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EVALUATION OF THE STEROIDAL AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS TREATMENTS IN SUBACUTE THYROIDITIS AMONG SYRIAN PATIENTS

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ABSTRACT
Subacute thyroiditis (SAT) is a transient inflammation in thyroid gland, which etiology is completely unclear. The treatment is aimed at first place to mitigate inflammation. This research was performed due to the recent increase in the number of cases of subacute thyroiditis in the Syrian Arab Republic, the spread of infections during the COVID-19 pandemic, and the lack of local studies on the differences between the treatments used in patients with SAT. The aim of this retrospective study was to compare the therapeutic effects of prednisolone and non-steroidal anti-inflammatory drugs in terms of the time needed for treatment (TT), the time needed for symptoms to disappear (TS), and the return of laboratory values to their normal state. In this study, 50 consecutive Syrian patients—44 females (88%), 6 males (12%)—who had been diagnosed with SAT were treated either with corticosteroids (n = 27), NSAIDs (n = 19) or NSAIDs with corticosteroids (n = 4). The time period for resolution of symptoms (TS) was shorter with prednisolone than NSAIDs (8.7±3.719, vs 16.31±6.07 days, p=0.00001); however, the time needed for full recovery (TT) was shorter under the NSAIDs drugs than prednisolone but the difference was not statistically significant (35.52±19.59, vs 38.222±15.4 days, p=0.372). The time required for the symptoms to disappear, and the time required for total treatment are longer in the case of severe infections than in cases of moderate infections, regardless of the type of treatment used. There were no statistically significant differences in these times between mild and moderate cases.

KEYWORDS: Subacute thyroiditis (SAT), NSAIDs, prednisolone, corticosteroids, Therapeutic effectiveness.

INTRODUCTION
Subacute thyroiditis (SAT) (also called De Quervain`s thyroiditis) is a thyroid inflammatory disease, with unclear pathogenesis and etiology.[1, 2] SAT is usually associated with inflammation-related symptoms; the main symptoms are usually pain in the thyroid, jaw and ears; the other common symptoms are malaise, fatigue, and tenderness.[3] Diagnosis of SAT is based on laboratory evidence of thyrotoxicosis, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), free thyroxine (FT4) concentration, free triiodothyronine (FT3) and thyrotropin (TSH), the clinical history, physical examination, and radioactive iodine uptake test (RAIU).[3] The main goal of treatment for SAT is to relieve pain and mitigate inflammation with anti-inflammatory drugs. NSAIDs and corticosteroids are the most common anti-inflammatory agents used in treatment.[1–3] To our knowledge, there is no clear and confirmed information about the differences in the time for symptoms to disappear, the time required for complete recovery, or the effect on laboratory values between treatment with NSAIDs and corticosteroids. The aim of this study was to compare the changes in laboratory values, the time for symptoms to disappear, and the time for complete recovery of corticosteroids and NSAIDs in patients with SAT.

PATIENTS AND METHODS
Patients
This study is a retrospective observation study involving 50 patients files (6 males 12% and 44 females 88%) of SAT patients were collected from private outpatient clinics for endocrinologists from several Syrian cities and governorates. The ages of the study sample ranged between 17 and 64 years. The anti-inflammatory drug

selected by the physicians included PSL (n = 27), NSAIDS (n = 19) or NSAIDS +PSL (n=4).

Methods

1. Data

The data involved personal and health information for each patient within the practical study. The most important of this information is pathogenic precedents, clinical symptoms, symptoms of hyper thyroiditis, symptoms of thyroid palaces, the appearance of symptoms before visiting the clinic, laboratory values of the most important laboratory examinations, assessment of infection.

