بسم الله الرحمن الرحيم

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Faculty of Graduate Studies and Scientific Research

Correlation between Erythrocyte Sedimentation Rate and C – Reactive Protein in Arthritis Patients in Shendi Locality – River Nile State

A Thesis Submitted for fulfillment of The M.Sc in Hematology

By

Altaf AbdAlla Siddig Elbashier

B.Sc Medical Laboratory Science- University of Shendi (2007)

Supervisor

Dr: Mohammed Osman Ali Mohammed (PhD)

Assistant professor of Haematology-Faculty of Medical Laboratory Sciences-Shendi University

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الآيـــــة

بسم الله الرحمن الرحيم

قال تعالي

﴿ قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَاۖ إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴾

صدق الله العظيم

سورة البقرة :الآية ٣٢

DEDICATION

To my dear parents:

Thinking of you today with love in every thought,

Thinking all the joy we have thought, the happiness you have brought,

Thinking of just have nice it is and how like “you ,your guidance meant more than your even guess

To my brothers , sisters, and husband.

ACKNOWLEDGEMENT

First of all I thank the Almighty Allah who helped me to complete this study I would like to express endless thanks to my supervisor

Dr : Mohammed Osman Ali

For his great efforts and guidance. I thank the staff of Elgawda center.

Also I would like **Dr Mohammed Elhassan Eltyeb** who help me in the statistical analysis for this research, I would also like to thank all the participants (patients)who gave the allowance to give sample of this research and many other whom I could not mention here, but their direct and in direct supports had already contributed in this study.

Abstract

Background: Arthritis is a chronic systemic inflammatory disease of unknown cause. An external trigger (e.g., cigarette smoking, infection, or trauma) that triggers an autoimmune reaction, leading to synovial hypertrophy and chronic joint inflammation. The aim of study is to identify the correlation between erythrocyte sedimentation rate and C-reactive protein in arthritis patients.

Method: This is across-sectional case control prospective analytical. The study conducted in shendi town to identify the correlation between erythrocyte sedimentation rate and C-reactive protein in arthritis patients in the period between (March to May2018) .The study included(50) patients who were diagnostic with arthritis disease and (25) healthy volunteers as control groups.

Blood samples were collected from the (two)groups to perform Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP+) .Data was collected by using structured face to face questionnaire and then analyzed by using (SPSS)version (18).

Result: The study revealed that the about (22%) of arthritis disease patients were male, while (78%) were female.

Also the result of this study showed that the mean of ESR in test group was (71mm/h), and control group was (19mm/h), while mean of CRP in test group was (18mg/l), and in control group was (3.0 mg/l),

Also the result of this study demonstrated that the mean of ESR and CRP level was higher in that group of age more than 40 years.

Also the result of this study showed that there was significant variation in CRP and ESR when compared the test group with control group.

مستخلص الدراسة

خلفية: مرض التهاب المفاصل هو التهاب مزمن غير معروف السبب .تعتبر(العدوى، الكدمات، التدخين) من المحفزات الخارجية لهذا الالتهاب المناعي الذاتي، يقود إلى ضمور والتهاب المفاصل المزمن. تهدف الدراسة لمعرفة معدل ترسب كريات الدم الحمراء وبروتين سي في مرضي التهاب المفاصل.

منهجية البحث:أجريت هذه الدراسة المقطعية الوصفية – الحالة في مدينه شندي لمعرفة معدل ترسب كريات الدم الحمراء وبروتين سي في مرضي التهاب المفاصل ما بين شهر (مارس – مايو ٢٠١٨). وكانت عينه الدراسة عبارة عن (٥٠) مريض مصابون بالتهاب المفاصل المزمن. وقورنت نتائج الدراسة مع (٢٥) متطوع سليم كمجموعة ضابطة.

جمعت عينات الدم من جميع المرضي وثم حللت معمليا لأجراء فحص معدل ترسيب كريات الدم الحمراء وبروتين سي المتفاعل. تم جمع المعلومات بواسطة الاستبيان ومن ثم استخدام برنامج الحزمة الإحصائية للعلوم الاجتماعية)SSPS)موديل(١٨) .

نتيجة الدراسة:

أظهرت نتائج الدراسة أن (٢٢%) من المرضي ذكور و(٧٨%) إناث. وكذلك أوضحت الدراسة أن متوسط الـــ ESR في المرضي (mm/h 71) وفي الأصحاء (19mm/h), وكذلك بينت أن متوسط CRP في المرضي (١٨mg/l) وفي الأصحاء (3mg/l) مع وجود فرق ذو دلاله إحصائية واضحة.

أيضا" أظهرت نتائج الدراسة أن معدل ترسيب كريات وبروتين سي أعلي في الفئة العمرية اكبر من ٤٠ سنة.

وكذلك أوضحت الدراسة وجود فرق ذو دلالة إحصائية في معدل ترسيب كريات الدم الحمراء وبروتين سي المتفاعل مقارنة مع المجموعة الضابطة.

List of abbreviation

ANF	Anti nuclear factor.
BSA	Bovine serum albumin
CD4	Cluster of differentiation
CRP	C-reactive protein.
COPD	Chronic obstructive pulmonary disease .
DAS	Disease activity score
DMARDS	Disease modifying anti rheumatic drugs.
EDTA	Ethylene di amine tetra acetic acid
ESR	Erythrocyte sedimentation rate
HS-CRP	High sensitivity –C-reactive protein
IBD	Inflammatory bowel disease.
RA	Rheumatoid arthritis.s
RANKL	Receptor activator of nuclear factor Kappa B linked.
RF	Rheumatoid factor.
SLE	Systemic lupus erythromatous.
SPSS	Statistical package for the social sciences.
Th	T helper.

