Whitney test between each two groups
- Fisher's exact test (expected value within cell < 5) for qualitative data between the groups
- Superscripts with different small letters refer to significant difference between each two groups
- *: Significant level at P value < 0.05

Table (2) ROC curve analysis of CRP for prediction of ITP

	CRP
Optimal cutoff point	>6527
AUC	0.778
95% CI	0.659-0.872
P value	***<0.001****
Sensitivity	63.83
Specificity	94.44
PPV	96.8
NPV	50
Accuracy	72.3

- AUC: Area Under Curve
- CI: Confidence Interval
- PPV: Positive Predictive Value
- NPV: Negative Predictive Value
- *: Significant level at P value < 0.05

Discussion

This study aimed to put some highlight on the role of CRP in predicting the treatment response in ITP patients. The results suggested that elevated CRP levels had a direct correlation with the severity and resistance of thrombocytopenia to steroid treatment. Nearly similar results were found by (Rama Kishore et al., 2017), as they suggested that increased C-reactive protein levels at diagnosis negatively predict platelet count recovery after steroid-treatment in newly diagnosed adult immune thrombocytopenia patients. It was also found that CRP levels are increased in ITP patients and correlate with platelet counts and bleeding severity and predict time to recovery (Kapur et al., 2015) .

Conclusions

Increased CRP levels were found at diagnosis of ITP, and the CRP levels dropped after corticosteroid treatment in newly diagnosed patients. Also, CRP levels increased at corticosteroid resistant cases predicting more difficult platelet count recovery in ITP. Thus highlighting the significance of measuring CRP level in ITP and its reflection on the course of the disease .

Recommendations

Our results may offer clues for reaching biomarkers for detection of ITP course and risk factors affecting the response of the disease to treatment. Hence, using agents that can target CRP levels.

Limitations of the study:

There are potential limitations of our study which include relatively small sample size, and lack of assessment of antiplatelet antibodies in the subjects.

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