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Article

Study the relation between thyroiditis markers (Anti-TPO and Anti TG) and autoimmune urticaria.

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ABSTRACT

The current study was focused to study Anti-TPO and Anti-TG , in (80) Chronic Urticaria patients were Clinically diagnosed by dermatologists in Specialized Center of Allergy in Baghdad/Al-Rusafa with age ranged between (11-60), as well as a control group 40 with age ranged between (11-60) from November 2021 to April 2022, The results of demographic and clinical characteristics revealed the rate of female patients was higher than male56.3%, 43.8% respectively, The results showed there was highly significant difference between the patients and the control in Anti-Tpo also the results showed Anti-TG were higher than control but no significant differences while the patient with age 21-30 year and 11-20 had highest Anti-Tpo and Anti-TG, the level of Anti-Tpo and Anti- TG between post-treatment and pre-treatment showed various results , Anti-Tpo and Anti- TG in post-treatment was lower than pre-treatment but higher than the control group significant difference between those group at $p \leq 0.05$ The results showed Finally The ROC showed the Anti-Tpo and Anti- TG were discriminated as accurate biomarkers for CSU.

Keywords: Anti-Tpo, Anti-TG, CUS, Age and treatment.

INTRODUCTION

Urticaria is a skin disorder with symptoms such as the sudden, unpredictable emergence of wheals (with or without) angioedema. According to the triggers, signs, symptoms and duration of wheal appearance, urticaria is classified into two classes, Acute Urticaria (AC) and Chronic Urticaria (CU), where Chronic Urticaria is classified into two subclasses; the first class is Chronic Inducible Urticaria (CIndU), while the second one is Chronic Spontaneous Urticaria (CSU)[1,2]. CSU is marked by angioedema and the appearance of wheals for more than six weeks in both adults and children. This subtype appears spontaneously without unknown causes[1]. Autoimmunity is characterized by inappropriate activation of the immune system towards its cells and tissues. This can be directed to a specific organ or cause systemic involvement[3]. The relationship

between CSU and autoimmune diseases was reported for the first time by Ravitch[4] in 1907. In the last decades, several authors have continued studying this relationship with ATD, which is more frequently associated with CSU, with association rates ranging from 4.3 to 57.4% in adults, compared with 3.5 to 8% in children[5].On the other hand, CSU is associated with the presence of IgG or IgE autoantibodies (AAbs) against FcεRIα, antibodies against IgE, and the antithyroid antibodies (ATAbs) TPOAbs and TGAbs[3] Autoimmune thyroid diseases are often coupled with the existence of anti- TSHR, anti-TG and anti-TPO[6]. The thyroid disorder (hyperthyroidism or hypothyroidism according to the thyroid gland function) in some chronic urticaria patients are both common[7].

MATERIALS AND METHODS

Patient diagnosis

This study included 80 Chronic Urticaria patients who were Clinically diagnosed by dermatologists in the Specialized Center of Allergy in Baghdad/Al-Rusafa with ages between (11 and 60), as well as a control group of 40 with ages ranging between (11 and 60) from November 2021 to April 2022.), which included name, age, occupation, accommodation location, therapy, and date of onset of all symptoms.

Collection of blood samples

The blood was obtained in the gel tube and coagulated at room temperature (20-25°C). After blood clotting, the gel tube was centrifuged at 3000 rpm for 5 minutes. Then, the serum was divided into equal parts into 3 sterile Eppendorf tubes, tightly closed and stored at-20°C.

Antithyroid antibodies assay

The Antithyroid antibodies in this current study represented (Anti-TPO and Anti-TG) the procedure in kit instructor (Mybiosource, USA) was followed.

Statistical analysis

The data was analyzed using the SPSS statistical approach (StatisticalPackage for the Social Sciences) version-26. For quantitative variables, the data for normality (Shapiro-Wilk and Kolmogorov-Smirnov Tests) and the levels have been given as (Mean ± Stander Error). Significant differences between medians were assessed by the nonparametric tests (Mann-Whitney and Kruskal-Wallis) probability value < 0.05 ROC curve (receiver operating characteristic curve). This graph was used to discriminate whether Antithyroid antibodies are biomarkers or not.

RESULTS AND DISCUSSION

Demographic characteristics of the study.