2. Treatment

There are no definite guidelines for the selection of drugs for the treatment of patients with SAT. Thus, the drug selected (NSAIDs or corticosteroids) and dose were determined by the attending endocrinologists depending on their experiences. In all patients, prednisolone (PSL) was tapered in 5 mg steps from the initial dose, which was given weekly in most cases and biweekly in a few cases. In all patients on NSAIDs, treatment was discontinued by the time of complete recovery. The time required for symptoms to disappear is defined as the disappearance of subjective symptoms. And the time required for complete recovery is defined as the normalization of thyroid hormones' data in addition to the disappearance of all SAT symptoms.

3. Statistical analysis

The mean and standard deviation (SD) have been calculated, and the statistical importance of the differences was evaluated between the values of the means of the laboratory values and the time necessary for the disappearance or improvement of symptoms according to each therapeutic group, by applying Test of Homogeneity of Variances, ANOVA, Welch and Brown-Forsythe, the value of $Sig<0.05$is considered 0.05 statistically important. Statistical analysis performed depending on the statistical package for social sciences (SPSS).

RESULTS AND DISCUSSION

Among the 50consecutive patients with SAT, the lowest age was 17, the highest age was 64 and the mean age for the sample was 36.8±10.2. The distribution of the study sample according to age is in table 1.

Table 1: Distribution of sample study according to age.

Age group	Number of patients	Percentage
15 – 24	8	16 %
25 – 54	39	78 %
55 – 69	3	6 %
SUM	50	100 %

Among the study sample patients, 78% of patients were between 25 and 54 years old, compared to only 6% in patients with ages over 55 years, and 16% in patients with ages under 24 years. The distribution of the disease between the ages of 25 and 55 may be attributed to factors such as depression, confusion, or, viral exposure, in addition to physical inactivity.[4,5]

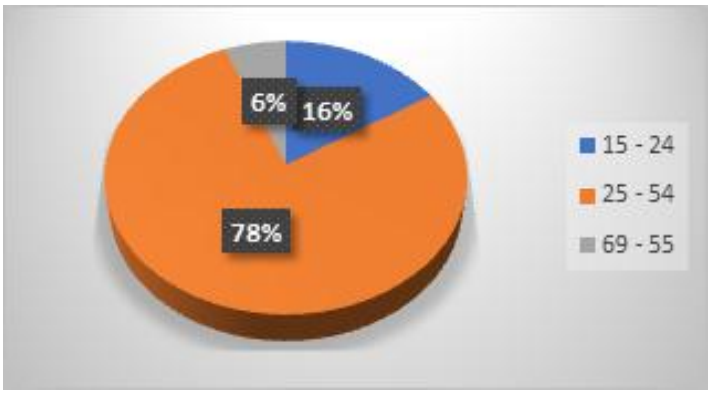

Figure 1: The percentage of the spread of the disease according to age groups.

The study sample comprised 50 patients, of which 88% were females (44 patients) and only 12% were males (6 patients). Our findings align with established scientific literature, which consistently reports a higher prevalence of subacute thyroiditis among females, with incidence rates approximately 8-10 times higher than in males.[5, 6] This discrepancy may be attributed to several factors: higher prevalence of autoimmune diseases among women[7], hormonal fluctuations during the menstrual cycle influencing thyroid hormone levels[8], increased susceptibility of women's bodies to hormonal changes[9], as well as stress and iodine deficiency commonly observed during pregnancy or menstruation.[10, 11]

Our study revealed that 64% of subacute thyroiditis cases were preceded by viral infections (including COVID-19), followed by 20% associated with bacterial infections, while 12% of patients had a history of allergies, and 2% lacked identifiable precedents. These findings corroborate existing scientific literature, suggesting that viral or bacterial infections may trigger the formation of nonspecific antibodies in susceptible individuals, while others may develop spontaneously due to autoimmune dysfunction.[2, 12, 13]

