Autoimmune Thyroid Diseases In Juvenile Systemic Lupus Erythematosus

Thesis

Submitted for Partial Fulfillment of M.D. Degree in Pediatric

By
Dr. Dalia Saber Morgan
(M.B.B.Ch. Ms C)

Supervised By Prof. Dr. Hala Salah

Professor of Pediatric Faculty of Medicine Cairo University

Prof. Dr. Gamal El-din Taha

Asst. Professor of Pediatric Faculty of Medicine Beni Sweif University

Prof. Dr. Fatma El Mougy

Professor of Clinical Pathology Faculty of Medicine Cairo University

Faculty of Medicine Cairo University 2007

Contents

	Page
List of Abbreviations	A
List of Tables	C
List of Figures	Е
Introduction and aim of the work	1
Review of Literatures	4
Patients and Methods	80
Results	93
Discussion	110
Conclusion	120
Recommendations	121
Summary	122
References	123
Arabic Summary	152

Abstract

Thyroid Function tests, anti microsomal and anti thyroglobulin antibodies level of 30 patients with Systemic Lupus Erythrematosus (SLE) and 30 healthy subjects were studied. The level of thyroid antibodies were higher in SLE patient's in comparison with control group although there is no significant difference in the level of thyroid hormones between the two groups.

Key wards:

Thyroid – Systemic Lupus Erythrematosus

List of Abbreviations

ACAs Anticardiolipin antibodies.

ACR American Collage of Rheumatology

ANA Anti nuclear antibodies

Anti T.G Anti thyroglobulin

Anti TPO Anti thyroid peroxidase **Anti-ds DNA** Anti double strand DNA

APLS Anti phospholipid syndrome

BILAG British isles lupus assessment group

C3 Complement 3
C4 Complement 4

CNS Central nervous systemCPK Creatinine phospho kinaseCT Computerized tomography

ECG Electro cardiography

F VIIIRAG Factor VIII related antigen

FT3 Free T3 Free T4

HLA Human leucocytic antigen

IgG Immunoglobin G

IVIg Intra venous immunoglobulin

LA Lupus anticoagulantLAI Lupus activity index

MRI Magnetic Resonance Image

NPLE Neuropsychiatric lupus Erythematosus
NSAID's Nonsteroidal anti-inflamatory drugs

PET Possitron emission tomography

SAHs Sub arachnoid hemorrhage

SLAM Systemic lupus activity measure

SLE	Systemic Lupus Erythematosus
-----	------------------------------

SLE-DAI SLE disease activity index

Tri- ido thyronnine

T4 Thyroxine

TIA's Transient ischemic attacks
TNF-α Tumor necrosis factor- α

TSH Thyroid stimulating hormone

UV Ultra violet light

List of Tables

		Page
Table1	Genes Associated With Systemic Lupus	10
	Erythematosus.	
Table 2	Causes of Drug-Induced Lupus.	15
Table 3	Evidence of Importance of Immune Complexes in	18
	Pathogenesis of Human Systemic Lupus	
	Erythematosus.	
Table 4	T lymphocyte Abnormalities in Systemic Lupus	19
	Erythematosus (SLE).	
Table 5	Auto antibodies in SLE.	20-21
Table 6	Manifestations of Systemic Lupus Erythematosus in	22
	58 Children.	
Table 7	Cutaneous Manifestations of Systemic Lupus	23
	Erythematosus in Children.	
Table 8	Frequencies of Central Nervous System	35
	Complications of Systemic Lupus Erythematosus.	
Table 9	Classification Criteria for Antiphospholipid	42
	Syndrome.	
Table 10	The 1982 revised ACR criteria.	48-49
Table 11	the SLE Disease Activity Index (SLE-DAI)	50-51
Table 12	Clinical classification of autoimmune thyroid disease.	
Table 13	Conditions associated with increased incidence of	72

	autoimmune thyroiditis.	
Table 14	Factors affecting maintenance dose requirements in	75
	thyroxine replacement therapy Increased requirements	
Table 15	Master sheet of patients group.	86-89
Table 16	Demographic data of the patients.	94
Table 17	Initial presentation of SLE in the study group.	95
Table 18	Frequency of the clinical data in patients with SLE.	97
Table 19	History of thyroid manifestations.	99
Table 20	Lab data of patients of the study group.	100
Table 21	ANA percentage and pattern in SLE patient group.	100
Table 22	Thyroid functions in patients and control.	101
Table 23	Anti Thyroglobulin in patients and controls.	103
Table 24	Anti microsomal in patients and controls.	104
Table 25	Correlation between Anti-thyroglobulin anti bodies	105
	and the age of the patients.	
Table 26	Correlation between Anti-thyroglobulin anti bodies	106
	and the lab data SLE patients.	
Table 27	Correlation between Anti-microsomal antibody and	107
	the age of the patients.	
Table 28	Correlation between Anti-microsomal antibodies and	107-
	the lab data of the SLE patients.	108

List of Figures

		Page
Figure 1	Malar erythema of acute SLE.	24
Figure2	Vasculitic purpura in a teenage girl with an	24
	acute exacerbation of SLE.	
Figure 3	Mucocutaneous ulcerations of acute SLE.	25
Figure 4	Calibration curve of FT3	90
Figure 5	Calibration curve of FT4	91
Figure 6	Calibration curve of TSH	92
Figure 7	Sex distribution of the study group.	93
Figure 8	Initial presentation of SLE in the study group.	96
Figure 9	Show frequency of the clinical data of the	98
	study group.	
Figure 10	The pattern of ANA in patients with SLE.	101
Figure 11	Comparison between FT3 among patients and	102
	control group.	
Figure 12	Comparison between FT4 among patients and	102
	control group.	
Figure 13	Comparison between TSH among patients and	103
	control group.	
Figure 14	Anti thyroglobulin antibodies in patients and	104
	control groups.	
Figure 15	Anti microsomal antibodies in patients and	105

control groups.

