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ORIGINAL ARTICLE

Occurrence of Autoimmune Thyroid Dysfunction in Juvenile SLE

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ABSTRACT

Objective: To define the occurrence of autoimmune thyroid dysfunction and its type i.e. sub-clinical hypothyroidism, hypothyroidism and hyperthyroidism in juvenile SLE.
Study design: Cross-sectional study.
Place and duration: The study was held at the rheumatology ward of the Children's hospital and the Institute of Child Health, Lahore from1st November 2019 to 30th April 2021.
Sample Technique: Non probability consecutive sampling
Material and methods: Inclusion Criteria had American college of rheumatology classification criteria for SLE filled by both female and male patients of 2-16 years. Consent was taken and all the data was written on pre designed proforma. Demographic data like age, gender and relevant history and examination was done to diagnose hypo or hyperthyroidism. Thyroid antibodies, 3 to 5 ml of venous blood for thyroid function tests of all patients were sent in laboratory and results were interpreted accordingly. Thyroid dysfunction and its types were labeled accordingly.
Results: In the present study, 55.56% (n=50) were between 9-16 years of age whereas 44.44% (n=40) were between 2-8 years of age, out of 90 cases. Mean and Sd. was calculated as 9.73+3.29 years, 30% (n=27) were male while 70%(n=63) were females, frequency of autoimmune thyroid dysfunction was recorded in 28.89%(n=26), frequency of type of autoimmune thyroid dysfunction was recorded as 10%(n=9) for sub-clinical hypothyroidism, 11.11%(n=10) for Hypothyroidism and 7.78%(n=7) for hyperthyroidism.
Conclusion: It is concluded that the occurrence of autoimmune thyroid dysfunction is higher in our population, however, some-other studies are required to validate our findings.
Keywords: Juvenile SLE, autoimmune thyroid dysfunction, hypothyroidism.

INTRODUCTION

Systemic lupus erythematous (SLE) is an aching disease which is caused by the immune complex formation, autoantibodies directed against self-antigens and immune deregulation which consequently damage to fundamental organs.[1] Though approximately all organs may be affected but most often joints, blood forming cells, joints, blood vessels, central nervous system and kidney are involved. Children and adolescents with systemic lupus erythematous have more severe disease as compare to adults. They also have more extensive organ contribution.[2] Pathogenesis is indefinite but, hormonal, environmental factors, genetics and various pathological contagions play part. In Children, frequency of is 1-6/100,000. In girls childhood SLE is more prevalent than boys (8:1). Systemic lupus erythematous can take place at any age in life but it is observed that it become more common after the age of five years. It is studies that it become more frequent after the first decade of life.[3]Thyroid gland secretes thyroid hormones (T3 and T4) which controls body's metabolic rate. In the body, every tissue is stimulated by thyroid hormones to increase the amount of oxygen and produce proteins used by cells. Secretion of thyroid hormones is influenced by TSH secreted from pituitary gland.[4] Many components of thyroid are targeted by anti-thyroid antibodies. The furthermost important are anti-thyroid peroxidase antibodies (anti-TPO), thyrotrophic receptor antibodies and thyroglobulin antibodies. Anti-TPO antibodies and thyroglobulin antibodies most commonly found in Hashimoto's thyroids, Graves' disease, nodular goiter, thyroid carcinoma and about 10-15% of normal individuals can have high titer of anti-TPO antibodies and about 3% of normal individuals can have high titer of thyroglobulin antibodies.[5,6] Thyroid abnormalities found to be 9.8% in rheumatological disorders.[7] Thyroid dysfunction is more common in Juvenile SLE as compared to general population. A study conducted in India in 2010 showed, 36% SLE patients were suffering from thyroid dysfunction as compared to healthy control group in which it was 8%. Out of these 36%, 14% were hypothyroid and 12% subclinical hypothyroidism, 2% subclinical hyperthyroidism, 8% with isolated low free T3.[8] A study published in "Egyptian Journal of Pediatric Allergy and Immunology" reveals 15% incidence of thyroid disorder in SLE,[9] all of them had subclinical hypothyroidism. Thyroid dysfunction is a curable cause of morbidity and studies showed that frequency of thyroid dysfunction is high in juvenile SLE patients as compared to general population. No statistics are available in Pakistan regarding frequency of thyroid disorders in Juvenile SLE. So this study was planned to determine the frequency of thyroid dysfunction in Juvenile SLE patients so that early detection and treatment should be started to prevent morbidity and improve future outcome.