The results of demographic and clinical characteristics revealed that the rate of female patients was higher than male % and 43.8%, respectively; finally, the mean age of patients was 34.8±1.5 years, as in Table 1.

Demographic character-istics	Patients N (%)	Controls N (%)
Groups	80 (50%)	40 (50%)
Gender: Male	35 (43.8%)	24 (60%)
Female	45 (56.3%)	16 (40%)
Treatment: Yes	58 (72.5%)	0 (0%)
No	22 (27.5%)	40 (100%)
Age (Mean± S.E.)	34.8±1.5	34.65±2.25

Table 1. Demographic and Clinical Characteristics of the Participants.

Antithyroid antibodies

The results showed a highly significant difference between the patients and the control in Anti-Tpo. Also, the results showed that the Anti-TG was higher than the control but no significant differences at $p \leq 0.05$, as in Table 1 and Figure 1.

Groups	N	Anti-Tpo U/ml	Anti-TG U/ml
Patients	80	22.75 ±1.14	9.68±1.27
Controls	40	7.23 ± 0.56	5.11 ± 0.17
p-value		0.001	0.9

Table 1. Comparison between the thyroid antibodies in study groups.

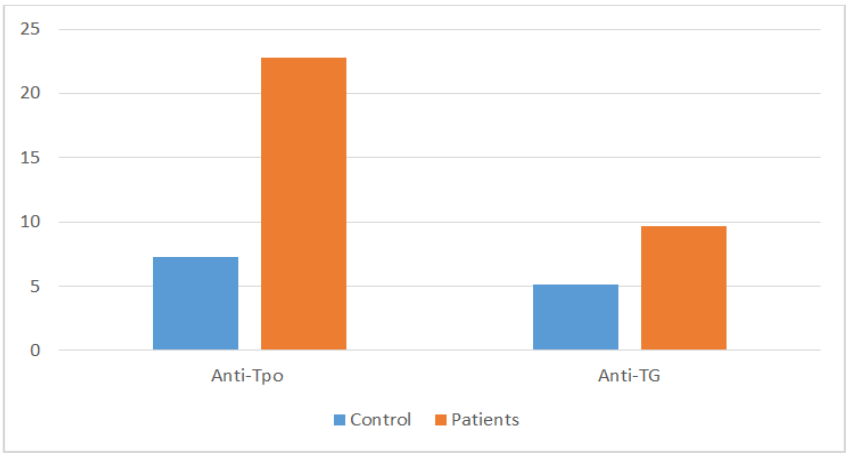

Figure 1. Antithyroid antibodies in study groups

Anti-thyroid antibodies and Age Distribution

The results of ages and Antithyroid antibodies are shown in table (2). The patients with age 21-30 years and 11-20 had the highest Anti-Tpo levels, 24.7±2.3 U/ml, and 23.57±3.21 U/ml, but patients with 21-30 years showed the highest Anti-TG levels with no significant differences; however, the patients with different ages recorded higher value than the control with the same age.

Groups	Age Group	N	Anti-Tpo U/ml (Mean± S.E.)	Anti-TG U/ml (Mean± S.E.)
Patients	**11-20**	13	23.57±3.21	10.61±3.61
	21-30	21	24.7±2.3	13.3±3.36
	31-40	22	20.2±1.7	6.8±1.26
	41-50	12	22.17±3.8	11.09±3.68
	51-60	12	23.58±2.53	6.21±1.57
Controls	**11-20**	5	9.16±1.87	5.5±0.46
	21-30	18	6.42±0.89	5.13±0.29
	31-40	4	8.98±1.98	4.8±0.42
	41-50	5	6.87±1.04	4.26±0.55
	51-60	8	7.82 ±1.16	5.42±0.33
p-value			**0.001**	**0.281**

Table 2. Antithyroid antibodies and Age Distribution in patients and control.

Anti-thyroid antibodies with treatment

The results of Anti-Tpo and AntiTG between post-treatment and pre-treatment patients showed various results; anti-tpo and anti-tg in post-treatment was lower than in pre-treatment, Anti-Tpo in post-treatment was 22.24±1.27 U/ml and in pre-treatment 24.09±2.50 U/ml while Anti- TG in the post and pre-treatment 8.98±1..26 U/ml,11.53±3.24 U/ml respectively but higher than the control group significant difference between those group at $p \leq 0.05$ as in table 3.