- Figure 16 Correlation between anti thyroglobulin 108 antibodies and the duration of illness.
- Figure 17 Correlation between anti microsomal 109 antibodies and the duration of illness.

Introduction and Aim of work

Lupus is a chronic autoimmune illness characterized by auto antibodies directed at nuclear antigens and causing a variety of clinical and laboratory abnormalities, including rash, arthritis, leucopoenia, thrombocytopenia, alopecia, fever, nephritis, and neurologic disease. (*Mihailova et al;1999*).

Most or all symptoms of acute lupus are attributable to immunologic attack on the affected organs. Many complications of long-term disease are attributable both to the disease and to its treatment. (Steere et al; 2001).

The term lupus applies to several variants of the illness, of which systemic lupus erythematosus (SLE) is the most serious and most common. SLE is the prototype of the systemic autoimmune illness, involving multiple organ systems in pathologically similar way. (*Rowell etal;1998*)

SLE may occur as an overlap syndrome that shares features with other autoimmune illnesses such as mixed or undifferentiated connective tissue disease,

Dermatomyositis, Sjogren syndrome, Rheumatoid arthritis and Scleroderma. Organ specific autoimmune diseases such as thyroiditis, autoimmune hemolytic anemia and idiopathic thrombocytopenia, frequently accompany and may be a part of SLE.(*Ramos-Casals et al;2000*).

Auto immune thyroid disease marked by the presence of antibodies directed against thyroid antigens, has been associated with a number of non specific rheumatological disorders, these associations include SLE and Sjogren syndrome. (*Pedersen*;1993)

It is postulated that thyroid disease is more common in SLE than in general population but there is disagreement as to whether both hypothyroidism and hyperthyroidism are more common or whether this finding is restricted to hypothyroidism alone.(*Pyne and Isenberg;2002*).

Both anti thyroglobulin and anti microsomal antibodies have been found with greater frequency in SLE than in the general population even in lupus

patients who do not have clinical thyroid disease. (Scofield; 1996).

The aim of the work is to estimate the thyroid functions and detect the presence of auto antibodies to thyroid gland in juvenile systemic lupus eryrhematosus (JSLE) patients also try to correlate the presence of this antibodies (if present) with the clinco-laboratory manifestations in the studied group.

Systemic Lulus Erythematosus

Introduction:

Systemic lupus erythematosus (SLE) is a multisystem connective tissue disease characterized by presence of numerous pathogenic antibodies and immune complexes and wide spread immunologically determined tissue damage. The clinical course of SLE is characterized by periods of remission and chronic or acute relapses (*Nuki*, 1995).

This disease occurs primarily in young women and ranges in severity from a mild disease with rash and arthritis to a devastating illness with renal failure and profound nervous system disturbances. Because of the variability in the course of SLE, the approach to therapy is individualized for each patient and is determined by the array of clinical manifestations present (*Pisetsky et al.*, 1997).

Epidemiology:

- Incidence and prevalence:

The overall incidence of SLE ranges from 1.8 to 7.6 cases per 100,000 (*Hopkinson*, 1992; *Hopkinson et al.*, 1993 and Hess and Farhey, 1994). The incidence varies

with age, race and sex (Lehman et al., 1989 and Singsen, 1990).

Prevelance among children younger than 18 years has been estimated at 0.53 (*Hocheberg et al.*, 1985) to 0.6 (*Siegel and Lee*, 1973) per 100,000.

The overall age-standardized one-year period prevalence rate as estimated by a recent study of a geographically complete cohort from Nottingham is at 24.7 per 100,000 (*Hopkinson et al., 1994*).

There are no accurate prevalence data in children, although it has been inferred that there are between 5000 and 10,000 children with SLE in the United States (*Lehman*, 1993).

• Sex ratio:

SLE is clearly more prevalent in women, particularly in reproductive years. In most studies of SLE, 90% of patients are women. (Wallace and Dubois, 1987; McCarty et al., 1995 and Cameron, 1997). For , 14-64 years age group, the ratios of age-specific and sex-specific Incidence rates show a 6-to 10-fold female excess, which is not noted in patient younger than 14 or older than 65 years of age. This effect of age and sex on the incidence and prevalence rates of SLE suggests a role of hormonal factors in its pathogenesis (Gladman and Urowitz, 1998).

• Age at onset.

Approximately 25% of all cases of SLE begin in the first two decades of life but the disease is extraordinary rare in children under the age of five (*Lahita*, 1999). In the pediatric series, the average age at diagnosis varied from I 1 to 14 years (median 12.2 years). The time from onset of symptoms to diagnosis varied from 8 months to 3.3 years (median 1.2 years). This median time of 1.2 years from symptoms to diagnosis emphasizes the difficulty in diagnosis or the lack of awareness of SLE in this age group (*Silverman and Eddy*, 1998).

Race and geography:

Many studies have highlighted the significant variation in the prevalence of lupus among different ethnic groups sharing much the same environment A study from Birmingham by Johnson et al reported prevalence rates of 36 2, 90.6 and 206/100,000 among women of Caucasian, Asian and Afro-Caribbean origin respectively (*Johnson et al.*, 1995).

In another study by McCarty et al., the incidence in African-American females was more than 2.5 times higher than that in white females. In males, incidence in African-Americans was almost twice as high as that in whites. thus rates of SLE were found to be highest in African-American