Department of Biochemistry at the Faculty of Medicine, University of Benghazi

DYSLIPIDEMIA IN RHEUMATOID PAITENTS

BY

SIHAM. ALI. A. ABASS. BDS

SUPERVISOR: Prof. FARAG. A. ELSHAARI

CO-SUPERVISOR: Prof. EMHEMED ABDULSALAM

Submitted in Partial Fulfillment of the Requirements of the Master's Degree of Science in Biochemistry

2016

Table of contents

List of Tables

List of Figures

8-Abbriviations

CA Cardiac Amyloidosis

CHF Congestive Heart Failure

CM Cervical Myelopathy

CNS Central Nervous System

CoV Coronary Vasculitis

CuV Cutaneous Vasculitis

CVD Cardiovascular Disease

CVS Cardiovascular System

DMARD: Disease Modifying Anti-Rheumatic Drugs

FS Felty's Syndrome

GN Glomerulonephritis

IDH Ischemic Heart Disease

ILD Interstitial Lung Disease

IN Interstitial Nephritis

KCS Kerato Conjunctivitis Sicca

MC Myocarditis

MM Mononeuritis Multiplex

NNA Normochromic-Normocytic Anaemia

NS Nervous System

OA Osteoarthritis

PC Pericarditis

PE Pleural Effusion

PNs Pulmonary Nodules

PS Pulmonary System

PUK Peripheral Ulcerative Keratitis

RNs Rheumatoid Nodules

RF Rheumatoid Factor

SPN Sensory Peripheral Neuropathy

SS Sjogren's Syndrome

SV Systemic Vasculitis

TNF Tumor Necrosis Factor

Th2 T-helper type 2 cells

VDs Valve Diseases

Abstract

Rheumatoid arthritis (RA) is associated with an excess mortality from cardiovascular disease (CVD) and this may be related to changes in lipid profile.

Cardiovascular features in RA are common, including: pericarditis, myocarditis, cardiac amyloidosis, coronary vasculitis, arrhythmia, valve diseases and most importantly congestive heart failure and ischemic heart disease (IHD).

The last two have been associated with an increased morbidity and mortality in RA patients compared with the general population due to an accelerated atherogenesis process that cannot be fully explained by the classic atherosclerosis risk factors. The presence of chronic inflammation and a possible genetic component are important contributing agents.

The increased prevalence of CVD among RA patients is probably due to an increase in both the traditional risk factors for atherosclerosis and the presence of chronic inflammation. Traditional risk factor for CVD including atherogenic dyslipidemia that involved elevation of plasma cholesterol, triglycerides or a low/high density lipoproteins that usually result from excessive dietary intake of saturated fat and cholesterol.

Dyslipidemias are disorders of lipoprotein metabolism, including lipoprotein overproduction and deficiency. They may manifest as one or more of the following: elevated total cholesterol, low-density lipoprotein (LDL), and triglyceride levels or as decreased high-density lipoprotein (HDL) level. Dyslipidemia is closely associated with atherosclerosis and is a major causal factor in the development of ischemic diseases. Ischemic cardiovascular and cerebrovascular events are leading causes of morbidity and mortality.

At Rheumatology Clinic Al-Hawari Hospital and Rheumatology Clinic 7th October Hospital, Benghazi-Libya , during period from January 2014 to June 2014, A prospective cross sectional study of 100 patients diagnosed as rheumatoid arthritis (RA) according to Eular/ACR criteria. Patients with diabetes , hypertension and history of familial hyperlipidemia were excluded in this study. Total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL) were measured. Nearly 58% of cases were female with age range (21-85years) and mean (47.87 ± SD 14.82), most of cases exceeding 1year in disease duration, whereas 13% of patients have disease duration less than 6 months. Approximately 51% of our patients exhibited active mode of rheumatoid arthritis. We noticed in present study that the majority of our patients were treated with methotrexate whereas the anti-TNF was the minor treatment in all patients.

Most frequent dyslipidemia was noticed in VLDL, the majority of the patients had at least one lipid out of range. There was only 4 patients had no dyslipidemia, while the 96% of the patients had at least one dyslipidemia. Hence, the majority had three lipoproteins and showed dyslipidemia (28%). There was a significant relation between duration of disease and the increase in the dyslipidemia i.e. the long duration of disease showed a high dyslipidemia level. In active patients the dyslipidemia was highly significant compared to the inactive patients. Dyslipidemia was slightly higher in females than males but this increase was non-significant. Dyslipidemia was highly significant in old age patients than the young age. Methotrexate as a common therapy used for rheumatoid arthritis showed a significant increase in dyslipidemia compared with other medications used in this study.

CERTIFICATE & APPROVAL

We the undersigned, certify that on October the 8th , 2016 have examined

SIHAM ALI. A. ABASS for her thesis entitled:

((DYSLIPIDEMIA IN RHEUMATOID PAITENTS))

The thesis has been accepted for partial fulfillment for the requirements for the degree of Master of Science in Biochemistry

EXTERNAL EXAMINER: **Prof. AHMAD ZAID**

Faculty of Medicine, Tripoli University

Signature: _____

INTERNAL EXAMINER: **Prof. ABDULLA M. JARARI**

Faculty of Medicine, University of Benghazi

Signature: _____

SUPERVISOR: **Prof. Farag Ali Elshaari**

Faculty of Medicine, University of Benghazi

Signature: _____

CO-SUPERVISOR: **Prof. Emhemed Abdulsalam**

Faculty of Medicine, University of Benghazi

Signature: _____

DATA COLLECTION SHEET

I. PATIENT NAME----------

AGE ---------- **SEX**----------**RESIDENCE** ----------

FILE NO---------- **HOSPITAL** ----------

II. DISEASE DURATION: ----------

III. DISEASE ACTIVITY: ACTIVE □ INACTIVE □

IV. DRUG HISTORY:

METHOTROXATE □

SALAZOPARINE □

ANTI-TNF □

HYDROCORTISONE □

STEROID □

V. LIPID PROFILE:

TC □ V---------- R----------

TG □ V---------- R----------

LDL □ V---------- R----------

HDL □ V---------- R----------

VLDL □ V---------- R----------

1- Literature Review

Rheumatoid arthritis (RA) is an immune-mediated chronic inflammatory disease. Despite being characterized by inflammation of the synovial membrane and progressive destruction of the articular cartilage and bone, RA is a systemic disease often associated with other extra-articular manifestations, with a significant impact on mortality and morbidity [Gabriel,2003].

A better control of disease activity in the last decades due to the availability of more effective drugs has resulted in a lower frequency of extra-articular manifestations of RA, as well as better outcomes in many patients.

Many different tissues and organs can be involved in RA patients in addition to the characteristic peripheral polyarthritis.

1.1. General Presentations of RA: Several general symptoms can represent a major problem during the course of RA, many of them also being present before its diagnosis. Weight loss, fever, prolonged early morning stiffness, fatigue, generalized muscle weakness, low mood, and depression are often responsible for a significant loss in the quality of life of patients. Fatigue is reported in 40–80% of RA patients as their most disabling symptom [Balsamo,2014].

As a result of the inflammatory process, RA patients frequently developed normo-chromic normocytic anemia [Wilson,2004].

Other manifestations associated with chronic inflammation include injury of exocrine glands with the development of a secondary Sjögren's syndrome (SS), sarcopaenia, and osteoporosis.

Rheumatoid nodules (RNs) are the most frequent skin manifestation. They occur in about 30% of RA patients, mostly in RF-positive subjects, and are usually located subcutaneously on pressure areas, including the olecranon process and proximal ulna, finger joints, sacral prominences, occiput, and Achilles tendon. Usually painless, they have a variable consistency from a soft, mobile to a hard, rubbery mass attached firmly to the periosteum. Histologically they are characterized by a central necrotic area rimmed by a corona of palisading fibroblasts that is surrounded by a zone of tissue affected by perivascular cellular infiltration enriched with lymphocytes, plasma cells, and histiocytes [Ziff, 1990].

Regression of nodules may occur during treatment with disease modifying anti-rheumatic drugs (DMARD). Paradoxically, in 8–11% of methotrexate treated RA patients, accelerated

rheumatoid nodules can occur, with nodules usually located in the fingers or in the metacarpophalangeal and proximal interphalangeal joints. The condition regresses when methotrexate is reduced or withdrawn and if hydroxy chloroquine or sulphasalazine treatment is started. Etanercept has also been related with the development of this type of nodules [Cunnane, 2002] no effective treatment is available.

1.2. Ocular Presentations: Ocular involvement occurs in 27% of RA patients [Zlatanovic, 2010] . Keratoconjunctivitis sicca (KCS), the most frequent and usually benign ophthalmologic manifestation, occurs in at least 10% of patients together with xerostomia, usually as a part of a secondary SS. Symptoms such as burning or a foreign body sensation can be warning signs. The diagnosis is supported by a positive Schirmer test and a reduced tear break-up time. On the other hand, a reduced salivary flow rate can confirm xerostomia. Some patients develop scleritis, episcleritis, peripheral ulcerative keratitis, or vasculitis involving retinal vessels. A clinical suspicion of such disorders in a patient with RA should lead to immediate referral to an ophthalmologist. Episcleritis, inflammation of the layer superficial to the sclera, usually correlates with the activity of RA. It presents in <1% of patients with RA and is generally a self-limiting condition. Symptoms are usually limited to focal redness and irritation of the eye without altering visual acuity.

Scleritis is a more aggressive process, characterized by an intensely painful inflammation of the sclera itself. It is seen in patients with vasculitis and long-standing arthritis. There are three types of anterior scleritis: diffuse, nodular, and necrotizing. The latter is also referred to as scleromalacia perforans, the most severe type. It is a degenerative thinning of the sclera that occurs in RF-positive female patients. It has been attributed to a vasculitis process with deposition of immune complexes. This condition is often painless and can evolve to scleral perforation when it goes untreated [Smith, 2007].

1.3. Pulmonary Presentations: Pulmonary involvement in RA is frequent, although not always clinically recognized, and includes RNs, pleural effusion (PE), interstitial lung disease (ILD), small airway disease, and pulmonary vasculitis. It is responsible for 10-20% of overall mortality [Bongartz, 2010; Young, 2007] and can occur before the development of joint symptoms. [Gizinski,2009; Chen,2013] Parenchymal pulmonary nodules (PNs) are usually asymptomatic, but may activate and cause PEs; they also increase the risk of infections and pneumothorax. They are

usually found in RF-positive patients with nodules elsewhere. Sometimes differentiation with neoplasms and infections can be difficult.

PE, usually an exudate with mixed cell counts and high protein concentration, is common but frequently asymptomatic; autopsy studies reported pleural involvement in 50% of cases, with only 10%clinically detected [Mielants, 2009].

ILD is the most important pulmonary manifestation of RA, being the commonest pulmonary cause of death and a significant contributor to morbidity[Kelly, 2007; Sihvonen, 2004].

The most frequent histopathological patterns of ILD in RA are usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP) (44–56% and 33–44%, respectively),[Lee, 2005] followed by mixed disease (0–12%).Other forms, such as obliterative bronchiolitis, are rare but associated with a high mortality [Devouassoux, 2009]. Although it tends to occur more often in RF positive male patients with long-standing nodular disease,[Anaya, 1995]studies in new onset RA have found lung abnormalities in a high percentage of patients.[Youssef, 2012; Wilsher, 2012] Clinical presentation and course are similar to that of idiopathic pulmonary fibrosis, but the response to immune suppressants is usually better.

Diagnosis is based on clinical presentation, blood gases, pulmonary function tests, and high resolution computed tomography (HRCT).[Lake, 2014] As abnormalities, can be detected by HRCT in about 50% of RA patients, but only 10% have clinically significant symptoms,[Lioté, 2008] diagnosis should be supported not only on clinical signs and symptoms, but also in abnormal pulmonary function tests and either a compatible HRCT or lung biopsy. Physiological abnormalities include a reduction in lung volume, a low diffusing capacity for carbon monoxide (which is the measure best associated with the extent of disease in ILDs and a poorer prognosis in RA-ILD27), and oxygen desaturation during a 6-minutes' walk test.

1.4. Neurological Presentations: On the contrary, neurological involvement in RA is rare, present in only 1% of patients. Disorders of the central nervous system (CNS) include cervical myelopathy, vasculitis, RNs located within the CNS, or meningitis. Stroke also occurs with increased frequency.[Avi̊a, 2008] CNS vasculitis is extremely rare.

