Effect of Hematologic Values in Determining the Resolution of Subacute Thyroiditis and Long-Term Hypothyroidism Risk

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Abstract: Subacute thyroiditis (SAT), which can be considered a disease with infectious signs and parameters, can affect humans and lead to permanent hypothyroidism. Haematological parameters play an essential role in SAT; these parameters begin to normalise after the thyrotoxic phase; however, there is still a gap in knowledge about how these parameters play a role in SAT prognosis. Therefore, we wanted to investigate haematological parameters and their impact on treatment response and recovery phase in patients with SAT. 51 SAT patients and 44 healthy controls were included in the study. ESR, CRP, NLR and MPV were recorded at the diagnosis and after resolution. The changes in these parameters were compared to determine the resolution phase. The ratio of permanent hypothyroidism after one year was studied, and its relevance with these parameters at the time of diagnosis was explored. 36 of 51 SAT patients were female in the study (70.5%). The mean age was 45.53 ± 11.46 years. In the acute phase, WBC, Neutrophil, platelet, ESR, N/L, and P/L were significantly higher (p<0.05). In the recovery phase, MPV and lymphocyte count were significantly higher (p: 0.002 and p=0.002). WBC, CRP, and ESR had the highest AUC values in ROC analysis (0.990, 0.959, 0.907, p<0.05). P/L and N/L ratios also had higher ratios for the acute phase (0.807, 0.98, p<0.05, respectively). Δ ESR, Δ CRP, Δ N/L, and Δ P/L had the highest AUC for the recovery phase (AUC= 0.990, 0.899, 0889,0.800, p<0.5, respectively). Permanent hypothyroidism after one year was 9/42 (21.4%). In addition to ESR and CRP, NLR, PLR and MPV were also successfully used to estimate SAT activity and response to treatment. Moreover, a decrease in NLR and PLR and an increase in MPV were associated with the treatment response and resolution phase. However, these parameters did not determine the long-term risk of hypothyroidism.

Keywords: Subacute thyroidism; erythrocyte sedimentation rate; mean platelet volume; neutrophil-lymphocyte ratio; platelet to lymphocyte proportion.

INTRODUCTION

Subacute thyroiditis (SAT), which predominantly affects women, is an inflammatory disease that can lead to permanent hypothyroidism in 22-26.8%. (Gorges et al., 2020) It could primarily result from a viral disease (Desailloud & Hober, 2009). However, the parameters erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often elevated in bacterial infections and are used as primary criteria for the diagnosis of subacute thyroiditis (Stasiak et al., 2020). Disease diagnosis is primarily based on clinical symptoms and physical examination, including neck pain, tenderness, fever, malaise (Stasiak, et al., 2020), and laboratory

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parameters. Inflammatory markers and elevated increased free thyroid hormones make up the primary picture. In addition, thyroid ultrasound ultrasonography, scintigraphy and autoantibodies can be helpful in the diagnosis (Ross et al., 2016)

In addition to ESR and CRP, mean platelet volume (MPV) and neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are popular parameters in the diagnosis and prognosis of acute and chronic infections. These parameters have been explored in inflammatory diseases and solid malignancies to predict prognosis and response to treatment. These studies have found that hematological parameters like NLR could present a cost-effective and easy reachable way in clinical practice. (Lagunas-Rangel, 2020) (Kuzucu et al., 2020) (Templeton et al., 2014) (Mirna et al., 2021). Up today, not so many studies have explored the role of hematological parameters in subacute thyroiditis prognosis. Therefore, we wanted to investigate the haematological parameters and their impact on the response to treatment and the recovery phase in patients with SAT.

MATERIALS AND METHODS

51 SAT Patients referred to the Department of Endocrinology and Metabolism, Istanbul Research and Education Hospital, between February 2020 and June 2022, were included in the study. Haematological values, Thyroid Stimulating Hormone (TSH), free T3, free T4, ESR, CRP, anti-TPO and TSH receptor antibody levels were recorded at the time of diagnosis. Thyroid ultrasound and scintigraphy reports were summarised and noted. The treatment method, type of treatment and duration were also recorded. The time taken for the symptoms to disappear was noted. Haematological values and thyroid hormone levels were measured at the end of treatment. The changes in MPV, NLR and PLR before and after treatment and their irrelevance with treatment methods were compared. 44 sex- and age-matched healthy control subjects were also included in the study. Male and female patients aged 18-70 were included in the study. Patients with pregnancy, acute or chronic inflammation, chronic renal failure, other endocrine disease and haematological or solid organ malignancies were excluded from the study. Patients taking medications affecting laboratory parameters and thyroid functions were also excluded from the study. Ethical approval was obtained from Istanbul Research and Education Hospital (20.05.2022/163). The Helsinki Declaration was followed.