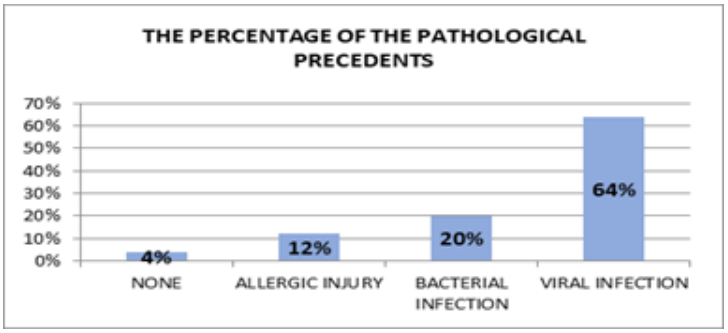

Figure 2: The percentage of the pathological precedents recorded before the SAT.

The clinical symptoms of subacute thyroiditis were meticulously documented across all participants of the study sample. These symptoms encompassed a spectrum ranging from neck pain, jaw pain, pain radiating to the ears, to difficulty swallowing. Moreover, clinical manifestations were further delineated into symptoms characteristic of hyperthyroidism and hypothyroidism, meticulously cataloged in the study sample questionnaire as delineated in Tab.3.

Table 2: Distribution of the study sample according to clinical symptoms.

Clinical symptoms	Details of symptoms	Number of patients	Percentage
Common general symptoms	Neck pain + jaw pain + pain extending to the ears + difficulty swallowing	50	100 %
Symptoms of hyperthyroidism phase	Weight loss + tension + palpitations + nervousness	41	82 %
Symptoms of hypothyroidism phase	Tiredness + feeling cold + constipation + weight gain	9	18 %

In our study sample, 82% of patients exhibited symptoms characteristic of the hyperthyroidism phase, including low weight, tension, palpitations, and nervousness, whereas only 18% presented symptoms indicative of thyroid failure, such as fatigue, feeling cold, constipation, and weight gain, marking the latter as the subsequent advanced phase of subacute thyroiditis (SAT). These symptoms arise from the initial surge in thyroxine and triiodothyronine during the hyperthyroidism phase, followed by their subsequent decline in the hypothyroidism phase, thereby manifesting common traits of hyperactivity and hypoactivity.[14]

The relatively low percentage of hypothyroidism cases compared to hyperactivity occurrences can be attributed to early SAT diagnosis and initiation of anti-inflammatory treatment during the hyperthyroidism phase, effectively averting the onset of hypothyroidism.

The duration of symptoms preceding specialist consultation and diagnosis varied significantly, spanning from one to 12 days, with an average duration of approximately four days. SAT severity classification, based on symptomatology and diagnostic laboratory values, ranged from mild to severe. Table 4 illustrates the distribution of our study sample according to SAT severity, with the majority of cases falling under the category of moderate severity.

Table 3: Distribution of the study sample according to the severity of SAT.

Severity of SAT	Number of patients	Percentage
Mild	7	14 %
Moderate	30	60 %
Severe	13	26 %
SUM	50	100 %

Treatment for the condition involved administering anti-inflammatory drugs, with some cases receiving non-steroidal anti-inflammatory drugs (NSAIDs) (n = 19), while others commenced treatment directly with corticosteroids (n = 27). In a few instances, a combination of both groups was employed (n = 4).

The group administered NSAIDs exhibited an average of 15 days until symptom improvement or resolution (TS), whereas patients receiving prednisolone (PSL) experienced a shorter duration (average of 11.5 days) until symptom amelioration or disappearance. Moreover, the average duration until complete recovery (TT) was shorter in the NSAID group. We posit that this disparity may be attributed to the time required for gradual cortisone tapering in the corticosteroid group.

Table 5: The differences in the time of total treatment and the time necessary to start the improvement of symptoms between the two study groups.