The diagnosis is supported by magnetic resonance imaging (MRI), alone or with magnetic resonance angiography (MRA), showing the segmental vascular stenosis characteristic of vasculitis [Caballol, 2010] Peripheral neuropathy is usually manifested

as sensorimotor neuropathy or mononeuritis multiplex. The underlying mechanism is small vessel vasculitis of the vasa vasorum of the nerves with ischemic neuropathy and demyelination as part of the rheumatoid vasculitis (RV) syndrome.

1.5. Renal Presentations: RA and kidney disease (KD) often coincide. There are several potential causes of nephropathy such as drug-related renal disease, secondary renal amyloidosis, and various types of glomerulonephritis (GN). Mesangial proliferative GN is the most frequent histological lesion followed by membranous GN [Nakano,1998; Helin,1995] The latter usually being related to gold or D-penicillamine, with both therapies not currently in use. Other infrequent causes of KD can be interstitial nephritis, minimal change glomerulopathy, IgA nephritis, focal proliferative GN, or rapidly progressive GN due to microscopic polyangitis [Palomar, 2005].

Secondary (reactive AA) amyloidosis can be seen in long-standing disease and poor response to therapy, and markedly influences these patients' outcomes [Lachmann, 2007].

Felty's Syndrome (FS) is an uncommon Ex RA, occurring in <1% of RA patients. It is defined as a combination of RA with neutropenia and splenomegaly, and occurs mostly among women around the age of 60 with a long history of severe articular disease, RF positive in association with antibodies to cyclic citrullinated peptides, and who have the HLA-DR4*0401 antigen [Campion, 1990]. Almost 75% of patients with FS will present cutaneous nodules. Other features that are usually present include lymphadenopathy, hepatopathy, vasculitis, leg ulcers, and skin pigmentation. Its poor prognosis is due to a higher incidence of severe infection related to neutropenia that normally accompanies it, whose cause lies in both decreased granulopoiesis and increased peripheral destruction of granulocytes [Breedveld,1987].

It is important to exclude hematopoietic malignancy when making the diagnosis of FS. The clinical significance of FS resides in the fact that often inactive joint disease distracts the clinician's attention from the severe extra-articular disease and neutropenia, causing recurrent, sometimes fatal infections. Furthermore, FS has been associated with an increased risk of malignant lymphoproliferative disease compared to other patients with RA. This highlights the importance of careful evaluation of these cases.

1.6. Cardiovascular presentations (CV): Cardiovascular features in RA are common, [Sarzi, 2010] including: pericarditis, myocarditis, cardiac amyloidosis, coronary vasculitis (CoV), arrhythmia, valve diseases and most importantly congestive heart failure [Nicola, 2005] and ischemic heart disease (IHD).

The last two have been associated with an increased morbidity and mortality in RA patients compared with the general population due to an accelerated atherogenesis process that cannot be fully explained by the classic atherosclerosis risk factors [Del Rincon, 2001; Dessein, 2005] .The presence of chronic inflammation and a possible genetic component are important contributing agents [Gonzalez, 2007; Rodriguez, 2011].

Within the classical cardiac manifestations, pericarditis is the most common. Both, Echocardiography and autopsy studies reveal evidence of pericardial inflammation in 50% of patients, although symptoms are relatively uncommon occurring in about 1–4% of patients. It usually occurs in RF-positive nodular RA, Conversely, symptomatic myocarditis, endocarditis, and CoV rarely occur, and are almost exclusively demonstrated by autopsy [Voskuyl, 2006].
Several investigators reported an excess of cardiovascular morbidity and mortality among RA patients. In active RA, the majority of cardiovascular deaths result from accelerated atherosclerosis [Gabriel, 2003; Goodson, 2002; Van Doornum, 2002]. Risk factors for atherosclerotic events and cardiovascular disease include male sex, old age, elevated plasma total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C), high blood pressure, smoking and diabetes mellitus [Castelli,1986; Cui, 2001]. Approximately 50% of atherosclerotic coronary artery disease (CAD) in the community occurs in the absence of traditional risk factors [Ross,1993].
The increased prevalence of CVD among RA patients is probably due to an increase in both the traditional risk factors for atherosclerosis and the presence of chronic inflammation [Satter, 2003].Traditional risk factor for CVD including atherogenic dyslipidemia that involved elevation of plasma cholesterol, triglycerides or a low/high density lipoprotein that usually results from excessive dietary intake of saturated fat and cholesterol [HY et al, 2007].
Active systemic inflammation has multiple effects which accelerate atherosclerosis these include changes to the endothelium by C-reactive protein (CRP) and cytokines. Induction of secondary dyslipidemia, altered glucose metabolism and creation of a hypercoagulable state due to platelet activation and increased production of clotting factors also play a role [Vanleuven et al, 2008]. The importance of inflammation in the development of atherosclerosis is supported by the association of cardiovascular death with elevated levels of CRP in patients with inflammatory polyarthritis [Goodson et al, 2005].

1.7. Lipid Profile:

In general, the lipid profile includes :- cholesterol, triglycerides, high-density lipoprotein (HDL), very low-density lipoprotein (VLDL), low-density lipoprotein (LDL) and various risk classifications for coronary heart disease (CHD), cholesterol to HDL ratio, and LDL to HDL ratio.

1.7.1. Cholesterol: Total cholesterol is used to measure lipid status and metabolic disorders. Cholesterol is necessary for life, but is also associated with atherosclerosis. It is used to make hormones, vitamin D, and cell membranes. About two-thirds of the body's cholesterol is made by the liver and one-third obtained through the diet. Increased cholesterol is found in high fat diets, primary hypercholesterolemia, the nephritic syndrome, hypothyroidism, primary biliary cirrhosis and in some cases of diabetes. Low levels have been found in malnutrition, malabsorption, severe liver disease, polycythemia Vera, etc.

The method to Measure total cholesterol is by spectrophotometry. Normal values are based on age. The "normal or reference ranges" has been lowered in recent years to combat the rapid increase in heart disease. In people under 19 years of age, the normal value is less than170 mg/dl. In people over 19 years of age, the normal value is less than 200 mg/dl.

1.7.2 Triglycerides: Like cholesterol, triglycerides (TG) are used to measure lipid status and metabolic disorders. A patient must absolutely be fasting for an accurate measurement. Triglycerides are the major component of chylomicrons (CM) and VLDL. They may be elevated in hypothyroidism, diabetes, chronic liver and kidney diseases, pancreatitis, some genetic types of hyperlipidemia, alcohol abuse, estrogen (pregnancy or oral contraceptive pills), and certain medications (thiazide diuretics).

The method to Measure TG is spectrophotometry. (< 150 mg/dl is normal, 150 – 199 mg/dl is borderline, 200 – 499 mg/dl is high and > 500 mg/dl is very high).

1.7.3. High-Density Lipoprotein (HDL): HDL is called the "good cholesterol". It tends to carry cholesterol away from tissues. The method to Measure HDL is spectrophotometry (< 40 mg/dl is low, and > 60 mg/dl is normal).

1.7.4. Low-Density Lipoprotein (LDL): LDL cholesterol is called the "bad cholesterol". It is part of the lipid profile and is one of the most important "risk factors" for atherosclerotic disease. LDL particles provide cholesterol to the peripheral tissues.

The method to Measure LDL is by calculation using the Fried Ewald formula. The formula can only be used when the TG are less than 400 mg/dl.

LDL core lipids contain about 10% TG and 145% cholesterol. (< 100 mg/dl is optimal, 100 – 129 mg/dl is near optimal, 130 – 159 mg/dl is borderline, 160 – 189 mg/dl is high and > 190 mg/dl is very high).

1.7.5. Very Low Density Lipoprotein (VLDL): VLDL is a type of lipoprotein and helps carry triglycerides from the liver to the blood to other parts of the body. Density refers to the amount of lipids versus proteins. Core lipids in chylomicrons contain about 85% triglycerides and 5% cholesterol, VLDL contains about 60% TG and 15% cholesterol. Elevated VLDL levels are found in Type IV hyperlipidemias.

1.7.6. Cholesterol to HDL Ratio: The Cholesterol to HDL ratio is a calculation of your risk for heart disease. It is optimal to have a low ratio. A low ratio indicates that total cholesterol is comprised mostly of HDL particles. This ratio is considered as the most important indicator for atherosclerosis. Average risk for male (5.5-9.6) and for female (4.5-7.1) respectively.

1.7.7. LDL to HDL Ratio: The LDL to HDL ratio is also a heart disease risk indicator. It is best to have a low ratio as this indicates there is sufficient HDL in relation to LDL to aid in prevention of atherosclerosis. Excessively high or low levels can indicate a problem. It is best to maintain these in proper balance to HDL. Average risk for male (3.7-6.3) and for female (3.3-5.0) [Vance, 1996; Vanleuven, 2001].

Many previous works revealed that rheumatoid arthritis is associated with an adverse lipid profile [Douglas, 2006]. RA likely influences lipoprotein metabolism leading to quantitative and qualitative alterations of low density lipoproteins. In addition, glucocorticoids may also alter carbohydrate and lipid metabolism. However, by reducing the inflammation level, the net effect on lipid parameters and on the CV risk may be favorable [Hansel, 2008]. Data from open follow-up studies would suggest that disease modifying therapy use is associated with a beneficial effect on lipid parameters and with a reduction in the incidence of CV disease [Sara, 2011].

In general, and with some variations between different studies, the lipid profile of patients with active or untreated RA is primarily characterized by a decrease in serum levels of HDL-C whereas contrasting results have been published on the serum levels of TC and LDL-C [Boers et al, 2003; Situnayake,1994]. Importantly, the reduction in HDL-C has as a consequence the increase in the TC/HDL-C ratio [Boers et al, 2003]. This ratio represents an atherogenic index, which is an important

prognostic marker for cardiovascular disease [Boers et al, 2003]. Indeed, the risk of myocardial infarction increases considerably when this ratio is higher than five, and it should ideally be four or less [Boers et al, 2003; Situnayake,1994]. The serum TC and HDL-C levels in RA are inversely related with disease activity [Boers et al, 2003]. suggesting a potential role for inflammation in the atherogenic profile and the higher atherosclerotic risk observed in RA [Park et al, 1999].

The cholesterol ester transfer protein (CETP) has a central role in HDL metabolism and in the regulation of HDL-C levels in serum. CETP exchanges cholesterol esters with triglycerides between HDL and apolipoprotein B-containing lipoproteins and thus significantly contributes to the reverse cholesterol transport pathway. High levels of CETP activity lead to a reduction in HDL-C levels and an atherogenic lipoprotein profile [Tall, 1993; Barter, 2002]. Thus mutations in the CETP gene associated with CETP deficiency are characterized by high serum HDL-C levels and reduced cardiovascular risk [Forrester et al, 2005].

Our knowledge about the effect of treatment on the lipid profile of patients with RA is limited and only cross-sectional and short term uncontrolled studies have been performed[Boers et al, 2003]. [Park et al, 1999; Lazarevic et al, 1992]. In addition studies on lipid profile and CETP activity, as well as studies on the effect of therapy on these parameters in RA patients, are scarce. On the other hand, atherosclerosis is a chronic process and only long-term changes of the lipid profile might affect cardiovascular disease.

1.8. Leptin: Leptin is a 16-kDa non-glycosylated protein encoded by the obese (ob) gene, which is located on human chromosome7. Leptin is mainly produced in white adipose tissue and regulates the balance between food intake and energy expenditure. Its plasma levels are correlated with total body fat mass. Leptin has a significant role in the immune system. It has structure similarity to the type I cytokine family and its receptor is a member of the class I cytokine receptor family. Centrally, leptin affects thymic function, leading to the generation and proliferation of naïve T lymphocyte. In the periphery, leptin augments the differentiation of T lymphocytes into T helper-1 lymphocyte, which predominately secrete pro-inflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-6 , and interferon(INF)-ϒ. [Sang-Won, et al, 2007].

IL-6 reduced TC and TG in animals and humans. Hence, inflammation reduces circulating lipid levels via the induction of IL-6. The exact mechanism by which IL-6 induces these changes still remains unknown. However we showed that IL-6 affects lipid metabolism by stimulating lipid

uptake via VLDL induction, increasing hepatic and adipose tissue lipolysis and decreasing hepatic lipid synthesis [Misato, 2011].

Rheumatoid arthritis (RA) is characterized by polyarticular synovitis and bony erosions, and the above mentioned proinfilamatory cytokines have been implicated in the development and progression of the disease. Thus, it is possible that leptin, another pro-inflammatory cytokines might have an important role in the pathogenesis and aggregation of RA. However, its role in the pathogenesis of RA remains controversial because the level of leptin is significantly affected by factors such as sex hormones, menopausal status, body mass index (BMI), and insulin resistance. Rheumatoid patients with high activity had significantly higher mean leptin levels than those with low activity, and mean leptin level adjusted to BMI (leptin\BMI) was also significantly higher in high –activity rheumatoid arthritis patients [Sang-Won, et al, 2007].