MATERIAL AND METHODS

It was a cross-sectional study held at the rheumatology department of the Children's hospital and the Institute of Child Health Lahore from 1st November 2019 to 30th April 2021. Inclusion criteria had American college of rheumatology classification criteria for SLE was filled by both female and male patients of 2-16 years. While patients with autoimmune diseases other than SLE like juvenile idiopathic arthritis, systemic sclerosis, dermatomyositis, diabetes (random blood sugar >200mg/dl), [1] celiac disease and already diagnosed cases of thyroid dysfunction on treatment were excluded. After taking informed consent from parents or guardian patients satisfying inclusion criteria were considered in the study. Demographic data like age, gender and relevant history and examination was done to diagnose hypo or hyperthyroidism. Thyroid antibodies and 3 to 5 ml of venous blood for thyroid function tests of all patients were sent in laboratory and results were interpreted accordingly. Thyroid dysfunction and its types were labeled accordingly. SPSS version 21 was used and analyzed through its statistical package. The quantitative variables like age, T_3, T_4, and TSH were presented as standard deviation and mean. Outcome variables like thyroid dysfunction and type i.e. hypothyroidism, hyperthyroidism and, family history of thyroid dysfunction and subclinical hypothyroidism were obtained as percentage and frequency. With effect modifiers, the data was stratified for gender, duration of SLE of deal and age. By taking p value <0.05 as significant, post-stratification chi square test was applied.

Sample Size:

Ninety cases were calculated with 85% confidence level Sample size of 90 cases was calculated with 10% margin of error and 85% confidence level. Expected percentage of autoimmune thyroid dysfunction was taken i.e. 36% in Juvenile SLE[8]

OPERATIONAL DEFINITIONS

1. Juvenile Systemic Lupus Erythematosus

Presence of at least 4 criteria's out of the following:

- Malar rash, (erythromatous rash over cheeks sparing visualized folds)
- Discoid rash (disc shape rash on clinical examination)
- Nasal or oral or ulcers (on clinical examination)
- Arthritis (nonerosive affecting two or more joints) (clinical examination+ X-ray of invalued)
- Serositis (peritonitis, pericarditis), (clinical examination+ investigations) CBC>11,000/m,^{2} ESR >40
- Seizures or psychosis (on history)
- Renal manifestations (persistent proteinuria >500mg protein/24 hrs or cellular cast, consistent renal biopsy),
- Photosensitivity
- Hematological appearances(hemolytic anemia<10g/dl, leukopenia<4,000/mm^3,lymphopenia<1,000/mm^3,thrombocytopenia <100,000/mm^3)
- Immunological manifestations (positive lupus anticoagulant ,false positive RPR test, , or elevated anticardiolipin immunoglobulin)
- Positive ANA test result [2]. (Qualitative test, assessed on medical record)

2. Autoimmune Thyroid Dysfunction

- Hypothyroidism: mean under active thyroid gland characterized by increase TSH level and decrease T3 and T4.
- Subclinical hypothyroidism is characterized by free T4 level or normal total or and a mildly elevated TSH (5–10mU/L).[10]
- Hyperthyroidism: TSH level and Total and free T3 and T4 were low. (For reference values see annexure 1).

Any of these types with positive anti-thyroid peroridase and antithyroglubyulin antibodies (any one or both) .