	NSAIDs	STEROIDS	F	Sig.
The mean of days of treatment (TT)± SD	35.52±19.59	38.222±15.4	0.868	0.372
The mean of days of treatment until the symptoms improve or disappear (TS)± SD	16.31±6.07	8.7±3.719	8.436	**0.00001**

Upon comparing the total treatment time (TT) and the time to symptom improvement (TS), a statistically significant difference (Sig = 0.00001) was observed between the two study groups regarding the period required for symptom resolution. This implies that the reduction in TS values is statistically significant when employing a steroidal anti-inflammatory compound compared to NSAIDs. Conversely, no statistically significant difference was found between the two study groups regarding the total treatment period (TT). The notable statistical disparity in the time required for symptom improvement between NSAIDs and prednisolone suggests the superior efficacy of prednisolone in addressing symptoms associated with SAT, potentially attributable to its broader inhibition spectrum of inflammatory mediators.[16] Nevertheless, the duration for laboratory values to normalize and achieve complete recovery is similar across both treatment groups, underscoring the importance of considering individual patient characteristics when selecting the appropriate treatment strategy. This finding aligns with the conclusions drawn in the study.[1]

Given the potential impact of SAT severity on symptom duration and total treatment time, we conducted a comparative analysis of TS and TT across patients categorized by SAT severity. The statistical analysis revealed significant differences in TS values between moderate and severe cases, as well as in TT values between moderate and severe cases. This indicates that the duration for symptom resolution and total treatment is prolonged in severe SAT cases compared to moderate ones, irrespective of the treatment modality employed, a conclusion that appears logical. No statistically significant differences in these durations were observed between mild and moderate cases (Table 6).

Table 6: The differences in the time of total treatment and the time required to start improving symptoms among patients according to the severity of the SAT

Dependent Variable	severity	severity	Mean Difference	Sig.
TT	mild	moderate	-9.31855	0.736
		severe	-54.55357	0.082
	moderate	mild	9.31855	0.736
		severe	-45.23502*	0.048
	severe	mild	54.55357	0.082
		moderate	45.23502*	0.048
TS	mild	moderate	3.33871	0.315
		severe	-6.63333	0.074
	moderate	mild	-3.33871	0.315
		severe	-9.97204*	0.000
	severe	mild	6.63333	0.074
		moderate	9.97204*	0.000

We studied the differences of the means of laboratory values of CRP, ESR, TSH, and FT4 after treatment by using steroidal and non-steroidal anti-inflammatory drugs (Table 7).

Table 7: The differences in the means of values of laboratory analyses after treatment between the two drug groups, NSAIDs and corticosteroids.

Laboratory Analyses	Drug group	Mean of value before treatment± SD	Mean of value after treatment± SD	F	Sig.
CRP	NSAIDS	54.72 ± 33.44	9.595 ± 4.73	**0.722**	0.402
	STEROIDS	55.36 ± 42.95	8.286 ± 4.183		
	NSAIDS +STEROIDS	42.475 ± 37.85	7.825 ± 3.704		

ESR	NSAIDS	71.02 ± 25.6	14.434 ± 6.33	0.010	0.923
	STEROIDS	74.709 ± 29.036	14.207 ± 9.72		
	NSAIDS + STEROIDS	85 ± 38.69	18 ± 10.36		
TSH	NSAIDS	0.2134 ± 0.42	2.83 ± 1.71	0.098	0.756
	STEROIDS	0.272 ± 0.671	2.71 ± 1.41		
	NSAIDS +STEROIDS	0.0505 ± 0.031	2.69 ± 1.699		
FT4	NSAIDS	4.44 ± 0.42	2.81 ± 4.06	0.081	0.777
	STEROIDS	4.661 ± 2.694	3.22 ± 4.34		
	NSAIDS +STEROIDS	4.216 ± 2.32	2.055 ± 1.584		

From Table 7, the analysis revealed no statistically significant differences in the studied laboratory parameters between the two groups receiving different drugs (Sig > 0.05). Among these parameters, CRP exhibited the highest sensitivity to changes, as indicated by the largest F value of 0.722. Furthermore, gender did not demonstrate any statistically significant differences in laboratory value changes among patients, irrespective of the treatment administered.