Patients with RA aged younger than 50years experience independent adiposity-driven leptin-endothelial activation relationship in the absence of leptin metabolic risk factor associations. Young but not older patients with RA may sustain obesity-induced endothelial activation that is directly mediated by leptin [Patrick et al, 2014].

Fasting patients with RA exhibit an improvement in clinical and biological parameters of disease activity, associated with decrease in leptin serum concentration and a shift toward Th2 cytokine production. These changes observed in RA patients and experimental models suggest that leptin may play a role in inflammatory mechanisms of arthritis [Bozena et al, 2008].

In patients with RA, chronic inflammation and its suppression during anti-TNF therapy have limited influence on plasma leptin concentrations, while significantly decreasing circulating adiponectin levels. Our findings question suggested key role of inflammatory markers in regulating adipocytokine patterns in RA [Calin et al, 2016].

A marked increase in plasma levels of leptin, adiponectin and visfatin was noted in patients with rheumatoid arthritis, whereas resistin levels were similar to those observed in healthy controls. Coordinated roles for adiponectin, leptin and visfatin are suggested in the modulation of the inflammatory environment in patients with rheumatoid arthritis, whereas the lack of modulation in resistin levels is predictive of an irrelevant role for this peptide, suggesting that resistin level is probably not one of the main signals associated with the pathogenesis of this disease [Otero et al, 2006].

Both early disease modifying antirheumatic drugs (DMARD)-naive and chronic RA were associated with higher plasma adiponectin compared to healthy controls, but lower plasma adiponectin than osteoarthritis (OA). Adiponectin increased 13% during MTX treatment. In patients with RA and OA body mass index, age, sex, and disease activity measures failed to explain the findings [Trine et al, 2009].

Altered adipokine production in RA is population specific. RA modifies adiponectin concentration metabolic risk factor relationships. Individual cardiovascular risk factors and particularly serum lipid concentrations require close monitoring upon employing interventions that alter adiponectin production or inhibit its effects in RA. However, whereas leptin and adiponectin inhibition could improve disease activity, this intervention may also not result in altered overall cardiovascular and disease in RA [Patrick et al, 2013].

2-Aim of the Study

In order to assess the disturbance in the lipid profile in rheumatoid arthritis patients and to evaluate the effect of drugs used at rheumatology clinics on the lipid levels in those patients.

A prospective, cross sectional study were taken to investigate lipid profile and disease activity in rheumatoid arthritis patients as well as the relationship between these parameters.

3- Materials and Methods

Total number of 100 patients diagnosed as rheumatoid arthritis were selected in this study according to Eular/ACR criteria. Assessment of their lipid profile as the following:

1-serum total cholesterol level.

2-serum total triglycerides level.

3-serum low density lipoprotein.

4-serum high density lipoprotein.

5-serum very low density lipoprotein.

3.1. Exclusion Criteria:

In the present study we excluded the following cases

1- Diabetic patients.
2- Hypertensive patients.
3- Patients with Familial Hyperlipidemia.

3.2. Type of the study: Cross sectional study.

3.3. Location of the study:

Rheumatology Clinic Al-Hawari Hospital and Rheumatology Clinic 7th October Hospital, Benghazi-Libya, during period from January 2014 to June 2014.

3.4. Estimation of lipid profile:

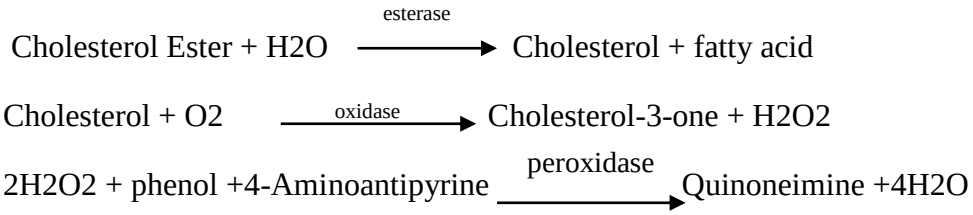
3.4.1. Blood collection:

Venous blood samples were drawn from all the participants after at least 12 hours fasting. Plain tubes and sera were separated from coagulated blood. Sera were analyzed for triacylglycerol, total cholesterol, HDL, LDL and VLDL.

3.4.2. Estimation of total cholesterol:

Test principle:

Determination of cholesterol is done following the enzymatic hydrolysis of cholesterol esters and oxidation of cholesterol. The colorimetric indicator is quinoneimine, which is generated from 4-aminoantipyrine and phenol by hydrogen peroxide under the catalytic action of peroxidase (Trinder's reaction).



The intensity of the pink/red color is proportional to the Cholesterol concentration in the sample. It is determined by measuring the increase the absorbance at 512nm.

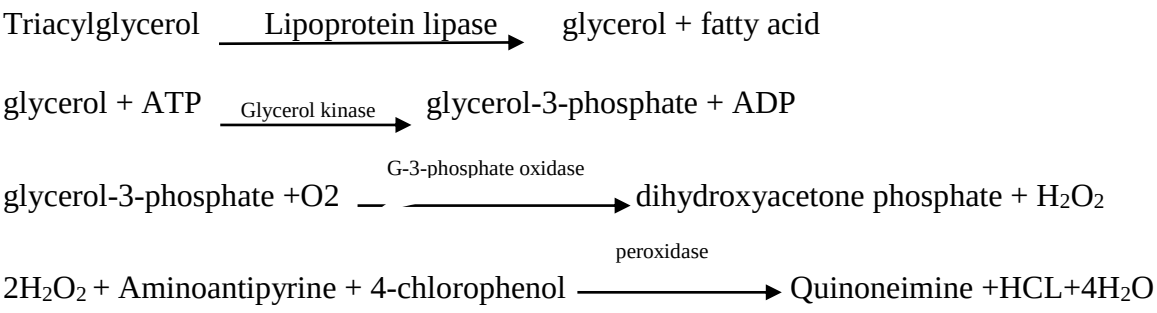
Calculation:

ChemWellanalyzer automatically calculate the analytic concentration of each sample.

3.4.3. Estimation of triglycerides:

Test principle:

Determination of triglycerides was carried out using the enzymatic splitting with lipoprotein lipase. The chromogen used is quinoneimine, which is generated from 4-aminoantipyrine and 4-chlorophenol by hydrogen peroxide under the catalytic action of peroxidase is used for TAG determination.



The absorbance of the colored complex was measured at 546nm, which is proportional to triglycerides concentration.

Calculation:

ChemWell analyzer automatically calculates the analytic concentration of each sample.

3.4.4. Estimation of high density lipoprotein cholesterol (HDL-C):

Test principle

Lipoproteins are particles comprising a mixture of lipids, phospholipids and apoproteins. There are four distinct groups of lipoproteins: chylomicron, very low density lipoproteins (VLDL), low density lipoproteins (LDL) and high density lipoproteins (HDL).

HDL cholesterol-AUTO Reagent, separation of the lipoprotein fractions is achieved by adding antibodies, which adsorb to the surface of the chylomicrons, VLDL and LDL. In a second step, adding detergent breaks up the HDL lipoproteins, and therefore making HDL cholesterol available for quantification, using the following enzymatic system.

LDL, VLDL and Chylomicrons $\xrightarrow{\text{Anti-human β lipoprotein antibodies}}$ Antigen-Antibodies complexes + HDL

HDL-cholesterol + H_2O +O_2 $\xrightarrow{\text{Esterase α oxidase}}$ cholesten-3-on +fatty acid + H_2O_2

H_2O_2 + 4-aminoantipyrine + N-Ethyl-N-(2-Hydroxy-3-sulfopropyl)-3,5-Dimethoxy-4-flouroanilline, sodium salt $\xrightarrow{\text{peroxidase}}$ blue coloured complex + H2O

The color intensity of the dye is directly proportional to the HDL-cholesterol concentration. It is determined by measuring the increase in absorbance at 583nm.

Calculation:

ChemWellanalyzer automatically calculates the analytic concentration of each sample.

3.4.5. Estimation of low density lipoprotein- cholesterol (LDL-C):

ChemWellanalyzer automatically calculate the LDL-cholesterol concentration of each sample using the Freidwald's formula.

LDL = (TCHOL – TAG/5)–HDL-C

3.5-Labratory working references:

Total cholesterol level (TC): 65-200 mg/dl

Triglyceride level (TG): 50-200 mg/dl

Low density lipoprotein (LDL) : <100 mg/dl

High density lipoprotein (HDL): 55-110 mg/dl

Very low density lipoprotein (VLDL): 8-25 mg/dl

3.6-Statistical analysis of the data:

Data were fed to the computer using IBM SPSS software package version 20.0.

Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test.

Quantitative data were described using mean and standard deviation for normally distributed data.

For normally distributed data, comparison between two independent population were done using independent t-test

Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

a- Mean value = $\frac{\sum x}{n}$.

Where X = the sum of all observations.

n = the number of observations.

b- The standard deviation S.D. = $\sqrt{\frac{\sum (x - \bar{x})^2}{n-1}}$

Where

$\sum$ (Xi – X)2 = the sum of squares of differences of observations from the mean.

c- Student (Unpaired-sample) “t” test:

It is used during comparison between the means of different sample groups. The "t" is calculated as follows:

$$t = \frac{X_1 - X_2}{\sqrt{\frac{S_1^2}{n_1} + \frac{S_2^2}{n_2}}}$$

Where

X1 = Mean of first group.

X2 = Mean of second group.

S1 = Standard deviation of the first group.

S2 = Standard deviation of the second group.

n1 = Sample size of the first group.

n2 = Sample size of the second group.

d- Chi-Square test:

It tests the association between qualitative nominal variables; it is performed mainly on frequencies. It determines whether the observed frequencies differ significantly from expected frequencies.

$$\text{Computed } X^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

Where E = expected frequency

O = observed frequency

$$E = \frac{\text{Raw total} \times \text{Column total}}{\text{Grand total}}$$

4-Results

This study was carried out on 100 patients diagnosed as rheumatoid arthritis according to Eular/ACR criteria, their lipid profile and other characteristic features assessed as following:

Table (1): Patients characterization.

	Number of Patients	Percent %
Sex		
Male	42	42.0
Female	58	58.0
Age		
< 50	56	56.0
> 50	44	44.0
Range	21-85	
Mean	47.87	
S.D.	14.82	
Hospital		
Al-Hawari H	41	41.0
7th October H	59	59.0
Disease duration		
< 6 months	13	13.0
6-12 months	26	26.0
> 1 year	61	61.0
Disease activity		
Active	51	51.0
Inactive	49	49.0

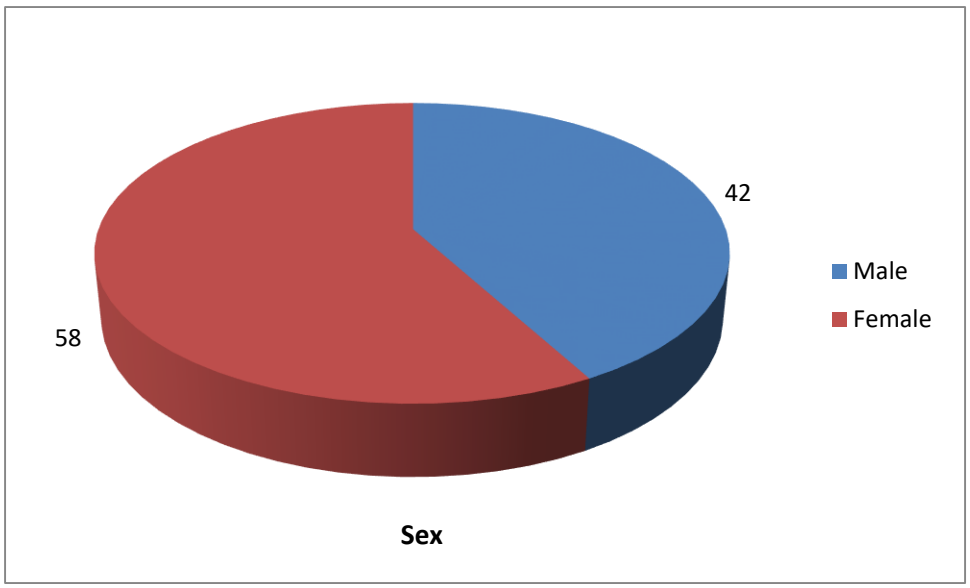


Figure (1a): Gender distribution.