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Chapter One

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1.1. Introduction

Erythrocyte sedimentation rate (ESR) and serum of C-reactive protein (CRP) are the acute phase reactants most commonly determined in patients with rheumatic diseases. The indices are affected by different factors, but both of them are applied for evaluation of the disease activity in patients with inflammatory disorders of the musculoskeletal system.

The erythrocyte sedimentation rate (ESR) is the oldest acute phase index. The phenomenon was described by John Hunter [1] and applied as a laboratory test by Edmund Biernacki [2]. Erythrocyte sedimentation rate was probably the most commonly used laboratory test in the 20th century. Currently, the clinical usefulness of ESR is questioned, and the C-reactive protein (CRP) level is widely applied. C-reactive protein was discovered in 1930 by William S. Tilled and Thomas Francis, and the test has experienced a revival in the last two decades due to the discovery of the role of inflammation in atherosclerotic disease [3, 4].

Despite the diminished role of ESR in modern diagnostics, the test is still used in rheumatology. Moreover, some disease activity indices are based on either ESR or CRP. This applies to the indices Disease activity score (DAS and DAS28) used to determine activity of rheumatoid arthritis [5].

The comparative value of ESR and CRP in measuring disease activity was investigated in groups of patients with certain rheumatic disorders. The erythrocyte sedimentation rate and CRP are found to be sensitive markers of disease activity in patients with rheumatoid arthritis, as reviewed by Roof and Stocky [7]. The juvenile arthritis disease activity score is calculated using ESR or CRP, and Nodal et al. [8] found that results of both ways of calculation of the score lead to very similar results. Thus they recommended both of them for assessing disease activity in patients with juvenile idiopathic arthritis. Several other reports indicate similar alterations in ESR and CRP in various diseases including systemic lupus erythromatous (SLE) [9] and rheumatoid arthritis (RA) [10, 11]. different measures are

used for evaluating disease activity in arthritis laboratory tests such as erythrocyte sedimentation rate (ESR) and C-reactive protein(CRP)have been integral part of the clinicians repertoire for many years used are markers of inflammation although there is still no clear consensus on when to use one (CRP) has recently become the mo\re preferred serological marker for evaluating acute disease activity.

The present study was designed to determine the correlation of ESR and CRP in patients admitted to the rheumatologic ward due to various rheumatic disorders

1.2. Rationale

Rheumatoid arthritis is common chronic disease that effects about (1%) of world population.

This study conducted to determine level of C reactive protein Erythrocyte sedimentation rate level with in arthritis patients specifically to help in early diagnosis and ,early treatment to avoid complicated of disease.

This study considers first step can help in diagnosis of arthritis disease. Futuristic we need more studies to clarify correlation between Erythrocyte sedimentation rate and C-reactive protein with in arthritis patients.

1.3. Objectives

1.3.1.General Objectives:

To determine the correlation between erythrocyte sedimentation rate and C-reactive protein in arthritis patients.

1.3.2. Specific objectives:

1. To measure ESR and C-reactive protein in arthritis patients.
2. To correlate the Frequency of arthritis according to age and gender.

Chapter tow

Literature review

2. Literature review

2.1. Definition of Arthritis

Arthritis is a joint disorder featuring inflammation. A joint is an area of the body where two bones meet. A joint functions to allow movement of the body parts it connects. Arthritis literally means inflammation of one or more joints. Arthritis is frequently accompanied by joint pain. Joint pain is referred to as arthralgia.[12]

2.1.1. Arthritis Causes:

The causes of arthritis depend on the form of arthritis. Causes include injury (leading to degenerative arthritis), abnormal metabolism (such as gout and pseudo gout), inheritance (such as in osteoarthritis), infections (such as in the arthritis of Lyme disease), and an overactive immune system (such as rheumatoid arthritis and systemic lupus erythematosus). Treatment programs, when possible, are often directed toward the precise cause of the arthritis.

2.1.2. Arthritis Risk Factors

Risk factors for arthritis include the following:

1. Age: The risk of developing many types of arthritis, including osteoarthritis (the most common type), increases with age.
2. Genetics: Most types of arthritis, including osteoarthritis, rheumatoid arthritis, gout, and ankylosing spondylitis, have a genetic (inherited) component.
3. Gender: Most types of arthritis are more common in females. Some types, such as gout and ankylosing spondylitis, are more common in men.
4. Overweight and obesity: Excess weight predisposes to many types of arthritis due to added wear and tear on the joints.
5. Injuries: Injured joints are more likely to develop osteoarthritis.
6. Infection: Many infections can attack the joints and cause arthritis.
7. Occupation: Occupations involving repetitive movements can predispose to the development of osteoarthritis and other musculoskeletal conditions.[13]

2.1.3. Classification of arthritis:

There are over 100 types of arthritis

There are several diseases where joint pain is primary, and is considered the main feature. Generally when a person has "arthritis" it means that they have one of these diseases, which include:

- Osteoarthritis.
- Rheumatoid arthritis.
- Gout and pseudo-gout.
- Septic arthritis.
- Ankylosing spondylitis.
- Juvenile idiopathic arthritis.
- Still's disease.

Joint pain can also be a symptom of other diseases. In this case, the arthritis is considered to be secondary to the main disease; these include:

- Psoriasis (Psoriatic arthritis).
- Reactive arthritis.
- Ehlers-Dandles Syndrome.
- Haemochromatosis.
- Hepatitis.
- Lyme disease.
- Sjogren's disease.
- Hashimoto's thyroiditis.
- Celiac disease.[14]
- Non-celiac gluten sensitivity.[15][16][17]
- Inflammatory bowel disease (including Crohn's disease and ulcerative colitis).
- Henoch–Schönlein purpura.
- Hyperimmunoglobulinemia D with recurrent fever.