Given that the choice of anti-inflammatory drugs hinges on the severity of SAT, clinicians typically prescribe NSAIDs for patients with mild symptoms, reserving glucocorticoids for those with moderate or severe symptoms. To elucidate previous findings, we examined the therapeutic efficacy of NSAIDs versus prednisolone in patients with moderate and severe SAT. Mild cases were excluded from the analysis due to the limited sample size.

Table 8: The differences in TT and TS between different drugs in the moderate-SAT group.

Drug	Mean of TT± SD (days)	F	P value	Mean of TS± SD (days)	F	P value
prednisolone	37.211± 17.980	0.15111	0.700313	7.579± 3.185	18.4354	**0.000179**
NSAIDs	34.583± 18.885			14.25± 5.496		

Table 9: The differences in laboratory tests between different drugs in the moderate-SAT group.

Drug	Mean of CRP± SD	P value	Mean of TSH± SD	P value	Mean of ESR± SD	P value	Mean of FT4± SD	P value
prednisolone	8.666± 3.464	0.6566	2.774± 1.282	0.5597	11.864± 3.966	0.2228	2.343 ± 2.635	0.54838
NSAIDs	9.7 ± 6		3.105± 1.845		13.6± 3.451		1.754 ± 0.870	

Table 10: The differences in TT and TS between different drugs in the severe SAT group.

Drug	Mean of TT± SD (days)	F	P value	Mean of TS± SD (days)	F	P value
prednisolone	87.273± 10.203	0.092941	0.765693	15.636± 11.843	6.66306	**0.022801**
NSAIDs	60± 0.0			32.5± 8.660		

Table 11: The differences in laboratory tests between different drugs in the severe SAT group.

Drug	Mean of CRP± SD	P value	Mean of TSH± SD	P value	Mean of ESR± SD	P value	Mean of FT4± SD	P value
prednisolone	8.2± 5.891	0.768	2.422± 1.583	0.484	18.909± 14.675	0.941	4.796± 6.184	0.780
NSAIDs	9.25± 3.862		3.06± 1.274		19.5± 8.505		5.935± 8.236	

Our study findings indicated that thyroid hormone levels in our patients mirrored those observed in previous studies conducted in other countries. However, the levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in our patients surpassed values reported in studies from other nations.[15]

While we recommend prednisolone (PLS) for patients with severe SAT, our analysis did not reveal significant differences in laboratory values between patients receiving PLS and NSAIDs, precluding definitive assertions regarding superior treatment outcomes. Nonetheless, our findings support the notion that PLS usage was associated with a shorter time to SAT symptom resolution (TS), aligning with data from similar studies advocating for the superiority of PLS over NSAIDs in symptom resolution.[1]

Despite providing valuable insights into subacute thyroiditis diagnosis and treatment, our study is subject to limitations including a relatively small sample size and a single-center design. Future investigations could encompass larger, multicenter studies to validate our findings and explore potential genetic and environmental factors influencing disease development and progression.

In summary, our study underscores a statistically significant difference between prednisolone and NSAIDs in terms of time to symptom improvement, favoring prednisolone, despite no notable disparity in total treatment time. Our results highlight the superiority of prednisolone usage, particularly in moderate and severe cases, due to its efficacy in resolving initial symptoms until thyroid function normalization occurs.

