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Original Article

Measurement of Some Physiological Parameters of Patients with Rheumatoid Arthritis

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Abstract:

Rheumatoid arthritis (RA) is a chronic, inflammatory, systemic autoimmune disease, affecting the joints with varying severity among patients.

The risk factors include age, gender, genetics, and environmental exposure (cigarette smoking, air pollutants, and occupational). Many complications can follow, such as permanent joint damage requiring arthroplasty, rheumatoid vasculitis, and Felty syndrome requiring splenectomy if it remains unaddressed. This Study was carried out in AL- Zahra Hospital.(25) adult male (men) ,(35-50) years old,were divided into (2) groups .The first group contained healthy men(10) and assisted as controller group (G1) ,men in next group were with Rheumatoid arthritis(15) (G2) , .In this present study we collect samples of blood to count the serum of Total cholesterol(TC),Triglycerides(TG),High density lipoprotein (HDL)and Low density Lipoprotein (LDL) . The results revealed that : Significant increase ($P<0.05$) in serum TC,TG and LDL levels in G2 compared with control group (G1) , Significant decrease ($P<0.05$) in serum HDL levels in G2 compared with G1. . From the data of the present research , it can be determined that Rheumatoid arthritis, effect on metabolism of fats in men.

Keywords: Rheumatoid Arthritis, Measurement, Physiological Parameters, Patients

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Introduction:

Rheumatoid arthritis (RA) is an inflammatory chronic, progressive disease, which belongs to the systemic connective tissue diseases and affects mostly peripheral joints (2). Although progressive, the disease has its phases of high and low disease activity, which is translated into symptoms and functional ability. Any worsening of the disease leaves irreversible changes in the joints (3). The characteristic clinical features of RA usually involve the following problems: morning stiffness lasting for more than 1 hour, pain (usually more pronounced at rest), swelling of joints, deformities, limitation of physical activity, and consequently decreased quality of life (QOL). Fassbender (4) defines three different determinants that describe complete picture of RA: exudative inflammatory process, which causes swelling, pain and stiffness; proliferative-destructive process that affects joint destruction; and enzymatic collagenolytic process, which can cause primary necrotizing of, e.g., myocardial muscle, blood vessels, and sclera of the eye.

Rheumatoid arthritis affects approximately 1% of the world population. The leading symptom of rheumatic diseases is a sense of pain, and it is usually the main reason for seeking consultation (5). Pain can be considered as a complex dual phenomenon; one part is the perception of pain, and the other is the patient's emotional reaction to it (6). Besides leading to unpleasant sensation, pain leads to the occurrence of depression in a number of patients (7, 8). According to Rezaei et al. (9), three illness perceptions significantly mediate the relationship between depression and pain: consequences, personal control, and emotional response. Pain is also brought into contact with a heightened sense of fatigue in this population. Thus, for example, Pollard et al. (10)

state that high level of fatigue is often noticed in RA patients and is mostly associated with pain and depression. Regarding pain perception, Lončarić-Katušin et al. (11)

in their study, conducted on a sample of 1090 subjects with various causes of chronic pain, found that moderate and severe sleep quality disorders were significantly more frequent in subjects over 65 years of age, as well as in subjects with musculoskeletal, neuropathic and back pain. In the same group of subjects, the higher intensity of pain and poor sleep quality also were the leading cause of deterioration of the Patients' Global Impression of Change Scale.

Quality of life in persons with rheumatoid arthritis

The World Health Organization (WHO) defines QOL as the individual's perception of their position in life regarding culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns. It is a wide concept that includes physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment (12).

Because RA affects different areas of personal existence, determinants that could define QOL in this population have been constantly tested. Considering the results of different investigations, it appears that people with RA have significantly worse results in physical functioning in particular (13-14).

However, RA also has a major impact on other areas of human life, e.g., social relationships, family life, and psychological well-being. Furthermore, because of RA, patients often are not able to perform everyday tasks in their private or professional life, and very often, they should change their profession or go to early retirement. Changes in self-perception in relation to painful stimuli, reduced functional ability, and labor and social inadequacy may also induce emotional and mental disorders. The overall negative effects of RA affect the patient QOL (15, 16).