Statistical evaluations were performed using IBM SPSS 22.0 (Statistical Package for the Social Sciences software version 22.0). Descriptive analyses were expressed as median (min-max) or mean ± standard deviation (SD) and percentages (%). Shapiro–Wilk test was used for normality. Where appropriate, the Chi-square test or Fisher's exact test was used for categorical variables. The student's t-test was used to compare the two groups normality distributed continuous variables. The Mann-Whitney U-test was used to compare the two groups' continuous variables that were not normally distributed.

RESULTS AND DISCUSSION

36 of the 51 SAT patients in the study were female (70.5%). The mean age was 45.53 ±11.46 years. All patients had negative thyroid receptor antibodies. Thyroid scintigraphy imaging of the patients was consistent with thyroiditis. ESR, free T3 and free T4 were elevated (table 1). In the acute phase, WBC, neutrophils, platelets, ESR, N/L, and P/L were significantly increased (p < 0.05). In the recovery phase, MPV and lymphocyte count were significantly higher (p: 0.002 and p=0.002) (Table 2). WBC, CRP and ESR had the highest AUC values in the ROC analysis (0.990, 0.959, 0.907,

p < 0.05). P/L and N/L ratios also had higher values for the acute phase (0.807, 0.98, p < 0.05, respectively). Δ ESR, Δ CRP, Δ N/L and Δ P/L had the highest AUC for the recovery phase (AUC= 0.990, 0.899, 0889,0.800, p < 0.5, respectively) (Table 3- acute phase) (Table 4- recovery phase) (Figure 1). Permanent hypothyroidism at one year was present in 9/42 (21.4%). CRP, MPV, WBC, ESR, NLL and PLL were not significantly associated with permanent hypothyroidism at baseline (p > 0.05).

Table 1. Characteristics of The Groups

	SAT (n=51)	Control (n=44)	p
Gender (Female/Male)	36/15	30/14	0.82
Age (years)	45.53±11.46	49.34±10.86	0.11
TSH mU/L	0.04±0.03	1.89±0.80	**0.00**
FreeT3 ng/dl	5.04±1.98	3.05±0.52	**0.00**
Free T4 ng/dl	11.7±1.64	5.30±8.94	**0.00**
ESR mm/h	78.46±28.38	23.15±19.51	**0.00**

*p < 0.05 = significant, significant values were expressed in bold

Table 2. Acute Inflammatory Phase and Recovery Phase Compassion

	Acute	Recovery	p	r
WBC (10^3/mm^3)	8781.73±2131.95	7183.91±2074.24	**0.003**	0.595
Neutrophil(10^3/mm^3)	5835.20±1875.93	3817.60±1520.94	**0.001**	0.635
Platelet(10^3/mm^3)	341555.55±87065.83	255370.81±93267.99	**0.005**	0.523
MPV (fl)	9.88±1.00	10.47±1.28	**0.002**	0.596
Sedimentation	57.38±36.28	27.98±21.23	**0.001**	0.525
Lymphocyte(10^3/mm^3)	1957.30±908.67	3611.92±7343.15	**0.002**	0.994
Neutrophil/Lymphocyte	3.55±2.25	1.96±1.05	**0.041**	0.411
Platelet /Lymphocyte	166.16±70.47	146.28±148.46	**0.011**	0.364
CRP	41.92±7.67	6.20±1.70	**<0.001**	0.511

*p < 0.05 = significant, significant values were expressed in bold

Table 3. ROC Analysis Of Parameters In Acute Phase

	AUC	p
Platelet/Lymphocyte	0.807	**0.008**
Neutrophil/Lymphocyte	0.798	**0,006**
MPV	0.472	0.686
Free T3	0.913	**0.001**
CRP	0.959	**0.045**
ESR	0.907	**<0.001**
WBC	0.990	**<0.001**

*p < 0.05 = significant, significant values were expressed in bold

Table 4. ROC Analysis Of Parameters In Recovery Phase

	AUC	p
Δ Platelet/Lymphocyte	0.800	**<0.001**
Δ Neutrophil/Lymphocyte	0.889	**<0.001**
Δ MPV	0.771	**<0.001**
Δ CRP	0.899	**<0.001**
Δ ESR	0.990	**<0.001**
Δ WBC	0.720	**0.011**