- Sarcoidosis.
- Whipple's disease.
- TNF receptor associated periodic syndrome.
- Granulomatosis with polyangiitis (and many other vasculitis syndromes).
- Familial Mediterranean fever.
- Systemic lupus erythematosus.

An *undifferentiated arthritis* is an arthritis that does not fit into well-known clinical disease categories, possibly being an early stage of a definite rheumatic disease[18] .

The most common types of arthritis is:

2.1.3.1.Osteoarthritis

Osteoarthritis is the most common form of arthritis. It can affect both the larger and the smaller joints of the body, including the hands, wrists, feet, back, hip, and knee. The disease is essentially one acquired from daily wear and tear of the joint; however, osteoarthritis can also occur as a result of injury. In recent years, some joint or limb deformities, such as knock-knee or acetabular overcoverage or dysplasia, have also been considered as a predisposing factor for knee or hip osteoarthritis. Osteoarthritis begins in the cartilage and eventually causes the two opposing bones to erode into each other. The condition starts with minor pain during physical activity, but soon the pain can be continuous and even occur while in a state of rest. The pain can be debilitating and prevent one from doing some activities. Osteoarthritis typically affects the weight-bearing joints, such as the back, knee and hip. Unlike rheumatoid arthritis, osteoarthritis is most commonly a disease of the elderly. More than 30 percent of women have some degree of osteoarthritis by age 65. Risk factors for osteoarthritis include prior joint trauma, obesity, and a sedentary lifestyle.[19]

2.1.3.2.Rheumatoid arthritis:

Bone erosions by rheumatoid arthritis.

Rheumatoid arthritis (RA) is a disorder in which the body's own immune system starts to attack body tissues. The attack is not only directed at the joint but to many other parts of the body. In rheumatoid arthritis, most damage occurs to the joint lining and cartilage which eventually results in erosion of two opposing bones. RA often affects joints in the fingers, wrists, knees and elbows, is symmetrical (appears on both sides of the body), and can lead to severe deformity in a few years if not treated. RA occurs mostly in people aged 20 and above. In children, the disorder can present with a skin rash, fever, pain, disability, and limitations in daily activities. With earlier diagnosis and aggressive treatment, many individuals can lead a better quality of life than if going undiagnosed for long after RA's onset. The drugs to treat RA range from corticosteroids to monoclonal antibodies given intravenously. Treatments also include analgesics such as NSAIDs and disease-modifying antirheumatic drugs (DMARDs), while in rare cases, surgery may be required to replace joints, but there is no cure for the disease[20]

Treatment with DMARDs is designed to initiate an adaptive immune response, in part by CD4+ T helper (Th) cells, specifically Th17 cells.[Th17 cells are present in higher quantities at the site of bone destruction in joints and produce inflammatory cytokines associated with inflammation, such as interleukin-17 (IL-17).[21]

Bone erosion is a central feature of rheumatoid arthritis. Bone continuously undergoes remodeling by actions of bone resorbing osteoclasts and bone forming osteoblasts. One of the main triggers of bone erosion in the joints in rheumatoid arthritis is inflammation of the synovium, caused in part by the production of pro-inflammatory cytokines and receptor activator of nuclear factor kappa B ligand (RANKL), a cell surface protein present in Th17 cells and osteoblasts.[20] Osteoclast activity can be directly induced by osteoblasts through the RANK/RANKL mechanism.[22]

2.1.3.3. Lupus

Lupus is a common collagen vascular disorder that can be present with severe arthritis. Other features of lupus include a skin rash, extreme photosensitivity, hair loss, kidney problems, lung fibrosis and constant joint pain.[23]

2.1.3.4.Gout

Gout is caused by deposition of uric acid crystals in the joint, causing inflammation. There is also an uncommon form of gouty arthritis caused by the formation of rhomboid crystals of calcium pyrophosphate known as pseudo gout. In the early stages, the gouty arthritis usually occurs in one joint, but with time, it can occur in many joints and be quite crippling. The joints in gout can often become swollen and lose function. Gouty arthritis can become particularly painful and potentially debilitating when gout cannot successfully be treated.[24] When uric acid levels and gout symptoms cannot be controlled with standard gout medicines that decrease the production of uric acid (e.g., allopurinol, febuxostat) or increase uric acid elimination from the body through the kidneys (e.g., probenecid), this can be referred to as refractory chronic gout or RCG.

2.1.3.5.Comparison of types

Comparison of some major forms of arthritis[25]

	Osteoarthritis	**Rheumatoid arthritis**	**Gouty arthritis**
Speed of onset	Months	Weeks-months[26]	Hours for an attack[27]
Main locations	Weight-bearing joints (such as knees, hips, vertebral column) and hands	Hands (proximal interphalangeal and metacarpophalangeal joint) wrists, ankles, knees and hips	Great toe, ankles, knees and elbows

Inflammation	May occur, though often mild compared to inflammation in rheumatoid arthritis	Yes	Yes
Radiologic changes	• Narrowed joint space • Osteophytes • Local osteosclerosis • Subchondral cysts	• Narrowed joint space • Bone erosions	• "Punched out" bone erosions
Laboratory findings	None	Anemia, elevated ESR and C-reactive protein (CRP), rheumatoid factor, anti-citrullinated protein antibody	Crystal in joints
Other features	• No systemic signs • Bouchard's and Heberden's nodes	• Extra-articular features are common • Ulnar deviation, swan neck- and Boutonniere deformity of the hand	• Tophi • Nephrolithiasis