For this purpose, the aim of this research was to get an insight into the QOL in subjects with RA in connection with their functional ability and pain perception.

Pathophysiology

Rheumatoid arthritis is best considered a clinical syndrome spanning several disease subsets. (17)

These different subsets entail several inflammatory cascades, (18)

which all lead towards a final common pathway in which persistent synovial inflammation and associated damage to articular cartilage and underlying bone are present.

Inflammation:

One key inflammatory cascade includes overproduction and overexpression of TNF

This pathway drives both synovial inflammation and joint destruction. .(19)
TNF overproduction has several causes, including interactions between T and B lymphocytes, synovial-like fibroblasts, and macrophages. This process leads to overproduction of many cytokines such as interleukin 6, which also drives persistent inflammation and joint destruction. (20)
Overproduction of other proinflammatory cytokines (eg, interleukin 1) differs from the process for interleukin 6 in that production is either less marked or is specific to one or more disease subsets, as best shown by the effects of interleukin 1 blockade in subforms of juvenile idiopathic arthritis or adult-onset Still's disease.

Synovial cells and cartilage cells:
The dominant local cell populations in joints affected by rheumatoid arthritis are synovial and cartilage cells. Synovial cells can be divided into fibroblast-like and macrophage-like synoviocytes. Overproduction of proinflammatory cytokines is believed to be led predominantly by macrophage-like synoviocytes. Fibroblast-like synoviocytes show abnormal behaviour in rheumatoid arthritis. In experimental models, co-implantation of fibroblast-like synoviocytes with cartilage leads to fibroblasts invading cartilage, (21)
behaviour that correlates with joint destruction. (22)
Considerable information has accumulated about joint destruction and the role of osteoclast activation as a key process leading to bone erosion. This association is proven because specific inhibition of osteoclast activation can reduce joint destruction yet not affect joint inflammation. (23)
We are unclear about whether arthritis starts as a primary problem in the bone and subsequently moves to the joint, or the other way around. (24)
One argument for rheumatoid arthritis starting in the joint is the observation that fibroblast-like synoviocytes showing altered behaviour can spread between joints, suggesting how polyarthritis might develop. (25)
Regulation of immune inflammation depends on balances between the number and strength of different cell types. Control of arthritogenic immunoresponses has been studied in mice in which the specific antigen is known. Infusion of low numbers of T cells with specific characteristics ameliorates arthritis in a rodent model of the disease, showing T cells can be protective. (26,27)
Ongoing research should translate these experimental findings into clinical practice.

Autoantibodies:

Rheumatoid factor is the classic autoantibody in rheumatoid arthritis. IgM and IgA rheumatoid factors are key pathogenic markers directed against the Fc fragment of IgG. Additional (and increasingly important) types of antibodies are those directed against citrullinated peptides (ACPA). Although most, but not all, ACPA-positive patients are also positive for rheumatoid factor, ACPA seem more specific and sensitive for diagnosis and seem to be better predictors of poor prognostic features such as progressive joint destruction. (28)

Ongoing research aims to identify antibody specificities relevant for different patients' subsets and disease stages. 50–80% of individuals with rheumatoid arthritis have rheumatoid factor, ACPA, or both. Composition of the antibody response varies over time, with limited specificities in early rheumatoid arthritis and a mature response—in which more epitopes are recognised and more isotypes used—in late disease

(**figure 1**). (29,30)

Evidence from animal models and in-vivo data suggest that ACPA are pathogenic on the basis of induction of arthritis in rodent models and because immunological responses are present in ACPA-positive patients in a citrulline-specific manner.(31,32)