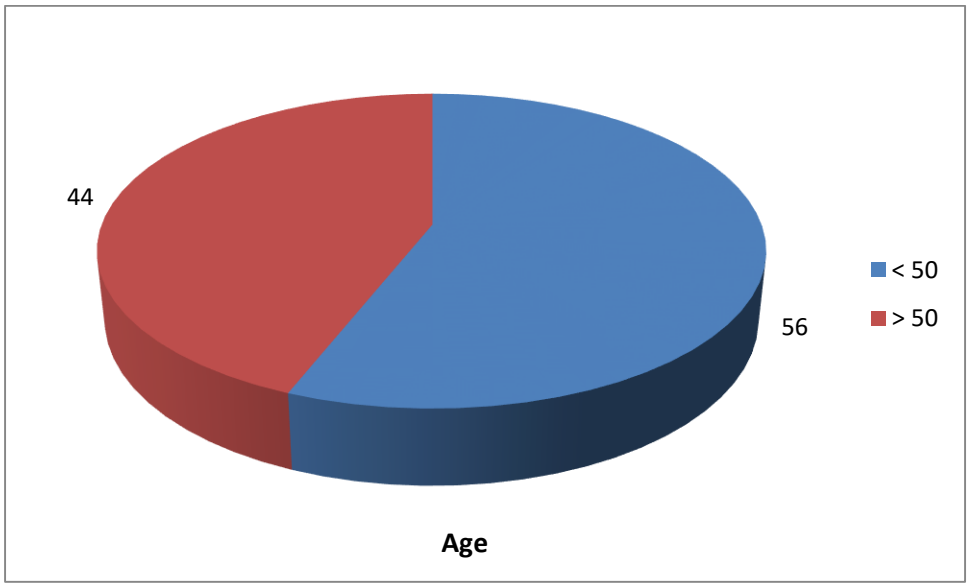


Figure (1b): Age distribution.

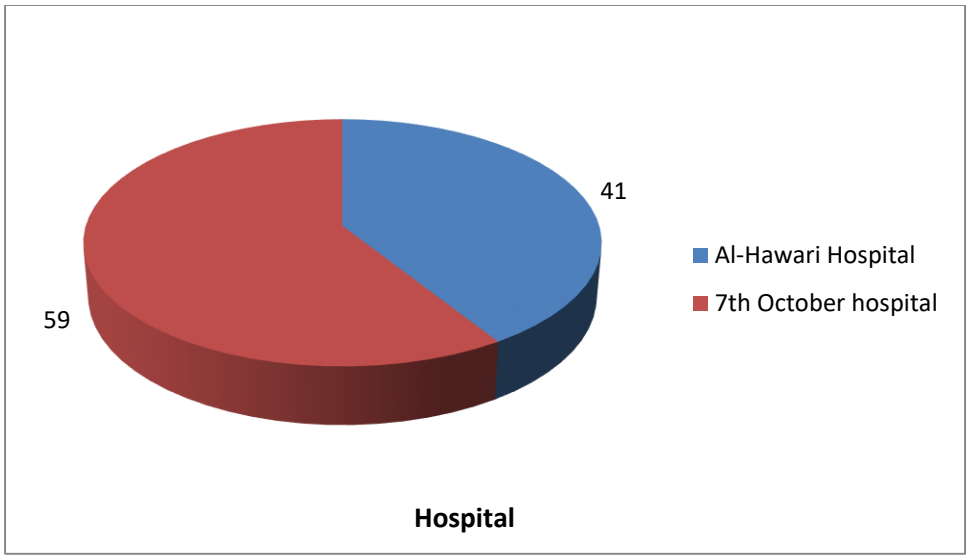


Figure (1c): Hospital distribution.

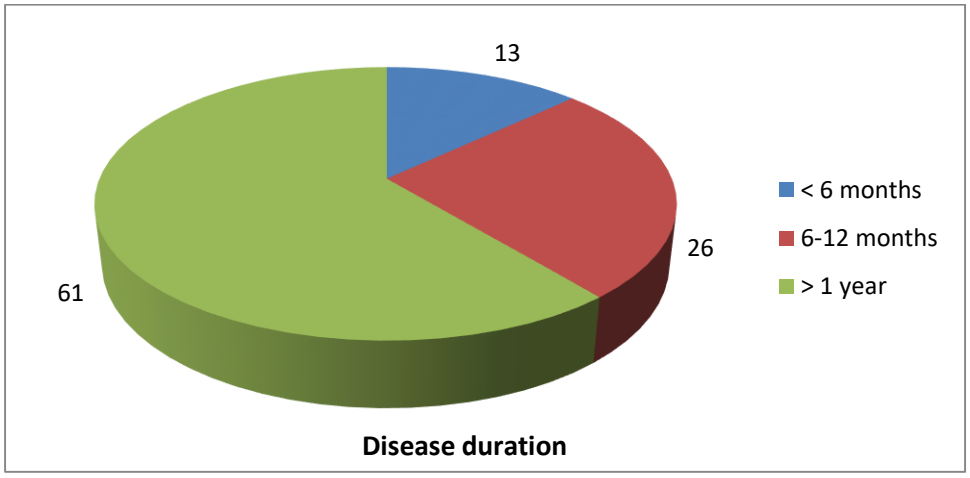


Figure (1d): Disease duration.

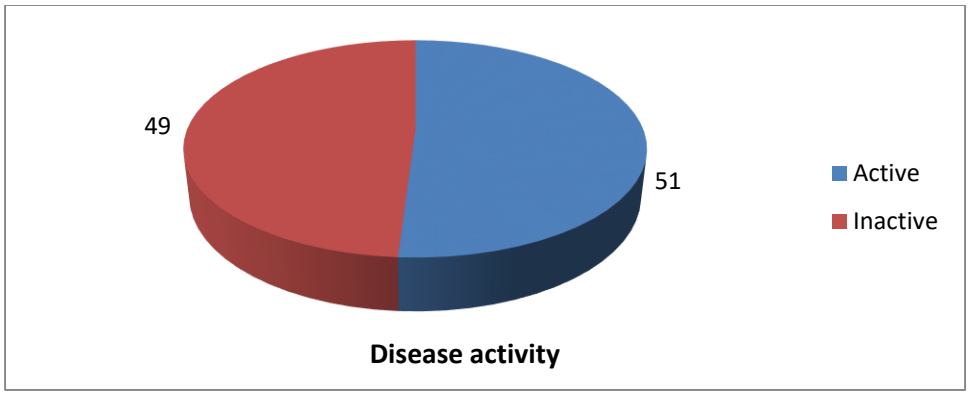


Figure (1e): Disease activity.

4.1. Patients gender: most of our studied patients were female (58%) (Table: 1& Figure:1a).

4.2. Patients age: age Range was 21-85 with Mean (47.87 +_SD 14.82) (Table:1& Figure:1b).

4.3.Duration of the disease: 61% of patients had long disease duration exceeding one year whereas 13% of patients have disease duration less than 6 months (Table:1& Figure:1c).

4.4. Hospital of study: 59 cases were received at 7th October Hospital, while rest of patients were at Al-Hawari Hospital (Table: 1& Figure:1d).

4.5. Disease activity: 51% of our patient's exhibit active mode of rheumatoid arthritis (Table: 1& Figure: 1e).

Table (2): Type of medication in the studied group.

	Number of Patients	Percent %
Methotrexate	87	87
Salazoparine	17	17
Anti-TNF	9	9
Hydrocortisone	54	54
Steroid	15	15

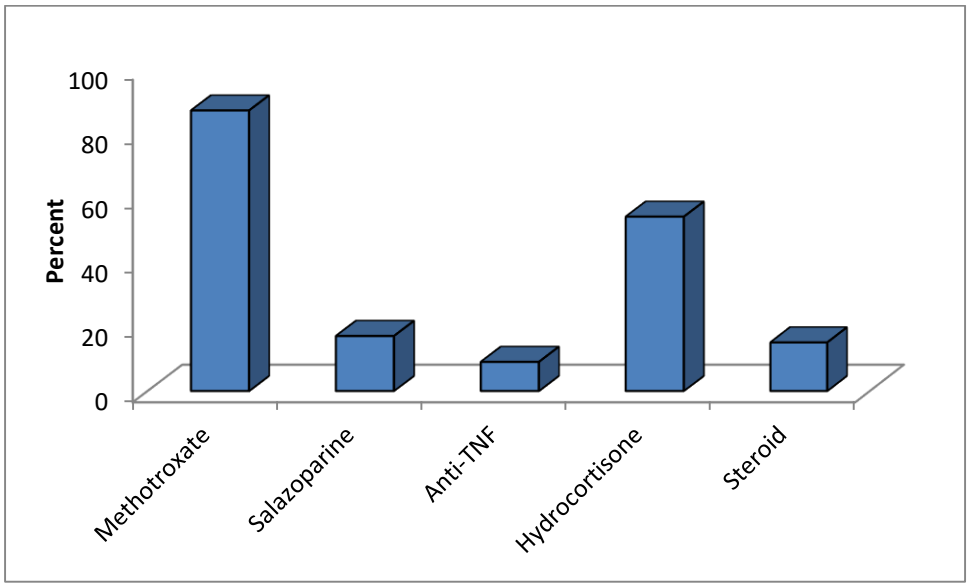


Figure (2): Type of medication in the studied group.

4.6. Type of medication in the studied group: it was found that the majority of the patients were received methotrexate, and the anti-TNF was the minor treatment in all patients (Table: 2& Figure: 2).

Table (3): Distribution of the studied patients regarding dyslipidemia.

Lipid profile	Number of Patients	Percent %
TC	67	67
TG	61	61
LDL	52	52
HDL	63	63
VLDL	84	84

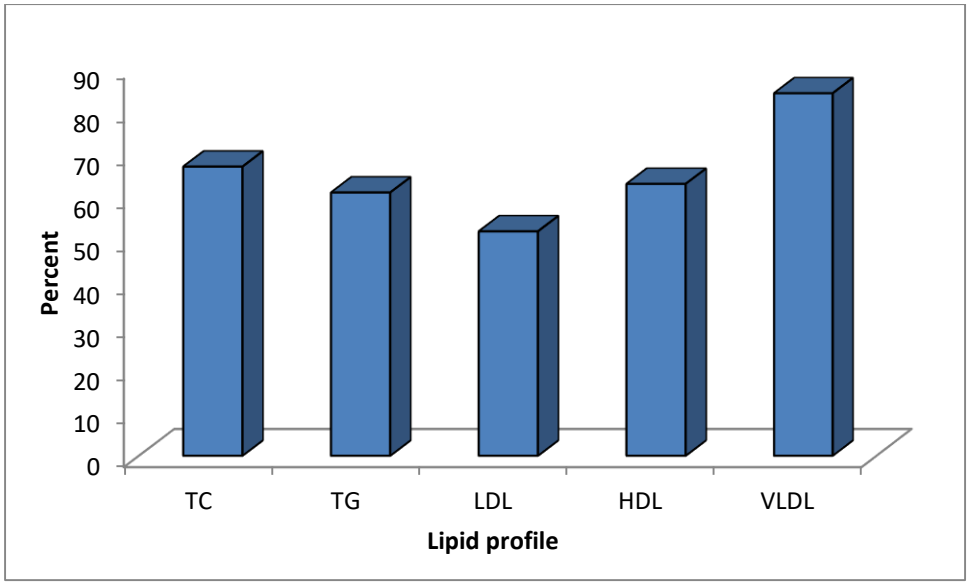


Figure (3): Distribution of the studied patients regarding dyslipidemia.

4.7. Distribution of the studied patients regarding dyslipidemia: it was found that the most frequent dyslipidemia was noticed in VLDL, the majority of the patients had at least one lipid out of range (Table: 3& Figure: 3).

Table (4):Distribution of the studied patients regarding the number of lipoproteins.

