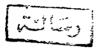
LIPOPROTEIN PROFILE IN JUVENILE RHEUMATOID ARTHRITIS

Thesies

Submitted in Partial Fulfilment of the Master Degree in Pediatrics



By

Amany Karam Mohamed El-Gindy

Supervised By

Prof. Yehia Mohamed El - Gamal

Professor of Pediatrics and Head of the Pediatric Allergy and Immunology Unit Ain Shams University

618.9272 A K

Assistant Supervisors

Dr. Elham Mohamed Hossny

Lecturer of Pediatrics - Ain Shams University

Dr. Mohamad Salah El - Deen Faheem

Lecturer of Pediatrics - Ain Shams University

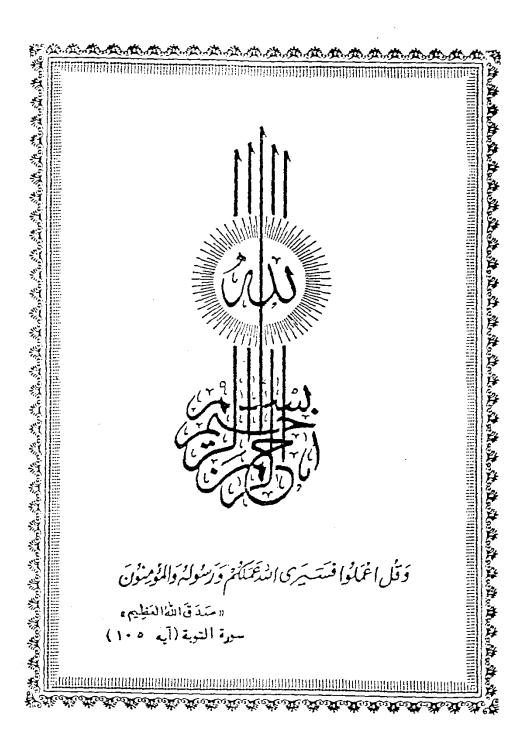
Dr. Nashwa Ahmed Adel El - Badawi

Lecturer of Clinical Pathology - Ain Shams University

Faculty of Medicine Ain Shams University

1992

48988





List of Contents

	Page	
☐ Introduction & Aim of the Work		
☐ Review of Literature		
* Juvenile Rheumatoid Arthritis		
• Etiology	1	
	1	
◆ Pathology	3	
	5	
 Clinical Manifestations 	5	
• Course & Prognosis	16	
Laboratory Investigations	17	
	23	
* Plasma Lipoproteins		
★ Lipoprotein Function	26	
	26	
† Plasma Lipid & Lipoprotein Levels	32	
	35	
* Lipoprotein Disturbances in Children	37	
☐ Subjects & Methods	40	
□ Results	51	
□ Discussion	89	
☐ Recommendations	103	
□ Summary	104	
□ References	106	
☐ Arabic Summary		

List of Abbreviations

ANA Antinuclear antibody

APO Apolipoproteins

C3 Third component of complement

Chylo chylomicron.