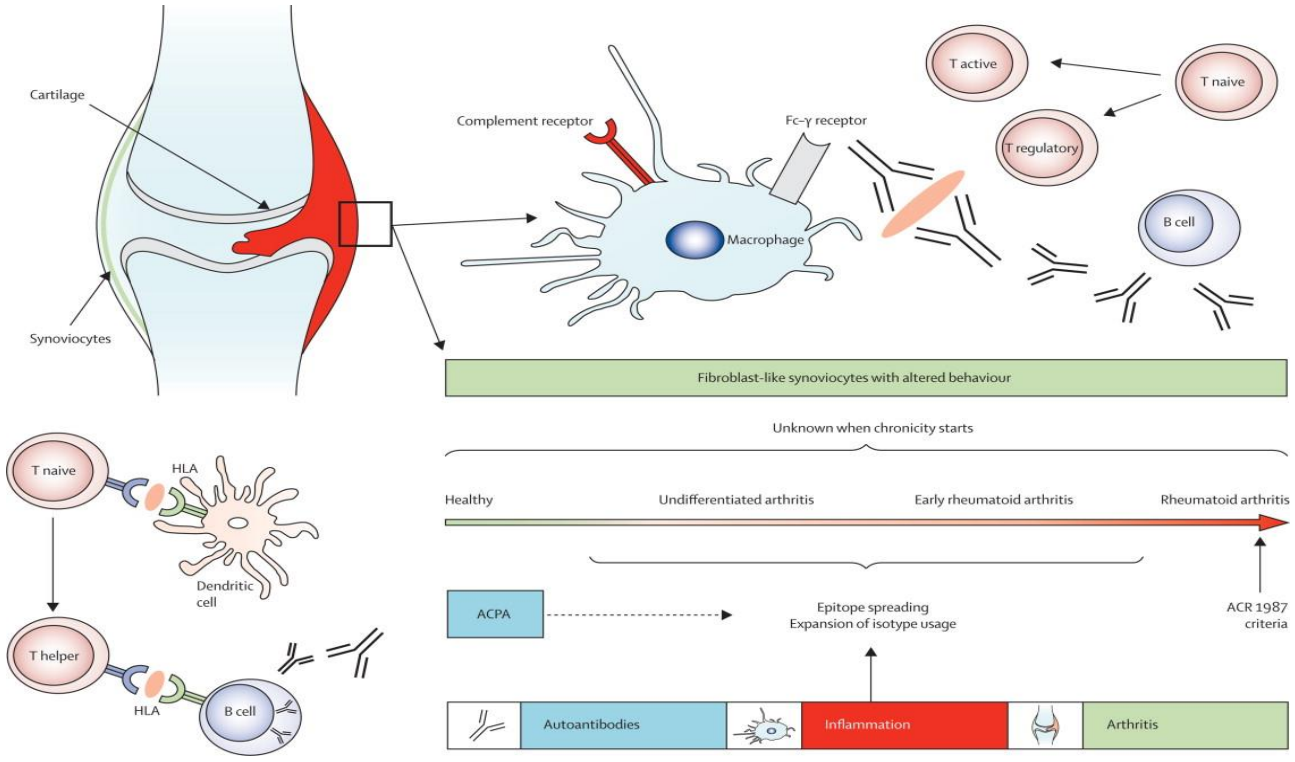


Figure 1: Key pathological changes in the synovium in rheumatoid arthritis.

The joint consists of two bones covered by cartilage and aligned by a capsule. The inner surface of the capsule consists of fibroblast-like synoviocytes that produce synovial fluid. In a joint affected by rheumatoid arthritis, the synovium is swollen due to an infiltrate consisting of fibroblast-like and macrophage-like synoviocytes, macrophages, several populations of T cells, and B cells. Macrophages are activated to produce all kind of proinflammatory products (eg, tumour necrosis factor) partly by immune complexes binding to Fc-γ receptors and complement receptors on their surface. Evolution of chronicity in joint inflammation is controlled by so-called master switches, and prediction models suggest a pathway of autoantibodies, inflammation, and arthritis. Autoantibodies binding to citrullinated antigens (ACPA) have confined specificity and limited isotype use in healthy individuals, but epitope spreading and expansion of isotype usage happens in those with rheumatoid arthritis. ACR=American College of Rheumatology.