RESULTS

A total of 90 cases were included fulfilling the inclusion criteria. Regarding age distribution of the patients, 55.56 %(n=50) were between 9-16 years of age whereas 44.44% (n=40) were between 2-8 years of age, mean+SD was calculated as 9.73+3.29 years. Patient's gender distribution showed that 70 %(n=63) were females whereas 30 %(n=27) were male. Mean quantitative variables were recorded as 2.98+0.67 for T3, 1.71+0.92 for T4 and 3.24+1.47 for TSH levels. (Table No. 1).Frequency of autoimmune thyroid dysfunction was recorded in 28.89% (n=26) whereas 71.11% (n=64) had no thyroid dysfunction (Fig:1). Frequency of type of autoimmune thyroid dysfunction was recorded as 10% (n=9) for sub-clinical hypothyroidism,11.11% (n=10) for Hypothyroidism and 7.78% (n=7) for hyperthyroidism (Fig:2).

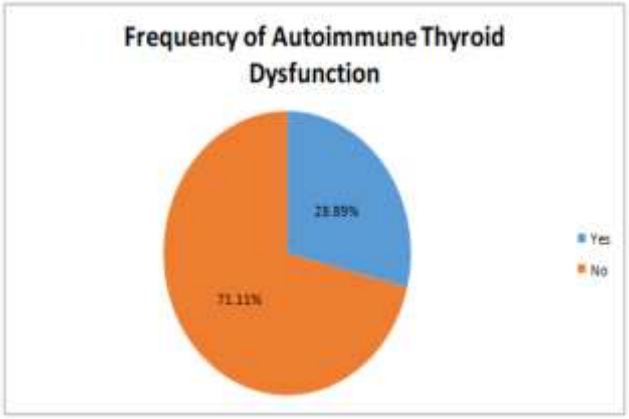

Fig 1: Frequency of autoimmune thyroid dysfunction

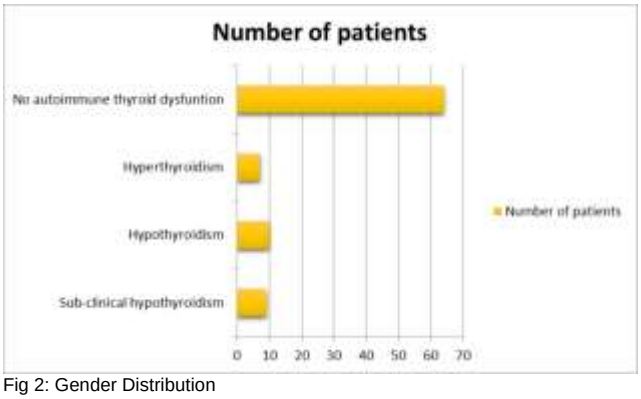

Fig 2: Gender Distribution

Table 1: Mean Quantitative Variables (n=90)

Variables	Mean	SD
T_3	2.98	0.67
T_4	1.71	0.92
TSH	3.24	1.47

DISCUSSION

Organ-specific and non-specific diseases are two types of autoimmune diseases (AID). Autoimmune thyroid diseases (AITD) are reflected as organ specific and represented by autoimmune thyroiditis (CAT), Graves' disease and Hashimoto's thyroiditis (HT). According to different journalists, presence of thyroid auto antibodies and abnormalities in thyroid functions have been commonly described in clients with rheumatologic diseases. As, thyroid dysfunction is a treatable cause of morbidity and studies showed that its frequency is high in juvenile patients of SLE as compared to common people. No statistics are available in Pakistan about occurrence of thyroid illnesses in SLE Juvenile. So this study was planned to record the occurrence of thyroid dysfunction in Juvenile SLE patients so that early detection and treatment should be started to prevent morbidity and improve future outcome. In this study, out of 90 patients, 55.56 %(n=50) were between 9-16 years of age whereas 44.44 %(n=40) were between 2-8 years of age, mean+sd was calculated as 9.73+3.29 years and 70%(n=63) were females while 30%(n=27) were male, frequency of autoimmune thyroid dysfunction was recorded in 28.89%(n=26), frequency of type of autoimmune thyroid dysfunction was recorded as 10%(n=9) for sub-clinical hypothyroidism, 11.11%(n=10) for Hypothyroidism and 7.78%(n=7) for hyperthyroidism. A previous study reveals that thyroid abnormalities found to be 9.8% in rheumatologic disorders.[7]