2.1.3.6.Other

Infectious arthritis is another severe form of arthritis. It presents with sudden onset of chills, fever and joint pain. The condition is caused by bacteria elsewhere in the body. Infectious arthritis must be rapidly diagnosed and treated promptly to prevent irreversible joint damage.[28]

Psoriasis can develop into psoriatic arthritis. With psoriatic arthritis, most individuals develop the skin problem first and then the arthritis. The typical features are of continuous joint pains, stiffness and swelling. The disease does recur with periods of remission but there is no cure for the disorder. A small percentage develop a severe painful and destructive form of arthritis which destroys the small joints in the hands and can lead to permanent disability and loss of hand function.[29]

2.1.4.Signs and symptoms

Pain, which can vary in severity, is a common symptom in virtually all types of arthritis. Other symptoms include swelling, joint stiffness and aching around the joint(s). Arthritic disorders like lupus and rheumatoid arthritis can affect other organs in the body, leading to a variety of symptoms.[29] Symptoms may include:

- Inability to use the hand or walk
- Stiffness, which may be worse in the morning, or after use
- Malaise and fatigue
- Weight loss
- Poor sleep
- Muscle aches and pains
- Tenderness
- Difficulty moving the joint

It is common in advanced arthritis for significant secondary changes to occur. For example, arthritic symptoms might make it difficult for a person to move around and/or exercise, which can lead to secondary effects, such as:

- Muscle weakness
- Loss of flexibility
- Decreased aerobic fitness

These changes, in addition to the primary symptoms, can have a huge impact on quality of life.

2.1.5. Disability

Arthritis is the most common cause of disability in the United States. More than 20 million individuals with arthritis have severe limitations in function on a daily basis.[30] Absenteeism and frequent visits to the physician are common in individuals who have arthritis. Arthritis can make it very difficult for individuals to be physically active and some become home bound.

It is estimated that the total cost of arthritis cases is close to $100 billion of which almost 50% is from lost earnings. Each year, arthritis results in nearly 1 million hospitalizations and close to 45 million outpatient visits to health care centers.[31]

Decreased mobility, in combination with the above symptoms, can make it difficult for an individual to remain physically active, contributing to an increased risk of obesity, high cholesterol or vulnerability to heart disease.[32] People with arthritis are also at increased risk of depression, which may be a response to numerous factors, including fear of worsening symptoms[33].

2.1.6.Diagnosis

Diagnosis is made by clinical examination from an appropriate health professional, and may be supported by other tests such as radiology and blood tests, depending on the type of suspected arthritis. All arthritides potentially feature pain. Pain patterns may differ depending on the arthritides and the location. Rheumatoid arthritis is generally worse in the morning and associated with stiffness; in the early stages, patients often have no symptoms after a morning shower. Osteoarthritis, on the other hand, tends to be worse after exercise. In the aged and children, pain

might not be the main presenting feature; the aged patient simply moves less, the infantile patient refuses to use the affected limb.

Elements of the history of the disorder guide diagnosis. Important features are speed and time of onset, pattern of joint involvement, symmetry of symptoms, early morning stiffness, tenderness, gelling or locking with inactivity, aggravating and relieving factors, and other systemic symptoms. Physical examination may confirm the diagnosis, or may indicate systemic disease. Radiographs are often used to follow progression or help assess severity.

Blood tests and X-rays of the affected joints often are performed to make the diagnosis. Screening blood tests are indicated if certain arthritides are suspected. These might include: rheumatoid factor, antinuclear factor (ANF), extractable nuclear antigen, and specific antibodies.[34]

2.1.6.1.Blood Tests to Diagnose Arthritis

In people with osteoarthritis, blood tests are not usually abnormal, but with other types of arthritis, including rheumatoid arthritis, certain tests will help with a proper diagnosis.

-Blood markers Are Used to Diagnose Rheumatoid Arthritis:Rheumatoid factors are a variety of antibodies that are present in 70% to 90% of people with rheumatoid arthritis (RA). Rheumatoid factor (RF), however, can be found in people without RA or with other autoimmune disorders. In general, when no rheumatoid factor is present in someone with RA, the course of the disease is less severe.

2.1.6.2.Erythrocyte sedimentation rate test:

The erythrocyte sedimentation rate (ESR) reflects the degree of inflammation in the body. In healthy people, the ESR is low and it climbs with inflammation. It doesn't point to any particular disease, but is a general indication of the amount of inflammation in the body. In lupus and polymyalgia rheumatica, the ESR often correlates with disease activity.[35]

2.1.6.3.C-reactive protein:

C-reactive protein (CRP) levels are an even better indication than ESR of the amount of inflammation present. In people with rheumatoid arthritis, if the CRP is high, it suggests that there is significant inflammation or injury in the body.

Both CRP and ESR levels are used to monitor disease activity and To monitor how well someone is responding to treatment.

2.2. Erythrocyte sedimentation Rate:

Erythrocyte Sedimentation Rate is a type of blood test that measures how quickly erythrocytes (red blood cells) settle at the bottom of a test tube that contains a blood sample. Normally, red blood cells settle relatively slowly. A faster-than-normal rate may indicate inflammation in the body. Inflammation is part of your immune response system. It can be a reaction to an infection or injury. Inflammation may also be a sign of a chronic disease, an immune disorder, or other medical condition.[36]

Other names: ESR, SED rate sedimentation rate; Westergren sedimentation rate

An ESR test can help determine if you have a condition that causes inflammation. These include arthritis, vasculitis, or inflammatory bowel disease. An ESR may also be used to monitor an existing condition

results mean

- Infection.
- Rheumatoid arthritis.
- Rheumatic fever.
- Vascular disease.
- Inflammatory bowel disease.
- Heart disease.
- Kidney disease.
- Certain cancers.