Group	N	Anti-Tpo U/ml (Mean ± SE.)	Anti-TG U/ml (Mean ± SE.)
Patients post-treatment	58	22.24±1.27	8.98± 1..26
Patients pre-treatment	22	24.09±2.50	11.53±3.24
Controls	40	7.23±0.56	5.11±0.17
p-value		**a=0.001,b=0.05,c=0.001**	**A=0.7, b=0.4, c=0.9**

Table 3. The Comparison between post and pre-treatment patients and control. A= Serum level of anti-Tpo and anti-TG in patients-treatment compared with controls. B = Serum level of anti-Tpo and anti-TG in patients pre-treatment compared with patients post-treatment. C Serum level of anti-Tpo and anti-TG in patients post-treatment compared with controls.

The current finding agreed with[22] that after radioactive iodine (RAI) treatment, serum TPOAb showed a similar variation trend to serum TRAb. However, it increased at 3 months, elevated to peak at 6 months and decreased to baseline at 12 months in people with Graves' hyperthyroidism, as well as agreed with 23 of those who noticed there was increasing and decreasing after radioactive iodine (RAI) treatment. The proportion of patients in whom anti-TPO increased was 73%, and in 27%, it did not change or decrease. In the group in which anti-TPO increased, the median value at baseline raised from 158 (range 8–3,962) to 419 (range 10–9,999) IU/L after 3 months, and in the group without change or decrease in anti-TPO, the value changed from 144 (range 9–2,243) to 103 (range 7–1,936) IU/L after 3 months. Mentioned[24] Serum TRAb and thyroid peroxidase antibody (TPOAb) levels increased in the initial year of RAI treatment, and both antibodies decreased gradually after one year.

The Receiver Operating Characteristic (ROC).

The ROC results of Anti-TPO showed a cut-off value of (12.06) in the roc curve validity test dependent on clinical diagnosis. They found the most excellent sensitivity (98.8%%), specificity(85.0%), PPV(100.3%), NPV (92.9%), accuracy (85.0%)and area under the curve (0.957). Overall, there are highly significant differences between studied groups (P<0.001) as in figure2.

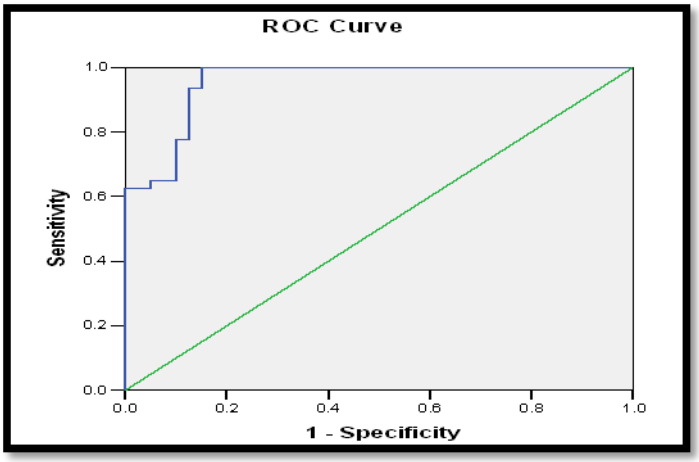

Figure 2. The ROC Curve of Anti-Tpo.

The ROC results[24] of Anti-TG showed a cut-off value of (7.28) in the roc curve validity test for Anti-TG dependent on clinical diagnosis and found the greatest sensitivity (27.5%), specificity(97.5 %), PPV(95.7%), NPV (40.6%), accuracy (25.3%)and area under the curve (0.506). Overall, there is a highly significant difference between the studied groups (P<0.001) as in figure3.