Thyroid dysfunction is more common in Juvenile SLE as compared to general population. Another study conducted in India in 2010 showed, 36% SLE patients were suffering from thyroid dysfunction as compared to healthy control group in which it was 8%. Out of these 36%, 14% were hypothyroid and 12% subclinical hypothyroidism, 2% subclinical hyperthyroidism, 8% with isolated low free T3.[8] A study published in "Egyptian Journal of Pediatric Allergy and Immunology" reveals 15% incidence of thyroid disorder in SLE, [9] all of them had subclinical hypothyroidism. Conclusions of this study are in contract with our study. Waldport and Weetman associated the frequency of abnormal thyroid-stimulating hormone (TSH) levels in 41 SLE patients, ThyAb, versus sex-matched and age- controls. An important higher frequency of ThyAb (51%) was perceived in SLE compared to controls which is 27%. Moreover, commonly in linked with circulating ThyAb, hypothyroidism was witnessed in 5 controls and 10 SLE patients. In the other study, positive ant microsomal antibodies were found in 18% of SLE patients. In 15% of SLE patients, euthyroid sick syndrome (ESS) was diagnosed. Initial primary hypothyroidism was observed in 5 and true hypothyroidism in 39% patients. 45% patients were having ThyAb with increased level of TSH. Families with more than one SLE patients were found to be suffering from autoimmune

thyroid disorders. In 1,138 SLE cases, 169 were identified patients of Sjögren's syndrome (SS), among these patients 50 were also having AITD. 119 patients had AITD among the 939 patients with SLE without SS whereas 44 had diagnosed primary SS and 16 (36.3%) of these also had autoimmune thyroid disease among 2,291 SLE-unaffected relatives. Autoimmune thyroid disease was in 265/2,247 (11.8%) subjects.

These results showed that among SLE patients with a diagnosis of secondary SS autoimmune thyroid disease was observed in excess. For thyroid disease, seventy-seven SLE patients were studied. Among 11.6% of SLE patients hypothyroidism was reported. There was no statistically major difference was perceived in the intensities of AbTPO or anti-thyroglobulin antibodies among the control group and the study group. There was no any was observed among the prevalence of ThyAb and the SLE disease activity (SLEDAI) score. Among 524 SLE patients, AITD were estimated. In particular hypothyroidism 32/524 (6.1%) SLE patients and 1/50 controls had symptomatic autoimmune thyroid dysfunctions. 89/524 (17%) had positive ThyAb in absence of thyroid dysfunctions and sixty (11.5%) SLE patients had subclinical thyroid diseases. Positive rheumatoid factor and SS were common in SLE patients with AITD. The presence of hyperthyroidism was connected with SLEDAI. Among 80 patients with SLE, frequency of AITD was significantly higher than in the 34 controls (24 versus 8%, $P < 0.05$). By assessing thyroid hormones, two hundred thirteen SLE patients were assessed. Among controls verses female SLE patients, the odds ratio (OR) was 2.9 (95% CI, 2.0–4.4) for thyroid autoimmunity, 2.6 (95% CI, 1.7–4.1) for AbTPO positivity and 4.5 [95% confidence interval (CI), 2.5–8.4] for subclinical hypothyroidism. Significantly, female SLE patients had higher AbTPO and mean $P < 0.01$) than controls. The journalists recommended that SLE patients had importantly high rate of matched controls than lower rate of hyperthyroidism and thyroid diseases.[11] This study could have some restrictions that can affect the finding: (1) data which was gathered in a retrospective cohort study was mainly poorer in statistical quality to those derived from randomized trials because of the potential biases for confounding variables related to adjustments [11]

(2) it was constructed on diagnostic codes released from The National Health Insurance Research Database, and because of this reason, presence of ThyAb, details on thyroid,SLE autoantibodies or serological assessments, were not obtainable. The above discussion reveals that the data varies according to different criteria and different regions of the world, however, by knowing the exact rate of this morbidity, we may plan proper guidelines for the management of this problem well-in-time and this data will be helpful for the pediatricians and general public as well, however, we are of the view that some other studies should be done so that or results may be correlated and validated.

CONCLUSION

We determined that the occurrence of autoimmune thyroid dysfunction is greater in our population, however, some-other studies are required to validate our findings.

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