Number of lipoproteins	Number of patients	Percent %
No dyslipidemia	4	4
Only one lipoprotein	8	8
Two lipoproteins	16	16
Three lipoproteins	28	28
Four lipoproteins	17	17
All lipoproteins	27	27

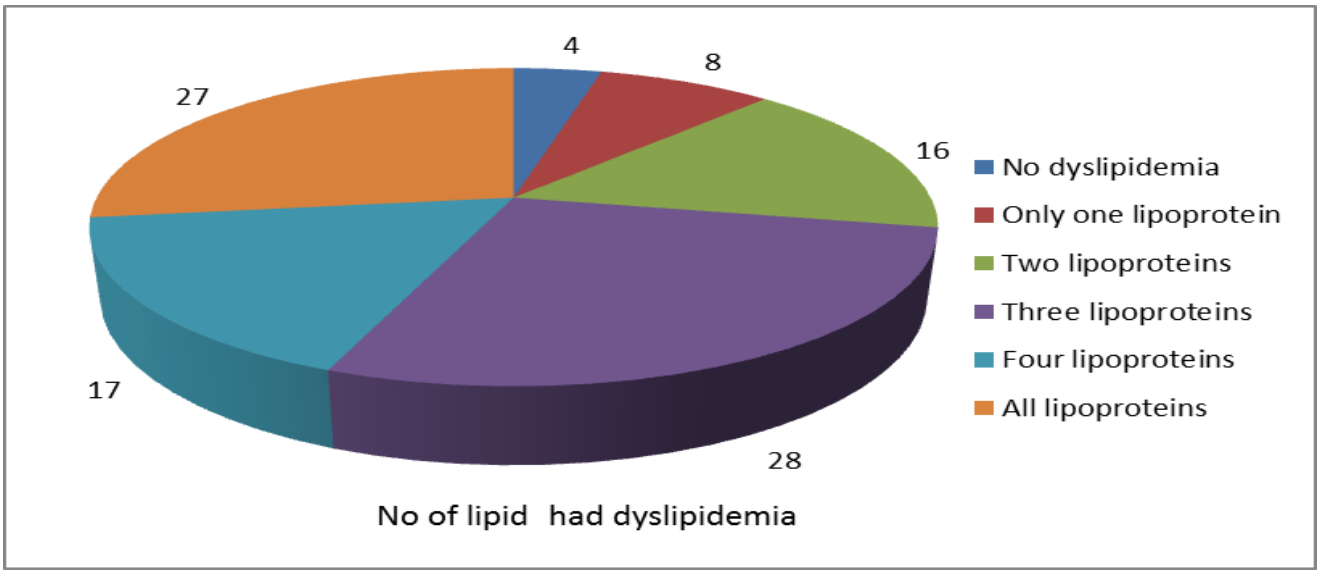


Figure (4): Distribution of the studied patients regarding the number of dyslipidemia.

4.8. Distribution of the studied patients regarding the number of dyslipidemia: it was found that there were only 4 patients had no dyslipidemia, while the 96 % of the patients had dyslipidemia, the majority had three lipoproteins show dyslipidemia (28 %)(Table: 4&Figure: 4).

Table (5): Relation between disease duration and lipid profile.

	< 6 months		6-12 months		> 1 year		p
	No.	%	No.	%	No.	%	
TC	2	15.4	6	23.1	59	96.7	0.001*
TG	3	23.1	7	26.9	51	83.6	0.0032*
LDL	2	15.4	8	30.8	42	68.9	0.013*
HDL	3	23.1	12	46.2	48	78.7	0.0027*
VLDL	7	53.8	20	76.9	57	93.4	0.001*
Total	13		26		61		

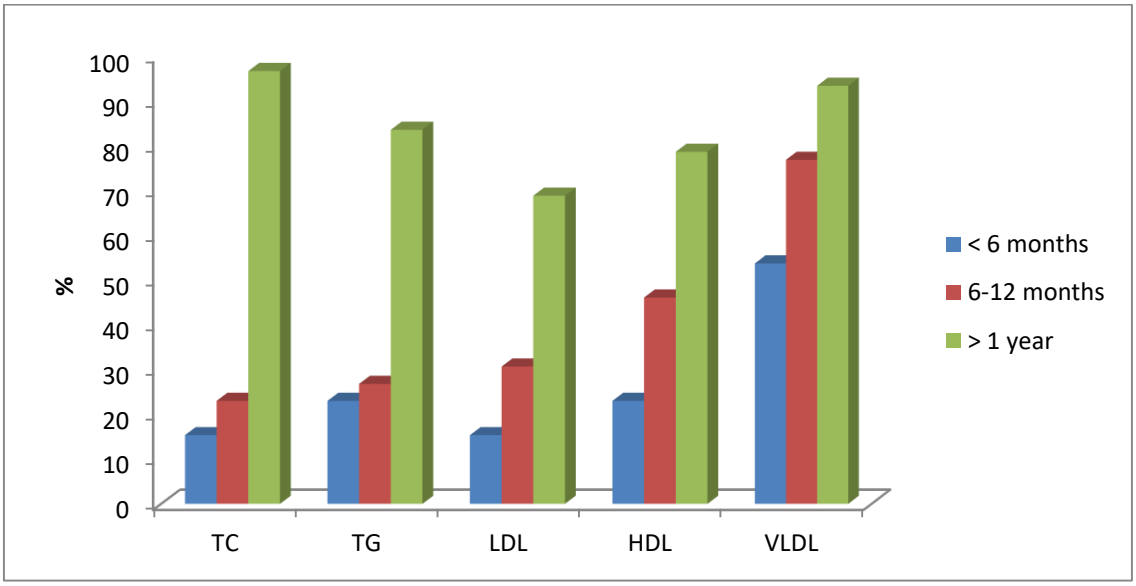


Figure (5): Relation between disease duration and lipid profile.

4.9. Relation between disease duration and lipid profile: it was found that there was a significant relation between duration of disease and the increase in the dyslipidemia. i.e. the long duration of disease show a high dyslipidemia level (Table:5& Figure:5).

Table (6): Relation between disease activity and lipid profile.

	Active		Inactive		p
	No.	%	No.	%	
TC	42	82.4	25	51.0	0.011*
TG	40	78.4	21	42.9	0.031*
LDL	39	76.5	13	26.5	0.001*
HDL	46	90.2	17	34.7	0.016*
VLDL	50	98.0	34	69.4	0.041*
Total	51		49		

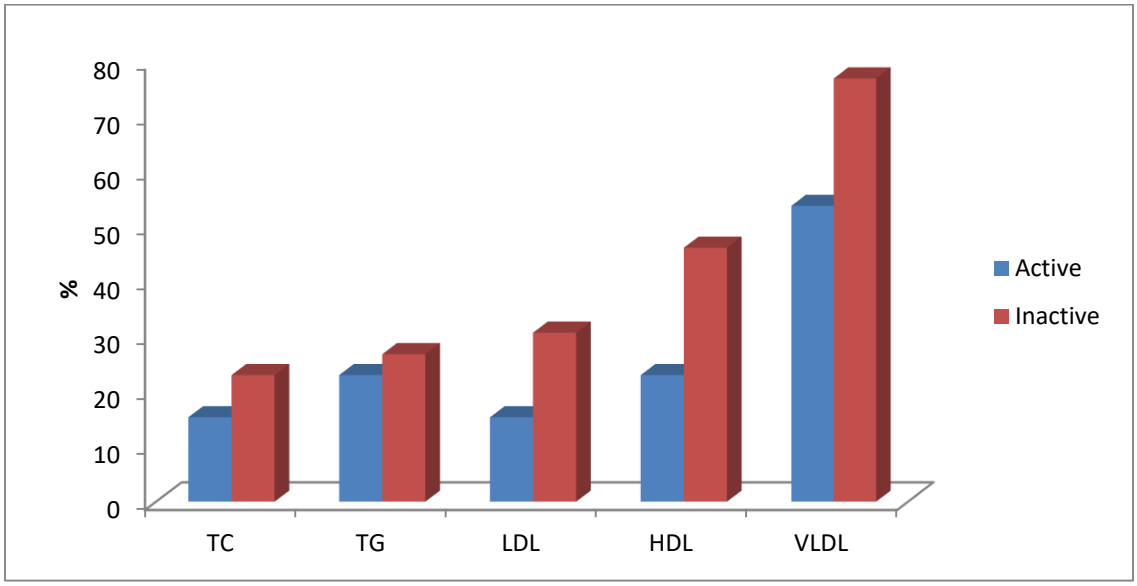


Figure (6): Relation between disease activity and lipid profile.

4.10. Relation between disease activity and lipid profile: we found a significant relation between the activity of disease and the increase in dyslipidemia, in active patients the dyslipidemia was significant higher than the inactive patients (Table: 6 & Figure: 6).

Table (7): Relation between sex and lipid profile.

	Male		Female		p
	No.	%	No.	%	
TC	32	62.7	35	71.4	0.089
TG	28	54.9	33	67.3	0.107
LDL	26	51.0	26	53.1	0.69
HDL	31	60.8	32	65.3	0.52
VLDL	40	78.4	44	89.8	0.33
Total	42		58		

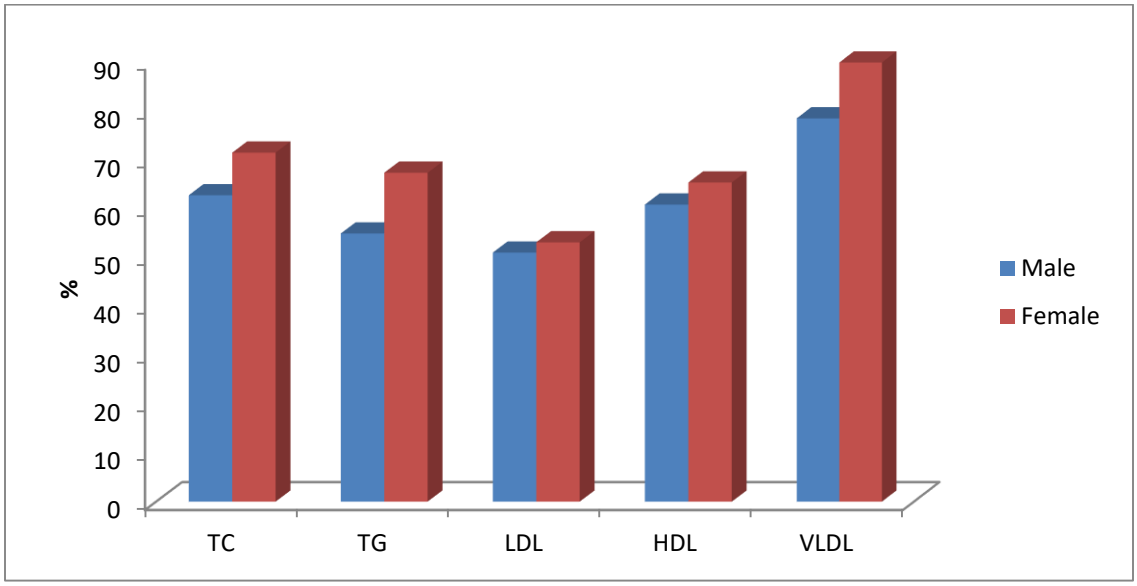


Figure (7): Relation between sex and lipid profile.

4.11. Relation between sex and lipid profile: it was found that the gender has no effect on the incidence of dyslipidemia, although the dyslipidemia was slightly higher in females than males but this increase was insignificant, (Table:7 & Figure:7).

Table (8): Relation between age and lipid profile.

	< 50 years		> 50 years		p
	No.	%	No.	%	
TC	28	54.9	39	79.6	0.023*
TG	22	43.1	39	79.6	0.017*
LDL	18	35.3	34	69.4	0.0036*
HDL	22	43.1	41	83.7	0.0021*
VLDL	43	84.3	41	83.7	0.698
Total	44		56		

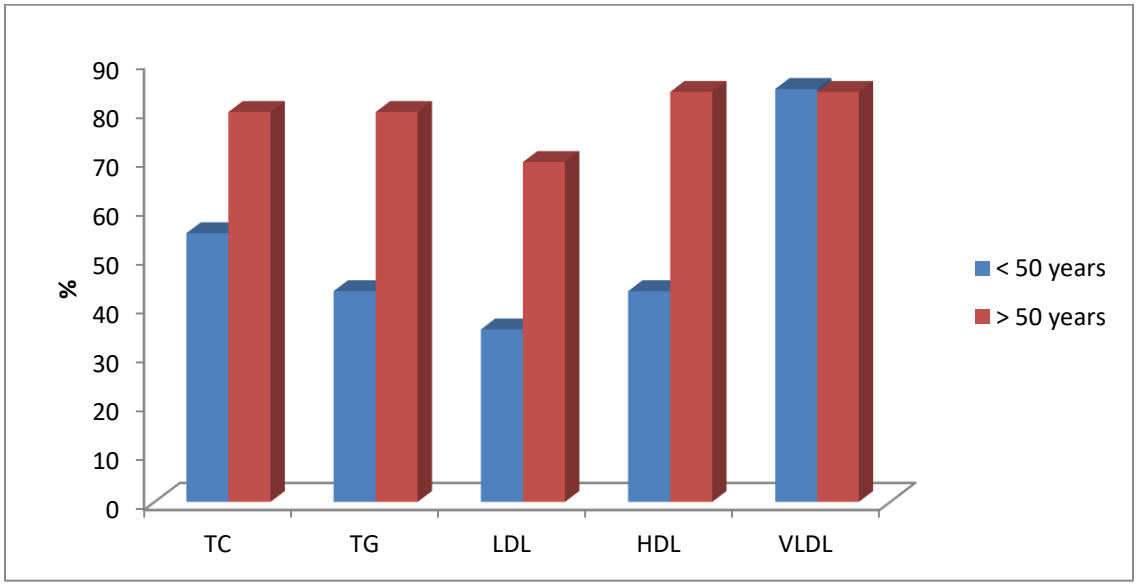


Figure (8): Relation between age and lipid profile.