Sometimes the ESR can be slower than normal. A slow ESR may indicate a blood disorder, such as:

- Polycythemia.
- Sickle cell anemia.
- Leukocytosis, an abnormal increase in white blood cells[37].
- If your results are not in the normal range, it doesn't necessarily mean you have a medical condition that requires treatment. A moderate ESR may indicate pregnancy, menstruation, or anemia, rather than an inflammatory disease. Certain medicines and supplements can also affect your results. These include oral contraceptives, aspirin, cortisone, and vitamin A. Be sure to tell your health care provider about any drugs or supplements you are taking.
- An ESR does not specifically diagnose any diseases, but it can provide information about whether or not there is inflammation in your body. If your ESR results are abnormal, your health care provider will need more information and will likely order more lab tests before making a diagnosis.[38]

2.3. C-reactive protein:

C-reactive protein (CRP) is a substance produced by the liver in response to inflammation. Other names for CRP are high-sensitivity C-reactive protein (hs-CRP) and ultra-sensitive C-reactive protein (us-CRP).

A high level of CRP in the blood is a marker of inflammation. It can be caused by a wide variety of conditions, from infection to cancer. High CRP levels can also indicate that there's inflammation in the arteries of the heart, which can mean a higher risk for heart attack. However, it's important to remember that the CRP test is an extremely nonspecific test, and CRP levels can be elevated in any inflammatory condition.CRP is first acute –phase protein to be describe d and is an exquisitely sensitive systemic marker of inflammation and tissue damage . The acute- phase response comprises the non specific physiological and biochemical

response of endothermic animals to most form of tissue damage ,infection ,inflammation ,and malignant neoplasia.[39] [40].The serum C RP level may arise from anormal level may arise from anormal level of (5mg/l to 500mg/l) during the body's general. Non- specific response to infectious and other acute inflammatory events. For some time ,the measurement of CRP concentration has been used is aclinical tool for monitoring auto immune disease and infectious processes, such as rheumatoid arthritis.[41] [42].

2.3.1.high CRP:

high CRP levels and an increased likelihood for heart attack or stroke.

The Physicians' Health Study found that among healthy adult men, those with a high level of CRP were three times more likely to have a heart attack than those with low levels of CRP. This was among men who had no previous history of heart disease. According to the Cleveland Clinic, the Harvard Women's Health Study showed that high CRP levels were more predictive of coronary conditions and stroke in women than were high cholesterol levels. High cholesterol is a more commonly cited risk factor. The Jackson Heart Study found that hs-CRP may play a role in the development of type 2 diabetes in African-Americans.

There is also new research that suggests CRP may be used as a predictor in health outcomes related to chronic obstructive pulmonary disease (COPD). Doctors may also order a CRP test to diagnose inflammatory autoimmune diseases, including:

- inflammatory bowel disease. (IBD)
- rheumatoid arthritis.
- lupus.

2.3.2.risks with the test:

- This is a routine test with low risk, but there's a slight chance of the following complications from the blood draw:
- Excessive bleeding.
- Dizziness or lightheadedness.

- Bruising or infection at the puncture site.

A CRP test can be helpful in assessing a person's risk of heart disease, especially in combination with high cholesterol levels. The benefits of this test outweigh potential complications, especially for those at risk for heart disease or stroke and those recovering from recent heart procedures.[43]

Results mean:

C-reactive protein is measured in milligrams of CRP per liter of blood (mg/L). In general, a low C-reactive protein level is better than a high one, because it indicates less inflammation in the body.

According to the Cleveland Clinic, a reading of less than 1 mg/L indicates you're at low risk of cardiovascular disease. A reading between 1 and 2.9 mg/L means you're at intermediate risk. A reading greater than 3 mg/L means you're at high risk for cardiovascular disease. A reading above 10 mg/L may signal a need for further testing to determine the cause of such significant inflammation in your body.

An CRP reading of greater than 10 mg/L is especially high and may indicate:

- a bone infection, or osteomyelitis.
- An autoimmune arthritis flare-up.
- IBD.
- Tuberculosis.
- lupus, connective tissue disease, or other autoimmune diseases.
- cancer, especially lymphoma.
- pneumonia or other significant infection.

Remember CRP levels may also be elevated if you're on birth control pills. However, other markers of inflammation are not necessarily abnormal in these individuals. Elevated CRP values in pregnancy may be a marker for complications, but more studies are necessary to fully understand the role of CRP and pregnancy.

If you're pregnant or have any other chronic infection or inflammatory disease, a CRP test is unlikely to accurately assess your risk for heart disease. Before having a CRP test, speak to your doctor about any medical conditions that may skew the test results. Since there are other blood tests that can be performed instead, you might wish to forego a CRP test altogether.[44]

2.3.3. Previous studies:

-Study done by Anna Kotulska, MagdalenaKopec-Medrek,and Eugeniusz J.Kuc harz showed asignificant correlation between ESR and CRP was fsound (ESR after 1 h/CRP:correlation coefficient 0.6944, ESR after 2 h/CRP:correlation coefficient 0.6126).

- Study done by LWalsh, PDavies, and B McConnkey showed Neither age nor duration of RA influenced ESR or serum CRP level, or relationship between the 2 values. There was apossitive correlation between ESR and CRP.