Genetics:

50% of risk of developing rheumatoid arthritis is attributable to genetic factors.24

Much progress has been made in identification of genetic regions tagged by structural variation (single nucleotide polymorphisms); more than 30 genetic regions are associated with rheumatoid arthritis. (33)

At present, apart from PTPN22 and HLA genes, no major pathogenic insights have come from these genetic associations. However progress is shown by the realisation that from a putative 2 m of DNA harbouring candidate variants, these 30 regions are all contained within 2 mm of DNA. With current sequencing methodology, 2 mm of DNA allows sequencing in large cohorts. So, we can reasonably expect new mechanisms to be identified in the next few years. Many risk alleles discovered in recent years are fairly common in the population as a whole; individually, they have modest effects on the risk of rheumatoid arthritis. However, ongoing research suggests that several risk loci are linked to other autoimmune diseases, and some genes fall within discrete biological pathways that are driving inflammation.

Findings of genetic studies show differences in ACPA status of patients with rheumatoid arthritis, related to the number of specific HLA-DRB1 alleles (**figure 1**). (34)

These HLA alleles share a common motive, which is known as the shared epitope. Currently, antigens are believed to

be modified by a process called citrullination; this step entails post-translational modification of the aminoacid arginine to citrulline. This change is thought to allow antigens to fit in the HLA alleles that harbour this shared epitope. The end result is breaking of tolerance that allows antibody formation against these antigens. (35)

Genetic risk factors associated with rheumatoid arthritis are, in the main, thought to be specifically associated with either ACPA-positive or ACPA-negative disease. The best-studied environmental factor for rheumatoid arthritis—smoking—seems to be a risk factor for ACPA-positive disease, especially in the context of positivity for HLA-DRB1 shared epitope alleles. (36)

Genetic research supports the idea that rheumatoid arthritis is a heterogeneous group of overlapping syndromes.

Symptoms and Causes

Signs and symptoms of rheumatoid arthritis may include:

- Tender, warm, swollen joints
- Joint stiffness that is usually worse in the mornings and after inactivity
- Fatigue, fever and loss of appetite

Early rheumatoid arthritis tends to affect your smaller joints first — particularly the joints that attach your fingers to your hands and your toes to your feet.

As the disease progresses, symptoms often spread to the wrists, knees, ankles, elbows, hips and shoulders. In most cases, symptoms occur in the same joints on both sides of your body.

About 40 percent of the people who have rheumatoid arthritis also experience signs and symptoms that don't involve the joints. Rheumatoid arthritis can affect many nonjoint structures, including:

- Skin
- Eyes
- Lungs
- Heart
- Kidneys
- Salivary glands
- Nerve tissue
- Bone marrow
- Blood vessels

Rheumatoid arthritis signs and symptoms may vary in severity and may even come and go. Periods of increased disease activity, called flares, alternate with periods of relative remission when the swelling and pain fade or disappear. Over time, rheumatoid arthritis can cause joints to deform and shift out of place.(37)

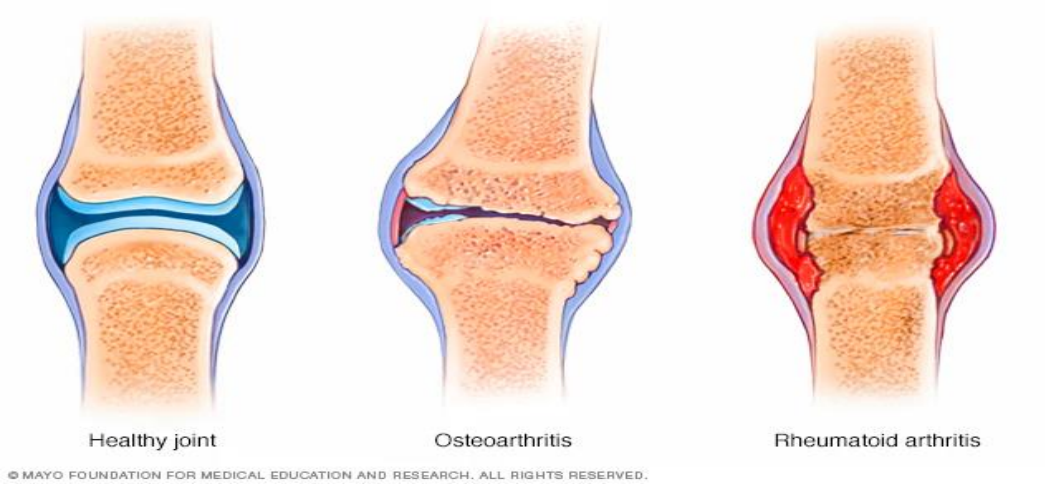
Causes:

Rheumatoid arthritis occurs when your immune system attacks the synovium the lining of the membranes that surround your joints.

The resulting inflammation thickens the synovium, which can eventually destroy the cartilage and bone within the joint.(38)

The tendons and ligaments that hold the joint together weaken and stretch. Gradually, the joint loses its shape and alignment.

Doctors don't know what starts this process, although a genetic component appears likely. While your genes don't actually cause rheumatoid arthritis, they can make you more susceptible to environmental factors such as infection with certain viruses and bacteria that may trigger the disease.(39)



Rheumatoid arthritis vs. osteoarthritis

Osteoarthritis, the most common form of arthritis, involves the wearing away of the cartilage that caps the bones in your joints. With rheumatoid arthritis, the synovial membrane that protects and lubricates joints becomes inflamed, causing pain and swelling. Joint erosion may follow.

Material and Methods:

In this study 15 patients (male) were completed all biochemical analysis tests . the range of their ages between 25-45 years, 10 apparently healthy male were selected as the control group . the range of their ages were equal to that of patients . blood were obtained from individuals in the morning and collected in plain tube for serum in order to rating some hematological and biochemical parameters : TC, TG, LDL-c, HDL-c, serum(TC) levels were measured by using (cholesterol kit BIOLABO company , France) (40) ,serum (TG) level were amounted by using (Triglyceride kit BIOLABO company , France) (41) , serum (HDL)

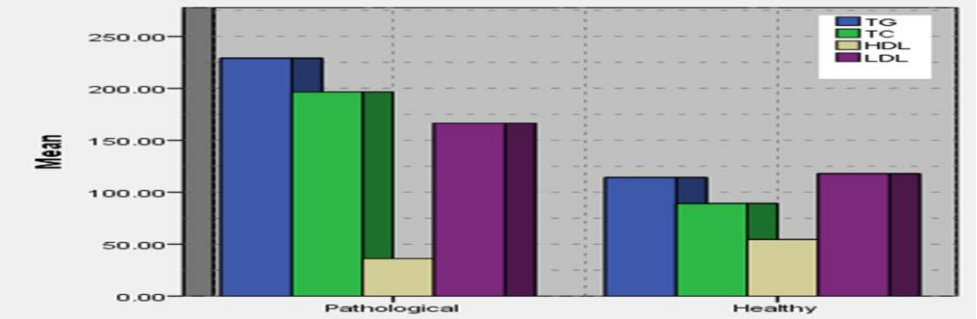
c) level were gauged by using (Rondo.United kingdom laboratories Ltd , co.Antrim) kit (42). Serum (LDL-c) level were measured by using : LDL= TC- (HDL+TG/5) (43).

The mean ±Std. Division(SD) of parameters measured from groups healthy and patients were determined with serum TC, TG, LDL and HDL.