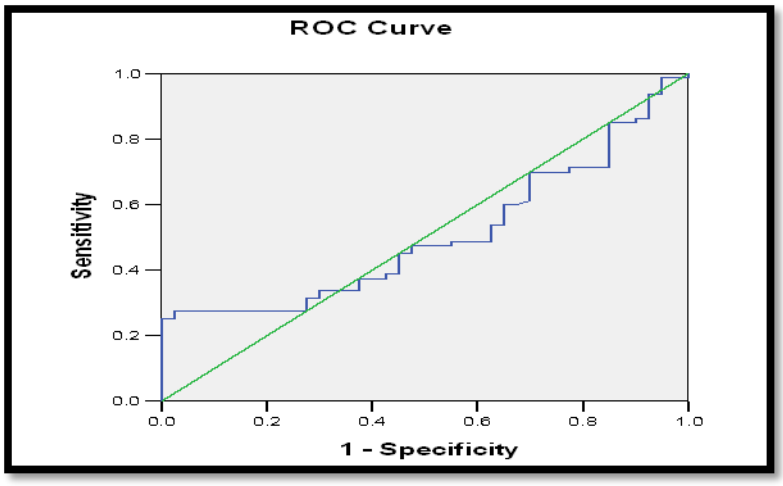

Figure 3. The ROC Curve pf Anti-TG.

DISCUSSION

These findings were similar to those that revealed that 19% of patients Smoked, and the females were higher than males 24/7 but with an age mean of 47.19. The results agreed with those who studied fatigue in chronic spontaneous urticarial patients and found that females with chronic spontaneous urticarial patients were higher than males, a literature review achieved by Maurer and his colleagues. The rate differences in chronic spontaneous urticaria between Europe and Central/South America reported the rate of females higher with significant differences; moreover[10] reported CSU affects females more often than males (females 68-80% of cases). Chronic urticaria (CU) is a common skin disorder with important repercussions on the quality of life and a relevant socioeconomic impact. CU is included among the skin diseases that exhibit a significant female preponderance, with an average female-to-male ratio of nearly [11] 2-1/4. This effect has been related to the estrogen-induced increased tissue expression of endothelial nitric oxide synthase and nitric oxide production, leading to vascular hyperpermeability. Regarding the immunological effects of sex hormones, it is known that androgens tend to have an immunosuppressive action through multiple mechanisms, and progesterone similarly seems to suppress immunity and inflammation. In contrast, estrogens can stimulate humoral immunity and antibody synthesis[12].

Furthermore, 13 found the anti-Tgand anti-TPO in the patients, similar to the obtained results. Although the triggers of mast cell activation in CSU are largely unknown and remain to be identified, several studies have allowed the identification in subgroups of CSU patients of IgG autoantibodies directed to thyroid peroxidase (TPO) and/or to IgE or their high-affinity IgE receptor[14] (FcεRI). Evidence of the role of autoimmunity in CSU stems from the observation that patients with CSU often have autoimmune disorders, including autoimmune thyroid disease. Levels of IgG anti-TPO antibodies were detected in up to 33% of CSU patients and have also been proposed as promising biomarkers for CSU since their presence is associated with a longer disease duration 16. Besides IgG anti-TPO, high levels of IgE anti-TPO antibodies have been recently

detected in a subpopulation of CSU patients. They might trigger mast cells and basophils degranulation binding to circulating antigens released after autoimmune thyroid damage[17].

These results agreed with 13; there was an increase, and Thyroid autoantibodies in patients ranged from 16 to 66 with a mean of 40.39 (14.39) and agreed with[18]. Thyroid autoantibodies were detected in 12 of the 54 female patients; their mean age was 31.5 years (median: 27 yrs, range: 21–47 years). 6 of these 12 patients had increased levels of anti-TPO antibodies, and 6 others had increased both anti-TPO and anti-TG antibodies. Reported[19] The prevalence of thyroid autoimmunity was 4.3%, much lower than that in adult series of chronic urticaria, but higher than the prevalence reported to date for age-matched children: in two population-based studies of the 10–11 to 18 year age group, Rallison and colleagues in 1991 reported a 1.27% prevalence of autoimmune thyroiditis in 4819 children, found[20] a prevalence of 1.6% in 6283 girls. Found[21] a prevalence of 0.35% in 5462 school-age children.

After 5 years from radioiodine treatment, The role of anti-TG in the pathogenesis of GD is unclear. However, in a previous study examining discontinuation of ATD, it was shown that patients with low levels of anti-TG at the diagnosis of GD had a lower chance to stop the treatment with ATD, indicating a higher activity of GD in these patients 25. A low level of anti-TPO at the diagnosis of GD has been coupled with an increased risk of developing GO both at diagnosis and during follow-up[26].