-Study done by Wolfe F.JRheumatol.1997. show the median values for CRP were 0.82mg/dl and ESR26mm/h. the average correlation with 7 clinical variables was0.248 for ESR compared to 0.259 for CRP . but partial correlation analysis showed that asubstantial portion of the correlation with ESR is explained by effect of immunoglobulins RF, and hemoglobin rather than the acute phase response. twenty–eight percent of result were discordant was explained by the above factors. When discordance occurred, CRP was better measure of disease activity than ESR.

Chapter three

Material and method

3. Material and methods

3.1.Study design:

This cross sectional case control study to correlate erythrocyte sedimentation rate and C-reactive protein which conducted in shendi locality River Nile state during the period of (March to May 2018) in patient suffering from arthritis disease,

3.2.Study area :

This study was conducted at Shendi town Shendi is a town in Northern Shendi is also about (45Km) southwest of the ancient city of Meroe .Located in the River Nile State ,Shendi is the center of the Ja'aliin tribe .any b00an important historic trading center. It's principal suburb on the west bank is Al-Matamma. A major traditional trade route across the Bayuda desert connects Al-Matamma to Marawi and Napata, (250Km) to the Northwest.

3.3.Study population:

A total of (50) patients with arthritis disease as test group and (25) healthy individuals as control group.

3.4. Inclusion criteria:

a. patients of both sexes with arthritis disease(Who take drugs or not take),

b. adult and children

3.5. Exclusion criteria:

a. Patients with other sever diseases such as renal failure, liver disease, hematological diseases and other medical conditions or receiving certain treatment that affect the results were excluded from study.

b. infants.

c.pregnant women.

3.6. Data collection tools:

Data was collected using questionnaire which specifically designed to obtain information that helped in study.

3.7.Sample processing:

Venous blood collected using sterile disposable plastic syringe after cleaning the vein puncture area with (70%) ethanol , 2.5ml of venous blood for ESR citrated blood was added to the anticoagulant and gently mix, while CRP blood was collected in EDTA. The sample centrifuge at (1300rpm) for (15min) to obtain plasma for (CRP). But the (ESR) put in tube do not need centrifuge.

3.8. Methods:

3.8.1. C-reative protein:

3.8.1.1. Principle

The test uses a sandwich immunodetection method, such that the detector antibody in buffer binds to CRP in sample and antigen-antibody complexes are captured to another CRP antibody that has been immobilized on test strip as sample mixture migrates nitrocellulose matrix. Thus the more CRP antigen in sample, the more antigen-antibody complexes accumulated on the test strip. Signal intensity of fluorescence on detector antibody reflects the amount of antigen captured and is processed by ichroma™ Reader to show CRP concentration in specimen. [53] [54]

3.8.1.2. Reference Range: < 10 mg/L

3.8.1.3. Components and reagents:

Ichroma™ CRP consists of a 'Test cartridge', an 'ID chip', a Blood Collecting Capillary, and a 'Detection buffer tube'

- The test cartridge contains a test strip; on the membrane of which, murine antibodies against CRP and rabbit IgG have been immobilized at the test line and the control line respectively.
- Each test cartridge is individually sealed in an aluminum foil pouch containing a desiccant. (25) Sealed test cartridges are packed in a box which also contains an ID chip.
- The detection buffer pre-dispensed in a tube contains fluorochrome-labeled anti-CRP antibodies, fluorescent-labeled anti-rabbit IgG, bovine serum albumin (BSA)

as a stabilizer and sodium azide in phosphate buffered saline (PBS) as a preservative.

- The detection buffer is dispensed in each detection buffer tube. (25) detection buffer tubes are packed in a separate box which is further packed in a Styrofoam box provided with ice packs for the purpose of shipment.
- Blood collection capillary is used for picking up (10 μL) of whole blood, serum, plasma, or control solution.[55] [56]

3.8.1.4. Test procedure:

1. Collect the blood in EDTA container and then centerfuge the sample.
2. Take 10mm from serum by the sample collector capillary.
3. The excess serum wipes out outside of the capillary with paper towel.
4. Assembled the capillary into the detection buffer tube.
5. Shaking the sample with the detection buffer 10times or for 30sec.
6. Discard two drops from the mixture onto the paper towel before applying to the cartridge.
7. Apply only two drops onto the sample well of a cartridge
8. Insert it into the test cartridge holder of the ichroma™ Reader.
9. ichroma™ Reader will start scanning the sample-loaded test cartridge after 3 minutes.
10. The test result was read on the display screen of the ichroma™ reader. [57][58].

3.8.2. ESR test:

3.8.2.1. Principle:

When anti coagulated blood is allowed to stand in a narrow vertical glass tube, undisturbed for a period of time, the RBCs – under the influence of gravity- settle out from the plasma. The rate at which they settle is measured as the number of millimeters of clear plasma present at the top of the column after 1/2 hour (mm/1/2hr). This mechanism involves three Stage:

Stage of aggregation: It is the initial stage in which piling up of RBCs takes place. The phenomenon is known as Rouleaux formation. It occurs in the first 10-15 minutes. Stage of sedimentation: It is the stage of actual falling of RBCs in which sedimentation occurs at constant rate. , depending upon the length of the tube used. Stage of packing : This is the final stage and is also known as stationary phase. In this, there is a slower rate of falling during which packing of sedimented RBCs in column occurs due to overcrowding. It occurs in final 10 minutes in 1/2hour.