CNS Central nervous system

CRP C- reactive protein

DIC Disseminated intravascular coagulopathy

ESR Erythrocyte sedimentation rate

HDL(HDLs) High density lipoproteins

HDL-C High density lipoprotein cholesterol

IDL(IDLs) Intermediate density lipoproteins

Ig Immunoglobulin

JRA Juvenile rheumatoid arthritis

LCAT Lecithin cholesteral acyl transferase

LDL(LDLs) Low density lipoproteins

LDL-C Low density lipoprotein cholesterol

LPL Lipoprotein lipase

NSAID Non steroidal anti-inflammatory drug

PCAT Phosphatidyl choline cholesterol acyl transferase

RA Rheumatoid arthratis

RF Rheumatoid factor

VLDL (VDLs) Very low density lipoproteins

List of Tables

I Tabl	es in	Review of Literature	Page
Table	(1)	Criteria for the classification of JRA	4
Table	(2)	Classification of the types of onset of JRA	6
Table	(3)	Acute phase proteins	18
Table	(4)	Drug therapy for JRA	24 - 25
Table	(5)	Plasma cholesterol and triglyceride levels	34
		in childhood and adolescence	
II Tab	les of	Results	
Table	(6)	Inborn irrors of lipoprotein metabolism	38
Table	(7)	Acquired disorders of lipoprotein	
		metabolism	39
Table	(8)	Clinical & laboratory data of the control	
		group	52
Table	(9)	Clinical & laboratory data of rheumatoid	
		patients	54 - 55
Table	(10)	Serum lipids in rheumatoid patients	
		versus controls	57
Table	(11)	Serum lipids in rheumatoid patients in	
		activity versus controls	61
Table	(12)	Serum lipids in rheumatoid patients in	
		remission versus Controls	63

Table (13)	Serum lipids & ESR in rheumatoid	
	activity versus remission	65
Table (14)	Serum lipids in rheumatoid patients	
	receiving corticosteroids versus controls.	67
Table (15)	Serum lipids in the group of rheumatoid	
	patients receiving NSAID versus controls	69
Table (16)	Serum lipids in rheumatoid patients under	
	both Corticosteroids & NSAID versus	
	Controls	71
Table (17)	Serum lipids in rheumatoid patients not	
	receiving anti - rheumatic therapy versus	
	Controls	73
Table (18)	Serum lipids & ESR in the group of	
	rheumatoid factor positive versus	
	rheumatoid factor negative patients.	78

List of Figures

		Page
Figure (1)	Over view of lipoprotein inter relation	
	ships	32
Figure (2)	Serum HDL in rhumatoid patients versus	
	controls	58
Figure (3)	Serum Apo A ₁ in rheumatoid patients	
	versus controls	58
Figure (4)	Serum Apo B in rheumatoid patients in	
	activity versus controls	62
Figure (5)	Serum HDL in rheumatoid patients in	
	remission versus controls	64
Figure (6)	Serum Apo B/Apo A ₁ ratio in rheumatoid	
	patients in remission versus controls	64
Figure (7)	Serum HDL in rheumatoid patients under	
	various anti - rheumatic drugs versus	
	control group	74
Figure (8)	Serum LDL in rheumatoid patients under	
	varoius anti - rheumatic drugs versus	
	control group	74
Figure (9)	Serum triglycerides in rheumatoid	
	patients under various anti - rheumatic	
	drugs versus control group	75

Figure	(10)	Serum Apo B in rheumatoid patients	
		under various anti - rheumatic drugs	
		versus control group	75
Figure	(11)	Mean ApoB/ApoA ₁ ratio in rheumatoid	
		factor positive versus negative patients	79
Figure	(12)	Serum Apo B/Apo A ₁ and age in	
,		rheumatoid patients not under therapy	80
Figure	(13)	Serum LDL/ HDL and age in rheumatoid	
		patients not under therapy	81
Figure	(14)	Serum cholesterol /HDL and Age in	
		rheumatoid patients not under therapy	81
Figure	(15)	Serum Apo B/Apo A ₁ and body weight in	
		the whole rheumatoid patients	82
Figure	(16)	Serum LDL/HDL ratio and body weight	
		in the rheumatoid children not under	
		therapy	83
Figure	(17)	Serum cholesterol /HDL ratio and body	
		weight in the rheumatoid children not	
		under therapy	83
Figure	(18)	Serum ApoB/ApoA ₁ ratio and height in	
		the rheumatoid patients not under therapy	84
Figure	(19)	Serum LDL/ HDL ratio and height in the	
		rheumatoid patients not under therapy	85

Figure (20)	Serum cholesterol / HDL ratio and height	
	in the rheumatoid patients not under	
	therapy	85
Figure (21)	Serum triglycerides and ESR in	
	rheumatoid patients in activity	86
Figure (22)	Serum LDL/HDL ratio and ESR in	
	rheumatoid patients	87
Figure (23)	Serum cholesterol / HDL ratio and ESR	
	in rheumatoid patients	88
	List of Plates	
Plate (1) Plate	e for apolipoprotein A ₁ estimation	56
DI ((a)	e for apolipoprotein B estimation	60

Introduction & Aim of the Work

The metabolic changes in chronic inflammatory connective tissue diseases ought to be recognized not only because of their potentially tissue - damaging effect but also because treatment with anti-inflammatory and disease - modifying drugs may have metabolic side effects (Svenson et al., 1987).