Result:

Table 1 Shows the significant increase (P<0.05) in TC,TG and LDL levels, and Displays significant decrease (P<0.05) of HDL levels in Patient groups compared with the control group Figure(1).

p.value	S. E	S. D	Mean	N	groups	
0.00	17.44	67.55	228.93	15	Pathological	TG
	6.91	21.84	114.00	10	Healthy	
0.00	7.70	29.81	196.47	15	Pathological	TC
	5.26	16.64	89.00	10	Healthy	
0.00	1.06	4.12	36.13	15	Pathological	HDL
	1.64	5.19	54.40	10	Healthy	
0.00	10.78	41.76	166.48	15	Pathological	LDL
	6.91	21.85	117.76	10	Healthy	
0.87	1.67	6.46	36.53	15	Pathological	Age
	2.46	7.79	37.00	10	Healthy	



Figure(1) : comparison of serum TC,TG,LDL and HDL(mg/dl) levels in Patients men groups with control group

Discussion:

In this study we found increase significantly ($p<0.05$) in TC, TG and LDL Levels and decrease significantly ($p<0.05$) in HDL Levels of patients in comparison to healthy control and that result by excess production of reactive oxygen intermediate such us superoxide (O2-) , hydrogen peroxide (H2O2) that lead to oxidative stress and that lead to change in (Hydroxyle -3- methylglutary- co enzyme A(HMG-Co A) reductase activity and dysfunction of cholesterol esters and decrease in lipoprotein lipase activity and all that lead to rise in free fatty acids in blood, and excess tumar necrosis factors (TNF-α) and interleukin (IL-IB) which lead to raise levels of cholesterogenic enzyme such as HMG-Co A reductase and diminution levels of α- cholesterol – 17 hydroxylase that in charge of cholesterol catabolism in liver, and by oxidative stress that results form Rheumatoid arthritis may due to stress of endoplasmic reticulum and increase in gene expression of strol on endoplasmic reticulum membrane and that due to high levels of TC and TG(44). and the results display high levels of LDL – c in serum of patients with Rheumatoid arthritis compared with healthy group and this results may be induce by (hypersensitivity) of LDL-receptors in blood vessels to collection of lipoproteins in serum and result high rate of LDL-c in serum. HDL-c levels in serum correlated oppositely with LDL-c levels in serum, and HDL-c play role in carry cholesterol from tissues to liver and rise levels of LDL lead to reduce HDL-c levels in serum. (45)

REFERENCES

1. American College of Rheumatology ad hoc Committee on Clinical Guidelines(2002). Guidelines for the management of rheumatoid arthritis. Arthritis Rheum;46:328□46.
2. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, Healey LA, Kaplan SR, Liang MH, Luthra HS, etal.(1987). The American Rheumatism Association revised criteria for the classification of rheumatoid arthritis. ArthritisRheum 1988;31:315□24.
3. Deighton C, O□Mahoney R, Tosh J, Turner C, Rudolf M; (2009).Guideline Development Group. Management of rheumatoidarthritis: summary of NICE guidance. BMJ;338:710□2.
4. Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, van Zeben D, Kerstens PJ, Hazes JM, Zwinderman AH, Ronday HK, Han KH, Westedt ML, et al. (2005). Clinical and radiographic outcomes of four different treatment strategies inpatients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. Arthritis Rheum;52:3381□90.
5. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, GG, et al. (1998) .Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. ArthritisRheum;41:778□99.
6. Sluka KA. Osteoarthritis and rheumatoid arthritis. In: Sluka KA, editor. (2009). Mechanisms and management of pain for thephysical therapist. Seattle: IASP Press;. p. 349□360.
7. Arnett FC, Edworthy SM, Bloch DA et al. 1988 Revised criteria for the classification of rheumatoidarthritis. Arthr Rheum; 31: 315□24.

8. Barton JL. 2009 Patient preferences and satisfaction in the treatment of rheumatoid arthritis with biologic therapy. Patient Prefer Adherence; 3: 335□44.

9. Cohen M. Abatacept in focus. Internet J Rheumatol; et al. (2007). Efficacy of B-cell targeted therapy with rituximab in patients with rheumatoid arthritis. N Engl J Med 2004; 350: 2572□81.

10. Genant HK, Peterfy CG, Westhovens R. 2008 Abatacept inhibits progression of structural damage inrheumatoid arthritis: results from the long-term extension of the AIM trial. Ann Rheum Dis; 67: 1084□9.