4.12. Relation between age and lipid profile: it was found that the dyslipidemia was higher significant in old age patients than the young age (Table: 8 & Figure: 8).

Table (9): Relation between type of treatment and lipid profile.

	Methotrexate		**Salazoparine**		**Anti-TNF**		**Hydro-cortisone**		**Steroid**		p
	No.	%	No.	%	No.	%	No.	%	No.	%	
TC	42	48.3	6	35.3	2	22.2	10	18.5	7	46.7	0.013*
TG	50	57.5	1	5.9	0	0.0	7	13.0	3	20.0	0.021*
LDL	28	32.2	6	35.3	3	33.3	15	27.8	0	0.0	0.033*
HDL	40	46.0	4	23.5	2	22.2	11	20.4	6	40.0	0.098
VLDL	52	59.8	10	58.8	6	66.7	7	13.0	9	60.0	0.214
Total	87		17		9		54		15		

4.13. Relation between type of treatment and lipid profile: it was found that the methotrexate showed a significant increase in dyslipidemia than the other treatments (Table: 9).

5-Discussion

Patients with rheumatoid arthritis (RA) have higher rates of morbidity and mortality than the general population, which is highly attributed to an increased risk of cardiovascular disease (CVD) among RA patients [Maradit et al, 2005; Nicola et al, 2005]. The increased risk of CVD appears to be linked to coronary atherosclerosis [Full et al, 2009], [Gabriel et al, 2010] and may be directly caused by chronic inflammation or secondarily caused by physical inactivity and drugs used to treat RA [Turesson et al, 2008]. Not surprisingly, RA treatment guidelines reflect this increased CV risk among RA patients. Evidence-based and expert-opinion based recommendations from the European League Against Rheumatism (EULAR) for the screening and management of RA patients include annual CV risk assessment, management of identified CV risk factors, and aggressive suppression of the inflammatory process to further lower the CV risk [Peters et al, 2010].

Lipid levels appear to be altered as a result of RA disease activity. Data on total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels in RA patients are conflicting: some studies demonstrate similar [Park et al, 1999] or lower [Boers et al, 2003] levels of TC, while others demonstrate increased levels of TC and LDL-C in patients with early RA [Georgiadis et al, 2006]. Although reports on lipid profiles in RA patients vary, growing evidence suggests that patients with active untreated RA have reduced total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels [Georgiadis et al, 2006], [Choy, 2009], [Myasoedova et al, 2011]. Regardless of the TC changes in RA patients, with a decrease in HDL-C, several studies support the notion that RA leads to a more atherogenic lipid profile (TC to HDL-C ratio) which is correlated with disease activity and improves after treatment with antirheumatic medications [Park et al, 1999; Boers et al, 2003; Georgiadis et al, 2006; Van Halm et al, 2007].

Inflammation is a common denominator in both RA and atherosclerosis. A growing body of evidence supports the involvement of common pro-inflammatory cytokines, such as macrophage migration inhibitory factor (MIF), interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α) in the development and progression of both RA and atherosclerosis [Full et al, 2009; Di Micco et al, 2009]. Several studies have demonstrated that the use of disease-modifying anti-rheumatic drugs (DMARDs) and biologic agents that affect these cytokines reduce

inflammation in RA patients and may be associated with a reduced risk of CVD [Van Halm et al, 2007; Choi et al, 2002; Del Porto et al, 2007; Naranjo et al, 2008; Wijbrandts et al, 2009; Dixon et al, 2007; Listing et al, 2008; Reiss et al, 2008].

Given that inflammation in RA patients alters the lipid profile, it is not surprising that treatment to control inflammation in RA patients may affect also lipid levels. A recent meta-analysis of 24 observational studies evaluating the effect of TNF therapy on lipids in RA patients showed a small trend in an increase in TC, mostly due to an increase in HDL-C levels [Pollono et al, 2010].

In this study, the majority of the patients were on methotrexate therapy, and the anti-TNF was the treatment in minority of patients. The most frequent dyslipidemia was noticed in VLDL, and the majority of the patients had at least one lipoprotein out of normal range. Only 4 patients had no dyslipidemia, while the 96% of the patients had at least one dyslipidemia. There was a significant relation between duration of disease and the dyslipidemia, the longer the duration of disease the higher is the dyslipidemia level. Regarding relation between disease activity and dyslipidemia, there was a significant relation between the activity of disease and the increase in dyslipidemia and patients with active disease had higher dyslipidemia than patients with inactive disease. The dyslipidemia was higher in old age patients than the young age. Regarding type of treatment, methotrexate showed a significant increase in dyslipidemia than the other treatments used in this study.

It has been shown in previous studies that patients with RA had mean TC, LDL-C, and TG levels that were lower than osteoarthritis (OA) patients. Although RA patients were slightly more likely to be in a favorable ATP-III category, approximately 25% of RA patients had suboptimal lipid levels based on current ATP-III guidelines [3rd report NCEP]. Among RA patients initiating TNFi therapy and who had their TC and LDL-C re-tested within three months, mean TC and LDL-C increased 5 and 4 mg/dl after TNFi therapy was initiated.

Jeffrey et al., (2012) observed that while RA patients were only slightly less likely to receive any lipid testing than OA patients, approximately one-third of RA patients did not receive any testing during the observation period of more than 2 years.

Among RA patients not receiving lipid-lowering medications, Jeffrey et al., (2012) observed that treatment with TNFi was associated with modest increases in TC and LDL-C

levels. This is consistent with results from other studies that observed increases in lipid levels after treatment with biological agents.

In a recent meta-analysis of 24 observational studies evaluating the effect of TNFi therapy on lipids in RA patients, a small trend of an increase in TC was observed [Pollono et al, 2010]. Of the four controlled studies which measured the atherogenic index, one study found a significant increase of 8.9% in the TNFi therapy group and a significant decrease of 10.4% in the control group [Dahlqvist et al, 2006] , two studies reported non-significant decreases in the TNFi group with no changes in the control groups [Seriolo et al, 2007], [Seriolo et al, 2009] , and one study reported a significant decrease in cases compared to controls, but data were not provided [Popa et al, 2005].

In our study, we found changes in lipid profiles among RA patients who were treated with TNFi therapy. However, our results could not be compared with the meta-analysis since no similar sub-group analysis of lipid level changes among patients using lipid-lowering medication treatments was performed [Pollono et al, 2010].

Aside from TNFi, other biologic agents have been shown to affect lipid profiles. Tocilizumab (TCZ), which inhibits the pro-inflammatory cytokine interleukin-6 (IL-6) binding to its receptors,[Mihara et al, 2005] is associated with decreases in inflammatory markers [Genovese et al, 2008]. TCZ is associated with increased lipid levels in RA patients (e.g. an increase in LDL of 20 mg/dl among TCZ+MTX users), but has not been associated with an increase in CV events during short-term follow-up [Maini et al, 2006; Nishimoto et al, 2007; Van Vollenhoven et al, 2009; Van Vollenhoven et al, 2010].

In a recently completed long-term follow-up study of TCZ in RA patients (mean treatment duration of 2.4 years), TC, HDL-C, LDL-C, and TG levels increased after 6 weeks of treatment and remained relatively stable at the elevated level thereafter [van Vollenhoven et al, 2009; van Vollenhoven et al, 2010].

The clinical importance of lipid levels on CVD risk in RA is not completely understood. Recent evidence suggests that there may be a paradoxical effect of lipids on the risk of CVD in RA, where lower and not higher TC and LDL-C levels are associated with increased cardiovascular risk [Myasoedova et al, 2011].

Furthermore, although HDL-C is generally considered to be cardio-protective, both through its ability to promote cholesterol efflux from artery cell walls and anti-inflammatory

properties which protect LDL-C from oxidation. A growing body of evidence suggests that in inflammatory conditions such as RA and systemic lupus erythematosus, patients have non-protective "pro-inflammatory HDL" (piHDL) which promotes accumulation of oxidized phospholipids in LDL-C [Charles-Schoeman et al, 2009; Hahn et al, 2008].

Based upon what appears to be more favorable TC and LDL-C distributions in RA patients compared to OA patients, the results of this analysis suggested that lipid profiles in RA patients only partially explain the previously-observed excess CVD risk associated with the systemic inflammation of RA [Dessein et al, 2002]. Other inflammation-induced factors, such as increased oxidative stress, insulin resistance, endothelial dysfunction, pro-thrombotic state, and elevated homocysteine levels,[Ku et al, 2009] as well as non-inflammatory mechanisms, such as genetic polymorphism and CV toxicity associated with certain anti-rheumatic drugs (e.g., glucocorticoids) may also contribute to the increased CVD risk in RA[Ku et al, 2009].

6-Conclusion

Dyslipidemias are disorders of lipoprotein metabolism, including lipoprotein overproduction and deficiency. They may manifest as one or more of the following: elevated total cholesterol, low-density lipoprotein cholesterol (LDL), and triglyceride levels or as decreased high-density lipoprotein cholesterol (HDL) level. Dyslipidemia is closely associated with atherosclerosis and is a major causal factor in the development of ischemic diseases. Ischemic cardiovascular and cerebrovascular events are leading causes of morbidity and mortality.

In this study we aimed to evaluate lipid profile changes as well as the effect of treatment in rheumatoid arthritis patients. This study was carried out on 100 patients diagnosed as rheumatoid arthritis according to Eular/ACR criteria.

Our study revealed the following results:

- The majority of the patients were treated with methotrexate, and the anti-TNF was the minor treatment in all patients.
- The most frequent dyslipidemia was noticed in VLDL, the majority of the patients had at least one lipoprotein out of range.

- There were only 4 patients had no dyslipidemia, while the 96 % of the patients had at least one dyslipidemia. Therefore, the majority had three lipoproteins in which they showed dyslipidemia (28 %).

- There was a significant relation between duration of disease and the increase in the dyslipidemia i.e. the long duration of disease showed a high dyslipidemia levels.
- Regarding relation between disease activity and dyslipidemia, we noticed a significant relation between the activity of disease and the increase in dyslipidemia, in active patients the dyslipidemia was highly significant compared to the inactive patients.
- Relation between sex and dyslipidemia, we found that the gender has no effect on the incidence of dyslipidemia, although the dyslipidemia was slightly higher in male than females but this increase was non-significant.
- The dyslipidemia was highly significant in old age patients than young aged ones.

- We noticed in present study that the methotrexate revealed a significant increase in dyslipidemia compared with other treatments.

7-References

Anaya JM , Diethelm L, Ortiz LA. Pulmonary involvement in rheumatoid arthritis. Semin Arthritis Rheum. 1995; 24(4):242-54.

Avi̊a-Zubieta JA Hyon K. Choi, Mohsen Sadatsafavi, Mahyar Etminan, John M. Esdaile, Diane Lacaille. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum. 2008; 59:1690.

Balsamo S Diniz LR,Dos santos-Neto LL, Da mota LM . Exercise and fatigue in rheumatoid arthritis. Isr Med Assoc J.2014; 16(1):57-60.

Barter PJ: Hugh Sinclair Lecture: the regulation and remodeling of HDL by plasma factors, atheroscler Suppl 2002, 3:39-47.

Bongartz T , Carlotta Nannini, Yimy F. Medina-Velasquez, Sara J. Achenbach, Cynthia S. Crowson, Jay H. Ryu, Robert Vassallo, Sherine E. Gabriel, Eric L. Matteson. Incidence and mortality of interstitial lung disease in rheumatoid arthritis: a population-based study, Arthritis Rheum. 2010; 62(6): 1583–91.

Boers M, Nurmohamed MT, Doelman CJ, Lard LR, Verhoeven AC, Voskuyl AE, Huizinga TW, van de Stadt RJ, Dijkmans BA, van der Linden S. Influence of glucocorticoids and disease activity on total and high density lipoprotein cholesterol in patients with rheumatoid arthritis. Ann Rheum Dis. 2003; 62(9):842–845.

Boers M, Nurmohamed MT, Doelman CJ, Lard LR, Verhoeven AC, Voskuyl AE, Huizinga TW, van de Stadt RJ, Dijkmans BA, van der Linden S: Influence of glucocorticoid and disease activity on total and high density lipoprotein cholesterol in patients with rheumatoid arthritis. Ann Rheum Dis 2003, 62:842-845.