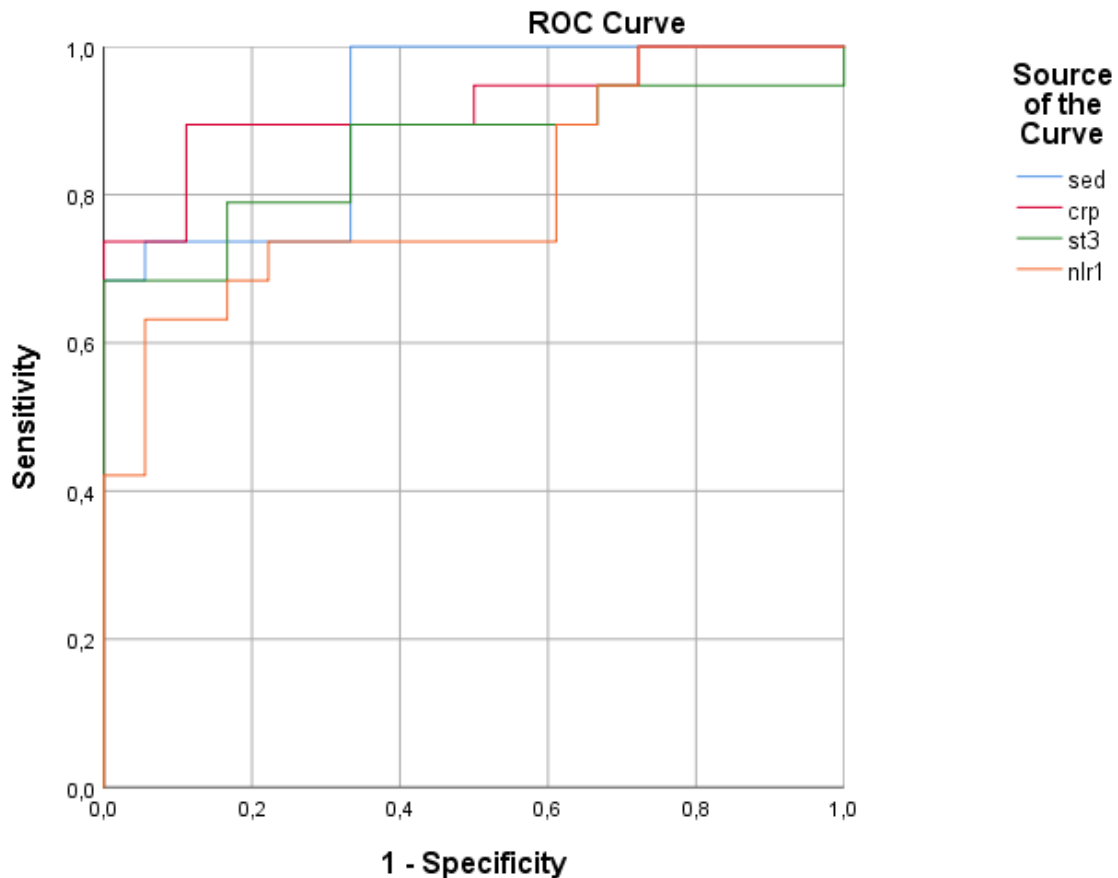*p < 0.05 = significant, significant values were expressed in bold

Figure 1. ROC Curve Analysis of Parameters

In line with the results of this study, we report that haematological parameters play an essential role in the diagnosis of subacute thyroiditis; changes in ESR, CRP and neutrophil/lymphocyte ratio were found to be the most valuable determinants of the recovery phase. 70.5% of the patients were female, and the mean age in this study was 45.53±11.46 years; the results seem reasonable and compatible with our studies (Stasiak, et al., 2020; Samuels, 2012). The rate of hypothyroidism at one year was 21.4%, consistent with previous results from other studies (Görges et al., 2020; Zhao et al., 2020). All acute inflammatory markers we studied were significantly higher in the SAT acute phase, as were NLR and PLR in this condition.

NLR is a commonly used, simple and practical marker that can separate infectious and non-infectious stimuli. Values of more than three are considered pathological (Zahorec, 2021). To the best of our knowledge, the NLRpredicts not only the infectious state in the body (de Jager et al., 2012) but also the progression of various tumour types (Chim et al., 2021; Arıman & Merder, 2021; Liontos et al., 2021). We found that NLR was significantly higher in the SAT group and the acute phase. A decrease in NLR after the resolution had a higher AUC (Table 2,4).

PLR has recently received attention as a prognostic marker in infectious and immunological events to assess prognosis (Koh et al., 2015; You et al., 2016) Both NLR and PLR were significantly higher in SAT to differentiate from Graves' disease (Taşkaldiran et al., 2019). We found significantly higher AUC values for decreased PLR at the resolution stage (Table 4). MPV is associated with inflammatory states and tumour progression (Seles et al., 2017). MPV decreased significantly in the SAT acute

phase, consistent with a previous study of 35 SAT patients (Fan & Tang, 2017). In addition, we saw an increase in MPV with the resolution of SAT. This is the first study to show an increase in MPV at SAT with treatment (Table 2).

In the analysis of ROC, we saw a decrease in ESR, and CRP had the highest AUC values for resolution (Table 4). However, a decrease in PLR and NLR and an increase in MPV were considered significant for the resolution phase. Previously, a few studies had examined these parameters for the diagnosis of SAT, but none of them examined the change in these parameters with resolution.

There are some important caveats to the study that should be mentioned. First, it was a single-farm study; second, the study population was not very large. This study carried out careful analysis and evaluation despite these limitations.

CONCLUSION

NLR and PLR were significantly increased, and MPV decreased in SAT patients, and the decrease in NLR and PLR and the increase in MPV could significantly estimate disease resolution. Therefore, these parameters could be successfully used to assess disease activity and response to treatment.

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CONFLICT OF INTEREST

The research reveals that there is no conflict of interest in this study.

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