REFERENCES

1. Sato, J., Uchida, T., Komiya, K., Goto, H., Takeno, K., Suzuki, R., Honda, A., Himuro, M., & Watada, H. Comparison of the therapeutic effects of prednisolone and nonsteroidal anti-inflammatory drugs in patients with subacute thyroiditis. Endocrine, 2017; 55(1): 209–214.
2. Stasiak, M., &Lewiński, A. New aspects in the pathogenesis and management of subacute thyroiditis. Reviews in Endocrine & Metabolic Disorders, 2021; 22(4): 1027–1039.
3. Bahn Chair, R. S., Burch, H. B., Cooper, D. S., Garber, J. R., Greenlee, M. C., Klein, I., Laurberg, P., McDougall, I. R., Montori, V. M., Rivkees, S. A., Ross, D. S., Sosa, J. A., Stan, M. N. Hyperthyroidism and other causes of thyrotoxicosis: Management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid: Official Journal of the American Thyroid Association, 2011; 21(6): 593–646.
4. Erdem, N., Erdogan, M., Ozbek, M., Karadeniz, M., Cetinkalp, S., GokhanOzgen, A., Saygılı, F., Yilmaz, C., Tuzun, M., &Kabalak, T. Demographic and clinical features of patients with subacute thyroiditis: Results of 169 patients from a single University Center in Turkey. Journal of Endocrinological Investigation, 2007; 30(7): 546–550.
5. Samuels, M. H. Subacute, silent, and postpartum thyroiditis. The Medical Clinics of North America, 2012; 96(2): 223–233.
6. Clinical Features and Outcome of Subacute Thyroiditis in an Incidence Cohort: Olmsted County, Minnesota, Study The Journal of Clinical Endocrinology & Metabolism | Oxford Academic. (n.d.). Retrieved November 2, 2022, from https://academic.oup.com/jcem/article/88/5/2100/2845301?.
7. Kronzer, V. L., Bridges, S. L., & Davis, J. M. Why women have more autoimmune diseases than men: An evolutionary perspective. Evolutionary Applications, 2020; 14(3): 629–633.
8. Jacobson, M. H., Howards, P. P., Darrow, L. A., Meadows, J. W., Kesner, J. S., Spencer, J. B., Terrell, M. L., & Marcus, M. Thyroid hormones and menstrual cycle function in a longitudinal cohort of premenopausal women. Paediatric and Perinatal Epidemiology, 2018; 32(3): 225–234.
9. Reproductive hormone sensitivity and risk for depression across the female life cycle: A continuum of vulnerability? - PMC. (n.d.). Retrieved November 2, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2440795/.
10. Skeaff, S. A. Iodine Deficiency in Pregnancy: The Effect on Neurodevelopment in the Child. Nutrients, 2011; 3(2): 265–273.
11. The Effects of Iodine Deficiency in Pregnancy and Infancy—Zimmermann—2012—Paediatric and Perinatal Epidemiology—Wiley Online Library. (n.d.). Retrieved November 2, 2022, from https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-3016.2012.01275.x.
12. Desailloud, R., &Hober, D. Viruses and thyroiditis: An update. Virology Journal, 2009; 6: 5. https://doi.org/10.1186/1743-422X-6-5.
13. Subacute Thyroiditis—Endocrine Surgery | UCLA Health. (n.d.). Retrieved November 2, 2022, from https://www.uclahealth.org/medical-services/surgery/endocrine-surgery/patient-resources/patient-education/endocrine-surgery-encyclopedia/subacute-thyroiditis.
14. Lanzo, N., Patera, B., Fazzino, G. F. M., Gallo, D., Lai, A., Piantanida, E., Ippolito, S., & Tanda, M. L. The Old and the New in Subacute Thyroiditis: An Integrative Review. Endocrines, 2022; 3(3): 3.
15. Angelopoulos N, Askitis DP, Androulakis I, Valvis N, Paparodis R, Petkova V, Boniakos A, Zianni D, Perogamvros I, Toulis K, Livadas S, Iakovou I. Clinical Aspects in Subacute Thyroiditis: A Real-Life Study on 226 Cases in Greece Amid the COVID-19 Pandemic. J Clin Med., 2023 Nov 18; 12(22): 7171. doi: 10.3390/jcm12227171. PMID: 38002783; PMCID: PMC10671895.
16. Puckett Y, Gabbar A, Bokhari AA. Prednisone. [Updated 2023 Jul 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534809/