Bozena Targonska-Stepniak, Maria Majdan, Magdalena Dryglewska. Leptin serum levels in rheumatoid arthritis pateints: relation to disease duration and activity. Rheumatology International .April 2008, Volume 28, Issue 6, pp 585–591

Breedveld FC , MD ; Wim E. Fibbe, MD ; Jo Hermans, PhD . Factors influencing the incidence of infections in Felty's syndrome. Arch Intern Med. 1987; 147: 915–20.

Caballol Pons N, Núria Montalà, José Valverde, Marta Brell, Isidre Ferrer, Sergio Martínez-Yélamos. Isolated cerebral vasculitis associated with rheumatoid arthritis. Joint Bone Spine 2010; 77(4):361–3.

Calin Popa, Mihai G. Netea, Jacqueline de Graaf, Frank H.J. van den Hoogen, Tiomthy R.D.J. Radstake, Helga Toenhake-Dijkstra, Piet L.C.M. van Riel, Jos W.M. van der Meer, Anton F.H.

Stalenhoef and Pilar Barrera. Circulating Leptin and Adiponectin Concentrations during Tumor Necrosis Factor Blockade in Patients with Active Rheumatoid Arthritis.the journal of rheumatology. September 2016, 43 (9)

Campion G, PG Madisson, N Gouldeng, I James . The Felty syndrome: a case-matched study of clinical manifestations and outcome, serologic features, and immunogenic associations. Medicine. 1990; 69:69–80.

Castelli WP, Garrison RJ, Wilson PW, Abbott RD, Kalousdian S, Kannel WB: Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham study. JAMA 1986, 256:2835-2838.

Choi HK, Hernan MA, Seeger JD, Robins JM, Wolfe F. Methotrexate and mortality in patients with rheumatoid arthritis: a prospective study. Lancet. 2002; 359(9313):1173–1177.

Choy E, Sattar N. Interpreting lipid levels in the context of high-grade inflammatory states with a focus on rheumatoid arthritis: a challenge to conventional cardiovascular risk actions. Ann Rheum Dis. 2009; 68(4):460–469.

Charles-Schoeman C, Watanabe J, Lee YY, Furst DE, Amjadi S, Elashoff D, Park G, McMahon M, Paulus HE, Fogelman AM, et al. Abnormal function of high-density lipoprotein is associated with poor disease control and an altered protein cargo in rheumatoid arthritis. Arthritis Rheum. 2009; 60(10):2870–2879.

Chen J, YH Shi, XP Wang, H Huang. Asymptomatic preclinical rheumatoid arthritis-associated interstitial lung disease. Clin Dev Immunol. 2013;2013:406927.

Cunnane G, Martha Warnock, Kenneth H, Fye, David I.Daikh . Accelerated nodulosis and vasculitis following Etanercept therapy for rheumatoid arthritis. Arthritis Rheum. 2002; 47(4):445–9.

Cui Y, Blumenthal RS, Flaws JA, Whiteman MK, Langenberg P, Bachorik PS, Bush TL: Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. Arch Intern Med 2001, 161:1413-1419.

Dahlqvist SR, Engstrand S, Berglin E, Johnson O. Conversion towards an atherogenic lipid profile in rheumatoid arthritis patients during long-term infliximab therapy. Scand J Rheumatol. 2006; 35(2):107–111.

Dessein PH, Stanwix AE, Joffe BI. Cardiovascular risk in rheumatoid arthritis versus osteoarthritis: acute phase response related decreased insulin sensitivity and high-density lipoprotein cholesterol as well as clustering of metabolic syndrome features in rheumatoid arthritis. Arthritis Res. 2002; 4(5):R5.

Del Porto F, Lagana B, Lai S, Nofroni I, Tinti F, Vitale M, Podesta E, Mitterhofer AP, D' Amelio R. Response to anti-tumour necrosis factor alpha blockade is associated with reduction of carotid intima-media thickness in patients with active rheumatoid arthritis. Rheumatology (Oxford) 2007; 46(7):1111–1115.

Del Rincon ID, Ken Williams, Micheal P .Stern, Gregory L .Freeman, Augustin Escalant . High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. Arthritis Rheum. 2001; 44:2737–45.

Dessein PH, BI Joffe, MG Veller, BA Stevens. Traditional and nontraditional cardiovascular risk factors are associated with atherosclerosis in rheumatoid arthritis.J Rheumatol.2005; 32:435-42.

Devouassoux G, V Cottin, H Liote. Characterisation of severe obliterative bronchiolitis in rheumatoid arthritis. Eur Respir J. 2009; 33: 1053–61.

Di Micco P, Ferrazzi P, Libre L, Mendolicchio L, Quaglia I, De Marco M, Colombo A, Bacci M, Rota LL, Lodigiani C. Intima-media thickness evolution after treatment with infliximab in patients with rheumatoid arthritis. Int J Gen Med. 2009;2:141–144.

Dixon WG, Watson KD, Lunt M, Hyrich KL, Silman AJ, Symmons DP. Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor alpha therapy: results from the British Society for Rheumatology Biologics Register. Arthritis Rheum. 2007; 56(9):2905–2912.

Douglas W, Sayed F, Alan D: Newzeland Med jour, 2006, 2006, 119(1240), 1-4.

Forrester SJ, Makkar R, Shah PK: Increasing high-density lipoprotein cholesterol in dyslipidemia by cholesteryl ester transfer protein inhibition. An update for clinicians. Circulation 2005, 111:1847-1854.

Full LE, Ruisanchez C, Monaco C. The inextricable link between atherosclerosis and prototypical inflammatory diseases rheumatoid arthritis and systemic lupus erythematosus. Arthritis Res Ther. 2009; 11(2):217.

Gabriel SE, CS Crowson, Hilal Haradite, Michele F Doran, Carl Toresson. Survival in rheumatoid arthritis: a population-based analysis of trends over 40 years. Arthritis Rheum.2003; 48(1):54–8.

Gabriel SE, Crowson CS, Kremers HM, Doran MF, Turesson C, O'Fallen WM, Matteson EL: Survival in rheumatoid arthritis: apopulation-based analysis of trends over 40 years. ArthritisRheum 2003, 48:54-58.

Gabriel SE. Heart disease and rheumatoid arthritis: understanding the risks. Ann Rheum Dis. 2010; 69(Suppl 1):i61–64. [PMC free article]

Georgiadis AN, Papavasiliou EC, Lourida ES, Alamanos Y, Kostara C, Tselepis AD, Drosos AA. Atherogenic lipid profile is a feature characteristic of patients with early rheumatoid arthritis: effect of early treatment--a prospective, controlled study. Arthritis Res Ther. 2006; 8(3):R82.

Genovese M, Smolen J, Emery P, Jones G, Lee J, Alecock E, Kremer J. Lipid and inflammatory biomarker profiles in patients receiving tocilizumab for rheumatoid arthritis: analysis of five phase 3 clinical trials. Arthritis & Rheumatism. 2008; 58(9):S531–S532.

Gizinski AM, M Mascolo, JL Louckes, A Kervitsky. Rheumatoid arthritis (RA)-specific autoantibodies in patients with interstitial lung disease and absence of clinically apparent articular RA. Clin Rheumatol. 2009; 28(5):611–3

Goodson N: Coronary artery disease and rheumatoid arthritis. Curr Opin Rheumatol 2002, 14:115-120.

Goodson NJ, Symmons DP, Scott DG et al: arthritis Rheum, 2005, 52, 2293-9.

Gonzalez-Gay MA, Carlos Gonzalez-Jaunatey, Maria J,Lopeze Diaze,Angela Pineiro . HLA–DRB1 and persistent chronic inflammation contribute to cardiovascular events and cardiovascular mortality in patients with rheumatoid arthritis. Arthritis Rheum. 2007; 57:125–32.

Hahn BH, Grossman J, Ansell BJ, Skaggs BJ, McMahon M. Altered lipoprotein metabolism in chronic inflammatory states: proinflammatory high-density lipoprotein and accelerated atherosclerosis in systemic lupus erythematosus and rheumatoid arthritis. Arthritis Res Ther. 2008; 10(4):213.

Hansel B, Bruckert E: Lipid profile and cardiovascular risk in patients with rheumatoid arthritis: effect of the disease and of drug therapy) Service d'endocrinologie-métabolisme et de prévention cardiovasculaire, hôpital de la Pitié-Salpêtrière, 2008, 47-83, boulevard de l'Hôpital, 75013 Paris, France.

Helin HJ, Markku M. Korpela MD, Jukka T.Mustoneen MD, Amos I Pasternack MD. Renal biopsy findings and clinicopathologic correlations in rheumatoid arthritis. Arthritis Rheum. 1995; 38:242–7.

HY, Chen DY, Lan JL, Chiang EP: Int J Epidemoiol, 2007, 36, 666-76.

Kelly C, Hamilton J. What kills patients with rheumatoid arthritis? Rheumatology (Oxford). 2007; 46(2):183–4.

Ku IA, Imboden JB, Hsue PY, Ganz P. Rheumatoid arthritis: model of systemic inflammation driving atherosclerosis. Circ J. 2009; 73(6):977–985.

Lachmann HJ, HJB Goodman. Natural history and outcome in systemic AA amyloidosis. N Engl J Med. 2007; 356(23):2361-71.

Lake F, Proudman S. Rheumatoid arthritis and lung disease: from mechanisms to a practical approach. Semin Respir Crit Care Med. 2014; 35: 222–38.

Lazarevic MB, Vitic J, Mladenovic V, Myones BL, Skosey JL, Swedler WI: Dyslipoproteinemia in the course of active rheumatoid arthritis. Semin Arthritis Rheum 1992, 22:172-178.

Lee HK,DS Kim, B Yoo, JB Seo. Histopathologic pattern and clinical features of rheumatoid arthritis-associated interstitial lung disease. Chest. 2005; 127(6):2019–27.

Lioté H. [Pulmonary manifestation of rheumatoid arthritis]. Rev Mal Respir. 2008;25(8):973-88.

Listing J, Strangfeld A, Kekow J, Schneider M, Kapelle A, Wassenberg S, Zink A. Does tumor necrosis factor alpha inhibition promote or prevent heart failure in patients with rheumatoid arthritis? Arthritis Rheum. 2008; 58(3):667–677.

Maradit-Kremers H, Crowson CS, Nicola PJ, Ballman KV, Roger VL, Jacobsen SJ, Gabriel SE. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population-based cohort study. Arthritis Rheum. 2005; 52(2):402–411.

Maini RN, Taylor PC, Szechinski J, Pavelka K, Broll J, Balint G, Emery P, Raemen F, Petersen J, Smolen J, et al. Double-blind randomized controlled clinical trial of the interleukin-6 receptor antagonist, tocilizumab, in European patients with rheumatoid arthritis who had an incomplete response to methotrexate. Arthritis Rheum. 2006; 54(9):2817–2829.

Misato Hashizume, Masahiko Mihara, IL-6 and lipid metabolism, mini review, Inflammation and Regeneration Vol .3 1 N o.3 May 2011.

Mihara M, Kasutani K, Okazaki M, Nakamura A, Kawai S, Sugimoto M, Matsumoto Y, Ohsugi Y. Tocilizumab inhibits signal transduction mediated by both mIL-6R and sIL-6R, but not by the receptors of other members of IL-6 cytokine family. Int Immunopharmacol. 2005; 5(12):1731–1740.

Mielants H, Van den Bosch F. Extraarticular manifestations. Clin Exp Rheumatol. 2009;27(4 Suppl 55):S56-61.

M Otero, R Lago, R Gomez, F Lago, C Dieguez, J J Gómez-Rein, O Gualillo. Changes in plasma levels of fat-derived hormones adiponectin, leptin, resistin and visfatin in patients with rheumatoid arthritis. Ann Rheum Dis 2006; 65:1198-1201 doi:10.1136/ard.2005.046540

Myasoedova E, Crowson CS, Kremers HM, Roger VL, Fitz-Gibbon PD, Therneau TM, Gabriel SE. Lipid paradox in rheumatoid arthritis: the impact of serum lipid measures and systemic inflammation on the risk of cardiovascular disease. Ann Rheum Dis. 2011; 70(3):482–487.

Nakano M, M Ueno, S Nishi, H Shimada. Analysis of renal pathology and drug history in 158 Japanese patients with rheumatoid arthritis. Clin Nephrol. 1998;50: 154–60.

Naranjo A, Sokka T, Descalzo MA, Calvo-Alen J, Horslev-Petersen K, Luukkainen RK, Combe B, Burmester GR, Devlin J, Ferraccioli G, et al. Cardiovascular disease in patients with rheumatoid arthritis: results from the QUEST-RA study. Arthritis Res Ther. 2008; 10(2):R30.