CONCLUSION

The obtained results showed that female was at higher than male risk of CSU, which was agreed with in different previous studies. Also, the study showed the Antithyroid antibodies in CSU patients were higher than in healthy people; at the same time, the values of biomarkers varied between immunotherapy and post-immunotherapy patients. However, the study revealed the ages 21-30 years and 11-20 years showed higher values in Anti-Tpo and Anti-TG, respectively, than other ages. Finally, the ROC showed Anti-Tpo and Anti-TG discriminated as accurate biomarkers for CSU.

References:

1. Song, W.J.; Choi, M.; Lee, D.H.; Kwon, J.W.; Kim, G.W.; Kim, M.H.; Kim, M.A.; Kim, M.H.; Kim, B.K.; Kim, S.; Kim, J.S.; Kim, J.E.; Kim, J.Y.; Kim, J.H.; Kim, H.J.; Kim, H.O.; Kim, H.B.; Roh, J.Y.; Park, K.H. and Park, K.Y.The KAAACI/KDA Evidence-Based Practice Guidelines for Chronic Spontaneous Urticaria in Korean Adults and Children: Part 1. Definition, Methodology and First-line Management. Allergy, Asthma & Immunology Research, 2020; 12(4), p.563. doi:10.4168/aair.**2020**.12.4.563.
2. Radonjic, Hoesli S, Hofmeier K.S.; Micaletto S, Schmid-Grendelmeier P, Bircher A, Simon D. Urticaria and Angioedema: an Update on Classification and Pathogenesis. Clin Rev Allergy Immunol. **2018** Feb;54(1):88-101. doi: 10.1007/s12016-017-8628-1. PMID: 28748365.
3. Berghi, N.O. Immunological mechanisms implicated in the pathogenesis of chronic urticaria and Hashimoto thyroiditis. Iran J Allergy, Asthma Immunol. **2017**;16(4):358–366.
4. Selvendran, S.S.; Aggarwal, N. Chronic urticarial and thyroid autoimmunity; a perplrxing association. Oxford Medical Case Reports, **2018**; doi; 10.1093/ omcr / omx099.
5. Kilic, G.; Guler, N.; Suleyman, A.; Tamay, Z. Chronic urticaria and autoimmunity in children. *Pediatric Allergy and Immunology*, **2010**; 21(5), pp.837–842. doi:10.1111/j.1399-3038.2010.00986.x.
6. Fröhlich E.; Wahl, R. Thyroid Autoimmunity: Role of Anti-thyroid Antibodies in Thyroid and Extra-Thyroidal Diseases. Front. Immunol. 2017; 8:521. doi: 10.3389/fimmu.00521