11. Goffe B, Cather JC. (2003). Etanercept: An overview. J Am Dermatol; 49(25 suppl): S105□11.

12. Kavanaugh A, Cohen S, Cush JJ. (2004).The evolving use of tumor necrosis factor inhibitors in rheumatoidarthritis. J Rheumatol; 31: 1881□4.

13. Koenders MI, Joosten LAB, van den Berg WB.(2006).Potential new targets in arthritis therapy: interleukin (IL)-17 and its relation to tumour necrosis factor and IL-1 in experimental arthritis.Ann Rheum Dis; 65(suppl iii): 29□33.

14. Assmann G ., Schute H . (1992) . Relation of high density lipoprotein cholesterol and Triglycerides to incidence of atherosclerotic coronary disease. CTIe procam experience. Am .J, cardiol ., 70:733-737.

15. Baccarelli , A .; Zanobetti , Martinelli ,L . Grillio , P .; Hou , L .; Guido , G.; Mannucci , P.; Pier Alberto , A and Schwartz , J (2007) . Air pollution , smoking , and plasma homocysteine . Environ Health perspect .,115:176-181. .

16. Badimon, J.;Zaman,A. and Helft , G .(2004) .Acute Coronary Syndromes .Pathophysiology and preventive priorities thromb.Haemostas . J., 82:997-1008.

17. Bischof and Islami D.(2002). Sexual hormons .8TH phostyraduate course fortraining reproductive medicine and reproductive biology. .Department of obstetvics and gynecology Geneva University Hospital.P:1-4.

18. Block, J.H. and Beal, J.M.(2004). Willson and Gisvolds Textbook of Pharmaceutical Chemistry .11th ed . Lippincott Williams and Willkins : 657-660.

19. Bostom, A G.; Shemin, D; Baylary, p. (2000). Contrlled comparion of L-5- methyltetrahydrofolate versus folic acid for the treatment of Hyperhomocysteinemia in hemodialysis patient's circulation. , 101: 2829-2832.

20. Denke, M. (2005). Weighing in before the fight: Low density lipoprotein cholesterol and non –high – density lipoprotein cholesterolversus apolipoprotein B as the best predictor for coranory heart disease and the best measure of therapy . Atheroscler. Thro. Vas. Biol., 112:3368-3377.

21. Ekaidem, M.S.: Akopanabiatu, M, I.: Uboh and Eka, O.U. (2007). Effect of folic acid and B12 administration on phentain induced toxicity in rats. Indian .J of Clin. Bioch. , 22(2):36-40.

22. Fernandez-Robredo,P.;Moy,D.;Rodriguez,J. and Garcia-Layana, A. (2005) .Vitamin C and E reduce retinal oxidative stress and nitric oxide metabolites and prevent ultrastructural alterations in povcine hypercholesterolemia. Investigative Opthalmology and Visual Science., 436:114-1146.

23. Finkleston, T. and Holbrok, N. (2000). Oxidants, Oxidative stress and the biology of aging .Nutrition . , 408(68):239-245

24. Neumann, E. et al. (2002). Local production of complement proteins in rheumatoid arthritis synovium. Arthritis Rheum. 46, 934–945.

25. Banda, N. K. et al. (2002).Mechanisms of effects of complement inhibition in murine collagen-induced arthritis. Arthritis Rheum. 46, 3065–3075.