Nicola PJ, Maradit-Kremers H, Roger VL, Jacobsen SJ, Crowson CS, Ballman KV, Gabriel SE. The risk of congestive heart failure in rheumatoid arthritis: a population-based study over 46 years. Arthritis Rheum. 2005;52(2):412–420.

Nicola PJ Maradit-Kremers H, Roger VL, Jacobsen SJ, Crowson CS, Ballman KV, Gabriel SE. The risk of congestive heart failure in rheumatoid arthritis: apopulation-based study over 46 years. Arthritis Rheum. 2005;52(2):412–20.

Nishimoto N, Hashimoto J, Miyasaka N, Yamamoto K, Kawai S, Takeuchi T, Murata N, van der Heijde D, Kishimoto T. Study of active controlled monotherapy used for rheumatoid arthritis, an IL-6 inhibitor (SAMURAI): evidence of clinical and radiographic benefit from an x ray reader-blinded randomised controlled trial of tocilizumab. Ann Rheum Dis. 2007;66(9):1162–1167.

Palomar R, O Castaneda, E Rodrigo. [Microscopic polyangiitis in a patient with rheumatoid arthritis.] Nefrologia. 2005;25:438–41.

Park YB, Lee SK, Lee WK, Suh CH, Lee CW, Lee CH, Song CH, Lee J: Lipid profiles in untreated patients with rheumatoid arthritis. J Rheumatol 1999, 26:1701-1704.

Park YB, Lee SK, Lee WK, Suh CH, Lee CW, Lee CH, Song CH, Lee J. Lipid profiles in untreated patients with rheumatoid arthritis. J Rheumatol. 1999;26(8):1701–1704.

Patrick H.dessein, Gavin R.Norton. Angela J.Woodiwiss, Linda Tsang , Ahmed Solomon.Age impacts on the independent relationships of leptin with cardiometabolic risk and surrogate markers of enhanced early atherogensis in black and white patients with rheumatoid arthritis: a cross sectional -study Rheumatology International.March 2014, Volume 34, Issue 3, pp 329–339

Patrick H. Dessein,Gavin R. Norton,Margaret Badenhorst,Angela J. Woodiwiss, and Ahmed Solomon. Rheumatoid Arthritis Impacts on the Independent Relationships between Circulating Adiponectin Concentrations and Cardiovascular Metabolic Risk. Mediators of Inflammation.Volume 2013 (2013), Article ID 461849, 9 pages.

Peters MJ, Symmons DP, McCarey D, Dijkmans BA, Nicola P, Kvien TK, McInnes IB, Haentzschel H, Gonzalez-Gay MA, Provan S, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis. 2010;69(2):325–331.

Pollono EN, Lopez-Olivo MA, Lopez JA, Suarez-Almazor ME. A systematic review of the effect of TNF-alpha antagonists on lipid profiles in patients with rheumatoid arthritis. Clin Rheumatol. 2010;29(9):947–955.

Popa C, Netea MG, Radstake T, Van der Meer JW, Stalenhoef AF, van Riel PL, Barerra P. Influence of anti-tumour necrosis factor therapy on cardiovascular risk factors in patients with active rheumatoid arthritis. Ann Rheum Dis. 2005;64(2):303–305.

Reiss AB, Carsons SE, Anwar K, Rao S, Edelman SD, Zhang H, Fernandez P, Cronstein BN, Chan ES. Atheroprotective effects of methotrexate on reverse cholesterol transport proteins and foam cell transformation in human THP-1 monocyte/macrophages. Arthritis Rheum. 2008;58(12):3675–3683.

Rodriguez-Rodriguez L. TNFA-308 (rs1800629) polymorphism is associated with a higher risk of cardiovascular disease in patients with rheumatoid arthritis. Atherosclerosis. 2011;216:125–30.

Ross R: The pathogenesis of atherosclerosis: a perspective for the 1990s. Nature 1993, 362:801-809.

Sang-Won Lee. Min-Chan park. Yong Beom Park. Soo-Kon Lee. Measurement of the serum leptin level could assist disease activity monitoring in rheumatoid arthritis. Rheumatology International, April 2007, Volume 27, Issue 6, pp 537–540

Sara I, Alexandra N, Janis B: Oxford Jour, Med, Rheum, 2011, 49 (Issu2), 295-307.

Sarzi-Puttini P, F Atzeni, R Gerli, E Bartoloni, A Doria. Cardiac involvement in systemic rheumatic diseases: an update. Autoimmun Rev. 2010;9:849–52.

Satter N, DW McCarey, H Capell, IB McInnes: Explaining how high –grade systemic inflammation accelerates vascular risk in rheumatoid arthritis., 2003, 108, 2957-63.

Seriolo B, Paolino S, Ferrone C, Cutolo M. Effects of etanercept or infliximab treatment on lipid profile and insulin resistance in patients with refractory rheumatoid arthritis. Clin Rheumatol. 2007;26(10):1799–1800.

Seriolo B, Paoliono S, Ferrone C, Cutolo M, Comments on the original article by Soubrier et al. Effects of anti-tumor necrosis factor therapy on lipid profile in patients with rheumatoid arthritis. Joint Bone Spine. 2009;76(1):117–118.

Sihvonen S, M Korpela, P Laippala. Death rates and causes of death in patients with rheumatoid arthritis: a population-based study. Scand J Rheumatol. 2004;33(4):221–7.

Situnayake R, Kitas G: Dyslipidemia and rheumatoid arthritis. Ann Rheum Dis 1997, 56:341-342.

Smith JR, F Mackensen, JT Rosenbaum. Therapy Insight: scleritis and its relationship to systemic autoimmune disease. Nat Clin Prac Rheumatol. 2007;3(4):219-26.

Tall AR: Plasma cholesteryl ester transfer protein. J Lipid Res 1993, 34:1255-1274.

Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report Circulation. 2002;106(25):3143–3421.

Trine Bay Laurberg, Jan Frystyk, Torkell Ellingsen, IB T. Hansen, Anette JØrgensen, Ulrik Tarp, Merete Lund Hetland, Kim HØrslev-Petersen, Nent Hornung, JØrgen Hjelm Poulsen, Allan Flyvbjerg , Kritian Stengaard-Pedersen. Plasma Adiponectin in Patients with Active, Early, and Chronic Rheumatoid Arthritis Who Are Steroid- and Disease-Modifying Antirheumatic Drug-Naive Compared with Patients with Osteoarthritis and Controls. The Journal of Rheumatology

Turesson C, Jacobsson LT, Matteson EL. Cardiovascular co-morbidity in rheumatic diseases. Vasc Health Risk Manag. 2008;4(3):605–614.

Van Vollenhoven R, Siri D, Furie R, Krasnow J, Alecock E, Alten R. Long term safety and tolerability of tocilizumab treatment in patients with rheumatoid arthritis and a mean treatment duration of 2.4 year. Arthritis Rheum. 2009;60(Suppl 10):1955.

Van Vollenhoven R, Scali J, Curtis J, Krasnow J, Vernon E, Alten R. Safety of tocilizumab in patients with rheumatoid arthritis: anyalysis of median of 2.6 years of treatment in long-tern extension studies. Ann Rheum Dis. 2010;69(Suppl3):544.

Van Doornum S, McColl G, Wicks IP: Accelerated atherosclerosis:m an extraarticular feature of rheumatoid arthritis. Arthritis Rheum 2002, 46:862-873.

Vanleuven SI, Franssen R, Kastelein JJ, et al, Rheumatology,2008, 47,3-7.

Vance, D.E., Vance, J.E. Biochemistry of Lipids, Lipoproteins, and Membranes. New York, Elsevier Science, 1996.

Vanleuven SI, Franssen R, Kastelein JJ,et al.NIH publication No.01-3305,JAMA, May2001, 285, 2486-97.

Van Halm VP, Nielen MM, Nurmohamed MT, van Schaardenburg D, Reesink HW, Voskuyl AE, Twisk JW, van de Stadt RJ, de Koning MH, Habibuw MR, et al. Lipids and inflammation: serial measurements of the lipid profile of blood donors who later developed rheumatoid arthritis. Ann Rheum Dis. 2007; 66(2):184–188.

Voskuyl AE. The heart and cardiovascular manifestations in rheumatoid arthritis. Rheumatology. 2006;45 Suppl 4:iv4-7.

Wilsher M, L Voight, D Milne, M Teh, N Good. Prevalence of airway and parenchymal abnormalities in newly diagnosed rheumatoid arthritis. Respir Med. 2012; 106(10):1441–6.

Wijbrandts CA, van Leuven SI, Boom HD, Gerlag DM, Stroes EG, Kastelein JJ, Tak PP. Sustained changes in lipid profile and macrophage migration inhibitory factor levels after anti-tumour necrosis factor therapy in rheumatoid arthritis. Ann Rheum Dis. 2009; 68(8):1316–1321.

Wilson A, HT Yu, LT Goodnough. Prevalence and outcomes of anaemia in rheumatoid arthritis: a systematic review of the literature. Am JMed. 2004; 116:50S–7S.

Young A, G Koduri, M Batley, E Kulinskaya.; Early Rheumatoid Arthritis Study (ERAS) group. Mortality in rheumatoid arthritis. Increased in the early course of disease, in ischaemic heart disease and in pulmonary fibrosis. Rheumatology (Oxford).2007; 46(2): 350–7

Youssef AA, SA Machaly, ME El-Dosoky. Respiratory symptoms in rheumatoid arthritis: relation to pulmonary abnormalities detected by high-resolution CT and pulmonary functional testing. Rheumatol Int. 2012; 32(7):1985–95.

Ziff M. The rheumatoid nodule. Arthritis Rheum. 1990;33(6):761–7.

Zlatanovic G, D Veselinović, S Cekić. Ocular manifestation of rheumatoid arthritis-different forms and frequency. Bosn J Basic Med Sci. 2010; 10(4):323–7.

الملخص العربي

التهاب المفاصل الروماتيزمي يؤدي الي ارتفاع نسبة الوفيات بسبب امراض القلب و الاوعية الدموية المتعلقة بتغيرات في مستوي دهون الدم ،في عيادات امراض الروماتزم في مستشفي الهواري ومستشفي 7 اكتوبر في بنغازي- ليبيا خلال الفترة من بداية يناير 2014 الي نهاية شهر يونيو 2014 قد اجريت دراسة مستقبلية لمئة 100 مريض يعانون من التهاب المفاصل الروماتزمي ، مستبعد منهم مرضي السكر وارتفاع ضغط الدم ومرضي يعانون من زيادة ارتفاع نسب دهون الدم العائلي،تمت اختبارات نسب دهون الدم المختلفة وادت الي النتائج التالية:85 % من الحالت كانت اناث بمدي عمر(21-85) ومتوسط عمر(47.87) معظم الحالات تعاني من المرض من اكثر من سنة بينما 13% منهم اقل من 6 اشهر، 51% من المرضي في الحالة النشطة للروماتزم و معظمهم يعالجون بعقار الميثوتريكسيت.

اغلب تغيرات كانت في مستوي بروتينات الدهون متدنية الكثافة و معظم المرضي لديهم تغير في مستوي واحد من بروتينات الدهون المختلفة و هناك 4 مرضي فقط لا يعانون من تغيرات في المستويات وهناك 96% من المرضي لديهم علي الاقل مستوي واحد متغير و 28% من الحالات لديهم تغير في 3 مستويات علي الاقل ، يوجد علاقة واضحة بين مدة المرض و زيادة التغير في نسبة دهون الدم علي سبيل المثال ،كل ما طالت مدة المرض تزداد نسب تغير الدهون في الدم ،واثبت ايضا ان زيادة التغير في نسبة دهون الدم ملاحظة بوضوح في مرضي في الحالة النشطة عن غيرهم من الحالات الغير نشطة.

تغير نسب الدهون في الدم كان اكثر في الاناث عن المرضي الرجال ولكنها لم تكن علاقة احصائية واضحة، التغير كان اوضح في المرضي المسنين اكثر من الاصغر سنا، عقار المثوتريكسيت كان العقار الاشهر في الاستخدام لدي المرضي وايضا له علاقة ذات دلالة احصائية واضحة مع تغير نسب الدهون في الدم.

قسم الكيمياء الحيوية

كلية الطب البشري- جامعة بنغازي

التغير في مستويات دهون الدم في مرضي الاءلتهاب الروماتزمي

مقدمة من

د.سهام علي الصديق عباس

تحت اشراف

ا. د. فرج علي الشاعري

قدمت هده الرسالة لاءستكمال متطلبات الحصول علي الماجستير في الكيمياء الحيوية

2016