7. Verneuil, L.; Leconte, C.; Ballet, JJ; Coffin, C.; Laroche, D.; Izard, J.P.; Reznik, Y.; Leroy, D. Association between chronic urticaria and thyroid autoimmunity: a prospective study involving 99 patients. Dermatology. **2004**;208(2):98-103. doi: 10.1159/000076480. PMID: 15056996.
8. Uysal, P. İ.; Hayran, Y.; Akdoğan, N.; Öktem, A.; Atılan, A.; Aksoy, G.G.; & Yalçın, B. Effect of Omalizumab Therapy on Coagulation Parameters and Total Immunoglobulin E Levels in Patients with Chronic Idiopathic Urticaria and Bullous Pemphigoid. *Turk Dermatoloji Dergisi*, **2018**;12(4), 159.
9. Erol, K.; Ertaş, Ş. K.; Ertaş, R. Fatigue is common and predicted by female gender and sleep disturbance in patients with chronic spontaneous urticaria. *The Journal of Allergy and Clinical Immunology: In Practice*, **2021**; *9*(1), 469-476.
10. Broder, M.S.; Raimundo, K.; Antonova, E.; Chang, E. Resource Use and Costs in an Insured Population of Patients with Chronic Idiopathic/Spontaneous Urticaria. *Am J Clin Dermatol*, **2015***;16(4)*, 313-321.
11. Cassano, N.; Colombo, D.; Bellia, G.; Zagni, E.; Vena, G.A. Gender-related differences in chronic urticaria. Giornale Italiano di Dermatologia e Venereologia: Organo Ufficiale, Societa Italiana di Dermatologia e Sifilografia, **2015**;151(5), 544-552.
12. Hox, V.; Desai, A.; Bandara, G.; Gilfillan, A.M. Metcalfe DD; Olivera A. Estrogen increases the severity of anaphylaxis in female mice through enhanced endothelial nitric oxide synthase expression and nitric oxide production. *J Allergy Clin Immunol* **2015***;135*:729-36.
13. Kasumagic-Halilovic, E.; Beslic, N.; & Ovcina-Kurtovic, N. Thyroid autoimmunity in patients with chronic urticaria. *Medical Archives*, 2017; *71*(1), 29.
14. Chanprapaph, K.; Iamsumang, W.; Wattanakrai, P.; Vachiramon, V. Thyroid autoimmunity and autoimmunity in chronic spontaneous urticaria linked to disease severity, therapeutic response, and time to remission in patients with chronic spontaneous urticaria. *BioMed research international*, **2018**;
15. Bracken, S.J.; Abraham, S.; MacLeod, A.S. Autoimmune theories of chronic spontaneous urticaria. *Frontiers in immunology*, **2019**; *10*, 627.
16. Viljanen, M.; Savilahti, E.; Haahtela, T.; Juntunen-Backman, K.; Korpela, R.; Poussa, T.; Kuitunen, M. Probiotics in the treatment of atopic eczema/dermatitis syndrome in infants: a double-blind placebo-controlled trial. *Allergy*, **2005**; *60*(4), 494-500.
17. Sánchez, J.; Sánchez, A.; Cardona, R. Causal relationship between anti-TPO IgE and chronic urticaria by in vitro and in vivo tests. *Allergy, asthma & immunology research*, **2019**; *11*(1), 29-42.
18. Nuzzo, V.; Tauchmanova, L.; Colasanti, P.; Zuccoli, A.; Colao, A. Idiopathic chronic urticaria and thyroid autoimmunity: Experience of a single center. *Dermato-endocrinology*, 2011; *3*(4), 255-258.
19. Levy, Y.; Segal, N.; Weintrob, N.; Danon, Y.L. Chronic urticaria: association with thyroid autoimmunity. *Archives of disease in childhood*, 2003; *88*(6), 517-519.
20. Marwaha, R.K.; Tandon, N.; Karak, AK; Gupta, N.; Verma, K.; Kochupillai, N. Hashimoto's thyroiditis: countrywide screening of goitrous healthy young girls in postiodization phase in India. *The Journal of Clinical Endocrinology & Metabolism*, **2000**; *85*(10), 3798-3802.
21. Jaksić, J.; Dumić, M.; Filipović, B.; Ille, J.; Cvijetić, M.; Gjurić, G. Thyroid diseases in a school population with thyromegaly. *Archives of disease in childhood*, **1994**; *70*(2), 103-106.
22. Dong, Q.; Liu, X.; Wang, F.; Xu, Y.; Liang, C.; Du, W.; &Gao, G. DYNAMIC CHANGES OF TRAb AND TPOAb AFTER RADIOIODINE THERAPY IN GRAVES'DISEASE. *Acta Endocrinologica (Bucharest)*, **2017**; *13*(1), 72.
23. Lindgren, O.; Asp, P.; Sundlöv, A.; Tennvall, J.; Shahida, B.; Planck, T.; Lantz, M. The effect of radioiodine treatment on TRAb, anti-TPO, and anti-TG in Graves' disease. *European Thyroid Journal*, **2019**; 8(2), 64-69.
24. Fang, Y.; Du, W.H.; Zhang, C.X.; Zhao, S.X.; Song, HD; Gao, G.Q.; Dong, M. The effect of radioiodine treatment on the characteristics of TRAb in Graves' disease. *BMC Endocrine Disorders*, **2021**; *21*(1), 1-9.
25. Katahira, M.; Ogata, H. Thyroglobulin autoantibodies are associated with refractoriness to antithyroid drug treatment for Graves' disease. *Internal Medicine*, **2016**; *55*(12), 1519-1524.
26. Lantz, M.; Planck, T.; Åsman, P.; Hallengren, B. Increased TRAb and/or low anti-TPO titers at diagnosis of Graves' disease are associated with an increased risk of developing ophthalmopathy after onset. *Experimental and Clinical Endocrinology & Diabetes*, **2014**; *122*(02), 113-117.

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