Dyslipoproteinemia is a feature of certain rheumatic diseases including adult rheumatoid arthritis (Lorber et al., 1985). This may explain the increased mortality reported in patients with rheumatoid arthritis - compared to the general population - with cardiovascular disease on the top of the list of causes of mortality (Mutru et al., 1985).

Increased concentrations of total cholesterol, low density lipoprotein cholesterol (LDL - C) and apolipoprotein B (Apo B) have been found to be associated with an increased risk of cardiovascular disease. Moreover, low concentrations of high density lipoprotein - cholesterol (HDL - C) and apolipoprotein A₁ (Apo A₁) have been found to be risk factors for cardiovascular disease (Kottke et al., 1986).

This study is aimed to outline the lipoprotein and apolipoprotein patterns in patients with juvenile rheumatoid arthritis and their possible relation to disease activity and therapy.

Juvenile Rheumatoid Arthritis

Juvenile rheumatoid arthritis (JRA) is a disease or group of diseases characterized by chronic synovitis and associated with a number of extra - articular inflammatory manifestations.

A confusing number of names have been applied, including juvenile arthritis, Still's disease, juvenile chronic polyarthritis, and chronic childhood arthritis (Harris, 1990).

Juvenile rheumatoid arthritis is one of the more frequent chronic illnesses of childhood and an important cause of disability and blindness. It may not represent a single disease but a syndrome of diverse etiologies (Cassidy et al., 1986).

As a matter of fact, it is the most common of the collagen vascular diseases in children (Rennebohm, 1988).

☐ Etiology:

The etiology of JRA is unknown. Among possible causes are infection, autoimmunity, trauma, stress, and immunogenetic predisposition.

An inflammatory arthritis of humans has been observed with infections from both mycoplasma and viruses (rubella and parvovirus) (Schwarz et al., 1987). Certain viral illnesses of

childhood such as rubella may result in a self - limited arthritis; persistent rubella virus infection has been demonstrated in the synovia of children with JRA (Chantler et al., 1985).

Chronic inflammation may be perpetuated by immune complexes formed from auto antibodies such as antinuclear antibody (ANA) or rheumatoid factor (RF) induced by infections.

It is observed frequently that onset of JRA may follow physical trauma to an extremity such as fall or an ankle sprain. It is also well documented that psychological stress appears to be particularly common in families of children with JRA (Henoch et al., 1978).

☐ Genetic background:

There are very few reported instances in which JRA has been observed in more than one family member. Although the cases are few in number, it is striking that within any one family JRA tended to be of the same type of onset (Rosenberg and Petty, 1980). Early studies of Ansell et al., 1962 reported that female relatives of children with JRA showed an increased frequency of seronegative erosive polyarthritis and that male relatives had an increased prevalence of sacroiliac arthritis (Ansell, 1977). One further association bears attention, that is the occasion occurrence of JRA and adult rheumatoid arthritis (RA) in the same family. Rossen et al.,

and concluded that susceptibility to arthritis was influenced by a dominant gene with variable penetrance and expressivity.

Pathology:

I) Articular.

Rheumatoid arthritis is characterized by chronic non suppurative inflammation of the synovium. Affected synovial tissues are edematous, hyperemic and infiltrated with lymphocytes and plasma cells. Secretion of increased amounts of joint fluid results in effusion (Schaller, 1980).

Projections of thickened synovial membrane from villi, which protrude into joint spaces. Hyperplastic rheumatoid synovia, may spread over and become adherent to articular cartilage (Pannus formation). With continuing chronic synovitis and proliferation of synovia, articular cartilage and other joint structure may become eroded and progressively destroyed.

Many children with JRA never incur perminent joint damage despite prolonged synovitis(Harris, 1990). However, once joint destruction has commenced, erosions of subchondral bone, narrowing of the "joint space" (loss of articular cartilage), destruction or fusion of bones, and deformity, subluxation, or ankylosis of the joints may result. Tenosynovitis and myositis may be present (Williams and Ansell, 1985).