26. Commentary: medicine, population, and tuberculosis. Int J Epidemiol. 2005; 34: 521-524

27. Advances in the genetics of rheumatoid arthritis point to subclassification into distinct disease subsets. Arthritis Res Ther. 2008; 10: 205

28. Differences in synovial tissue infiltrates between anti-cyclic citrullinated peptide-positive rheumatoid arthritis

and anti-cyclic citrullinated peptide-negative rheumatoid arthritis. Arthritis Rheum. 2008; 58: 53-60

29. Agca R, Heslinga SC, Rollefstad S, Heslinga M,et al. (2017).EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis.;76:17–28.
30. Choi HK, Seeger JD.(2005) .Lipid profiles among US elderly with untreated rheumatoid arthritis—the Third National Health and Nutrition Examination Survey. J Rheumatol. ;32:2311–2316.
31. Steiner G, Urowitz MB. (2009).Lipid profiles in patients with rheumatoid arthritis: mechanisms and the impact of treatment. Semin Arthritis Rheum. ;38:372–381.
32. Knowlton N, Wages JA, Centola MB, Alaupovic P. (2012). Apolipoprotein-defined lipoprotein abnormalities in rheumatoid arthritis patients and their potential impact on cardiovascular disease. Scand J Rheumatol. ;41:165–169.
33. Schulte DM, Paulsen K, Turk K, Brandt B, Freitag-Wolf S,. (2018).Small dense LDL cholesterol in human subjects with different chronic inflammatory diseases. Nutr Metab Cardiovasc Dis. ;28:1100–1105
34. Park Y, Chang M (2016). "Effects of rehabilitation for pain relief in patients with rheumatoid arthritis: a systematic review". Journal of Physical Therapy Science. 28 (1): 304–8.
35. Lopez-Olivo MA, Amezaga Urruela M, McGahan L, Pollono EN, Suarez-Almazor ME (2015). "Rituximab for rheumatoid arthritis". The Cochrane Database of Systematic Reviews. 1: CD007356.
36. Singh JA, Hossain A, Tanjong Ghogomu E, Mudano AS, Tugwell P, Wells GA (2016). "Biologic or tofacitinib monotherapy for rheumatoid arthritis in people with traditional disease-modifying anti-rheumatic drug (DMARD) failure: a Cochrane Systematic Review and network meta-analysis (NMA)". The Cochrane Database of Systematic Reviews. 11: CD012437.
37. Singh JA, Hossain A, Tanjong Ghogomu E, Mudano AS, Maxwell LJ, Buchbinder R, et al. (2017). "Biologics or tofacitinib for people with rheumatoid arthritis unsuccessfully treated with biologics: a systematic review and network meta-analysis". The Cochrane Database of Systematic Reviews. 3: CD012591.
38. Verhoef LM, van den Bemt BJ, van der Maas A, Vriezekolk JE, Hulscher ME, van den Hoogen FH, et al. (2019). "Down-titration and discontinuation strategies of tumour necrosis factor-blocking agents for rheumatoid arthritis in patients with low disease activity". The Cochrane Database of Systematic Reviews. 5: CD010455.
39. Maxwell L, Singh JA (2009). Maxwell L (ed.). "Abatacept for rheumatoid arthritis". The Cochrane Database of Systematic Reviews (4): CD007277.
40. Allain , C.C.; Poon, L.S.;Chan,Chan ;C.S.G.; Richmond , Wand Fup , C.(1974).The Merk Manual of diagnostic and therapy .Merk and Co .,Clin .Chem .13:56-59.
41. Fossati, P;andprencipe.; L.(1982). Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. clinical chemistry.,28 :2077-2080.
42. Lopez-Virella, M. F.; Stone, P.; Ellis, S. & Colwell, J. A. (1977). Cholesterol determination in high-density lipoproteins separated by three different methods.Clin. Chem.; 23:882-884.
43. Anderioli , T.E.; Carpenter , C.C.; Griggs, R.C.& Loscalza, J.(2004). Cecils essentials of medicine . USA., 392-399.
44. Denke, M. (2005). Weighing in before the fight: Low density lipoprotein cholesterol and non –high – density lipoprotein cholesterolversus apolipoprotein B as the best predictor for coranory heart disease and the best measure of therapy . Atheroscler. Thro. Vas. Biol., 112:3368-3377.
45. Gotto, A .M. (1992) . Lipid and lipoprotein disorders . Manual of lipid disorders . Pownall HJ (eds) . Baltimore , Williams and Wilkins CO ., pp . 95- 124.