3.8.2.2. Materials:

- Streck ESR vacuum tubes
- Streck ESR-10 Manual Rack
- Disposable plastic pipets
- ESR-Chex Assayed Hematology Controls
- Calibrated Timer

3.8.2.3. Test Procedure:

1. Collect blood in EDTA-lavender top vacutainer tube.
2. Withdraw blood from lavender-top tube using disposable plastic pipette, and fill vacuum tube to fill line indicated on label.
3. Replace stopper and mix by thoroughly inverting 6-8 times. Place tube in upright position in the ESR-10 rack with the menicus of the blood-air interface level with the zero measurement on the rack.
4. Insure that the bubble on the ESR-10 rack is centered , indicating rack is on level surface. Adjust rack if needed.
5. Set timer for 30 minutes.
6. Read ESR making sure that your eyes on the same horizontal level as the rack since reading at an angle will result in error.

3.8.2.4. Reference Range:

Men0-21 mm/hr

Women 0-28 mm/hr

3.9. Ethical consideration:

The consent of the selected individuals to the study was taken after being informed with all detailed objectives of the study and it is health emphasis in the future.

3.10. Data analysis:

The collected data code in master sheet and proceed for analysis using (SPSS) program. (mean, standard deviation, standard error mean, P.value by using independent T.test).

Chapter four

Results

4. Results

In this study the mean of (ESR) value in test group was (71.08mm/1h), while the mean in control group was(18.96mm/1/2h) as demonstrated in table (4-1).

Also in this study the mean of (CRP) value in test group was (17.8mg/l), while in control group was (2.87mg/l) as demonstrated in table (4-2).

ESR mean:

The mean of (ESR) in age group of (20-40years) was (73mm/1h), while in age group of (41-60years) was (72.65mm/1h), and in age group more than (60 years) was (69.2mm/1h) as noted in table (4-3). The mean of (ESR) value in male was (73.36mm/1h), while in female was (70.44mm/1h) which noted in table (4-.4).

Also the mean of (ESR) value in people suffer from other chronic disease was (70.95mm/1h), while in those no having chronic disease was (71.18mm/1h) as demonstrated in table (4-5).

Also the mean of (ESR) value in people take drugs was (70.95mm/1h), while people that don't take drugs were (71.18mm/1h) as noted in table (4-6).

The mean of (ESR) according of duration of disease less than one years was (76.9mm/1h), while in duration from (1-15) years was (70.08mm/1h), and in the duration from (16-30) years was (64mm/1h) as demonstrated in table (4-7).

Also in this study the mean of (ESR) value in people with tonsillitis was (97.5mm/1h), while no having tonsillitis was (69.98mm/1h) as noted in table (4-8),

The mean of (CRP) in age group of (20-40) years was (20.27 mg/l),while in age group of (41-60) years was (22.72mg/l),and in age group more than (60 years) was (12.49mg/l) as noted in table (4-9).

The mean of (CRP) value in male was (13.66mg/l), while in female was (18.99mg/l) as noted in table (4-10).

In the present study the mean of (CRP) value in people suffer from other chronic disease was (14.85 mg/l), while in those no having chronic disease was (20.15mg/l) as demonstrated in table (4-11).

Also the mean of (CRP) value in people take drugs was (14.85mg/l), while in people don't take drugs was (20.15mg/l) as noted in table (4-12).

The mean of (CRP) according of duration of disease less than one years was (46.8mg/l), while in duration from (1-15) years was (11.09mg/l), and in the duration from (16-30) years was (4.21mg/l) as demonstrated in table (4-13).

Also in this study the mean of (CRP) value in people with tonsillitis was (52.52mg/l), while in those no having tonsillitis was (16.37mg/l) as noted in table (4-14).

Table (4-1) Show the mean of ESR in test and control group:

ESR	N	Mean	Std. Deviation	Std. Error Mean
Test	50	71.08	21.529	3.045
Control	25	18.96	10.175	2.035

Table (4-2) Show the mean of CRP in test and control group:

CRP	N	Mean	Std. Deviation	Std. Error Mean
Test	50	17.8242	35.67897	5.04577
Control	25	2.8748	.74883	.14977

Table (4-3) Show the mean of ESR according to age :

Age groups	Mean	N	% of Total N
20-40yrs	73.00	4	8.0%
41-60yrs	72.65	23	46.0%
60+ yrs	69.17	23	46.0%
Total	71.08	50	100.0%

Table (4-4) Show the mean of ESR according to sex:

Sex	Mean	N	% of Total N
Male	73.36	11	22.0%
Female	70.44	39	78.0%
Total	71.08	50	100.0%

Table (4-5) Show the mean of ESR according to chronic disease :

Chronic diseases	Mean	N	% of Total N
Yes	70.95	22	44.0%
No	71.18	28	56.0%
Total	71.08	50	100.0%

Table (4- 6) Show the mean of ESR according to drugs in take :

Drugs	Mean	N	% of Total N
Yes	70.95	22	44.0%
No	71.18	28	56.0%
Total	71.08	50	100.0%

Table (4-7) Show the mean of ESR according to duration of disease:

Duration	Mean	N	% of Total N
Less than 1yrs	76.90	10	20.0%
1-15yrs	70.08	37	74.0%
16-30yrs	64.00	3	6.0%
Total	71.08	50	100.0%

Table (4-8) Show the mean of ESR according to tonsillitis:

Tonsillitis	Mean	N	% of Total N
Yes	97.50	2	4.0%
No	69.98	48	96.0%
Total	71.08	50	100.0%

Table (4-9) Show the mean of CRP according to age:

Age groups	Mean	N	% of Total N
20-40yrs	20.2775	4	8.0%
41-60yrs	22.7278	23	46.0%
60+ yrs	12.4939	23	46.0%
Total	17.8242	50	100.0%

Table (4-10) Show the mean the mean of CRP according to sex:

Sex	Mean	N	% of Total N
Male	13.6682	11	22.0%
Female	18.9964	39	78.0%
Total	17.8242	50	100.0%

Table (4-11) Show the mean of CRP according to chronic disease:

Chronic diseases	Mean	N	% of Total N
Yes	14.8573	22	44.0%
No	20.1554	28	56.0%
Total	17.8242	50	100.0%

Table (4-12) Show the mean of CRP according to drugs in take:

Drugs	Mean	N	% of Total N
Yes	14.8573	22	44.0%
No	20.1554	28	56.0%
Total	17.8242	50	100.0%

Table (4-13) Show the mean of CRP according to duration of disease:

Duration	Mean	N	% of Total N
Less than 1yrs	46.8040	10	20.0%
1-15yrs	11.0957	37	74.0%
16-30yrs	4.2100	3	6.0%
Total	17.8242	50	100.0%

Table (4-14) Show the mean of CRP according to tonsillitis:

Tonsillitis	Mean	N	% of Total N
Yes	52.5200	2	4.0%
No	16.3785	48	96.0%
Total	17.8242	50	100.0%

Chapter five

Discussion

Conclusion

Recommendations

5.1. Discussion

The arthritis disease that inflammatory condition, is very common but is not well understood actually, it's not a single disease, it is an informal way of referring to joint pain or joint disease.

The results of this study obtained demonstrated that the mean of (ESR) value in test group is higher, when compared with the control group. Statistical analysis show that there was significant varation. This result was similar to the result of study conducted by Lwalsh, P Davies and B McConnkey (50).

While the mean of (CRP) value in test group was also higher when compared with the control group which is low. Statistical analysis demonstrated that there was strong significant variation. This result was similar to the result of study conducted by L walsh, P Davies and B McConnky. (50)

The mean of (ESR) in age group of (20-40) years and (41-60) years is above from age group more than 60years. Statistical analysis noted that there was no significant variation. This result was similar to the result of study done by Anna Kotulska and his colleagues in USA at 2015 showed that, the patient older than 40 years had higher (ESR) (49).

While the mean of (CRP) for the age group of (20-40) years and (41-60) years is higher than that of age more than 60 years. Statistical analysis demonstrated that there was no significant variation. This result was similar to the result of study done by Anna Kotulska, Magdalenakope and his colleagues in USA at 2015 showed the patients older than 40years had higher CRP (49).

The present study revealed that the mean of (ESR) in male and female present simple different. Statistical analysis indicated that there was no significant variation. This result are similar to the result study done by Anna Kotulska, Magdalena and his colleagues' (49) in USA at 2015 whom revealed that there was no difference in (ESR) between male and female patients.

The mean of (CRP) in male and female demonstrated by present of simple difference. Statistical analysis noted that there was no significant variation .This result are similar to the results done by Anna Kotulska, Magdolena and his colleagues in USA at 2015 whom revealed that there was no difference in (CRP) between male and female patients.

The outcome of result obtained that the chronic diseases and drugs intake not affect in arthritis patients , The mean of (ESR) value in patients with chronic diseases and those whose intake drugs is similar to those whom are healthy and doesn't intake drugs. Statistical analysis demonstrated that there was no significant variation.

Also the present study denoted that the mean of (CRP) value in patients with chronic diseases and in those intake drugs was lower than that in patients whom don't suffer from chronic diseases and those whom don't intake drugs. Statistical analysis showed that there was no significant variation. The mean of (ESR) according to duration of disease less than one year is higher than duration from (1-15) years, and the duration from (16-30) years. Statistical analysis showed that there was no significant variation.

The mean of (CRP) according to duration of the disease less than one year also is higher than other durations. Statistical analysis noted that there was no significant variation. Also in this study the mean of (ESR) value of patients have tonsillitis is greater than those doesn't had tonsillitis. Statistical analysis noted that there was no significant variation.

Also in this the mean of (CRP) value of patients have tonsillitis disease above than that in patients whose don't have tonsillitis. Statistical analysis noted that there was no significant variation.

This study clarified there is strong correlation between ESR, CRP and arthritis disease.

5.2. Conclusion

By the end of this study we conclude that:

- Serum C-reactive protein level and ESR value was higher in arthritis patients compared to healthy individual.
- The arthritis disease was wide distributing in female rather than male.
- Serum C-reactive protein level and ESR value was higher in older age more than 40 years.
- The duration of arthritis disease can be effect in ESR and CRP.
- The ESR and CRP level have no effect by chronic disease and drugs intake.

5.3. Recommendations

1. Erythrocyte sedimentation rate and C-reactive protein tests should be checked regularly in arthritis patients.
2. The research in this topic should be continued with large sample size study with more sensitive by new markers should be conducted.
3. Large sample size with more sensitive biomarker should be conducted

Chapter Six

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Appendix

6.1. References

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6.1. Appendix

Questionnaire

University of Shendi

Faculty of post –graduate Studies

Faculty of medical laboratory sciences

Determination of the Correlation between Erythrocyte Sedimentation rate and C-reactive protein in arthritis patients:-

Age:

Sex:

Tribe:

Presence of Chronic disease:

Arthritis disease history:

Drugs intake:

Tonsillitis:

Result:

ESR:

CRP:

Appendix 11

إقـــرار بالموافقة

الاسم :----------

العمر :---------- العنوان :----------

أوافق بمحض إرادتي بالمشاركة في البحث العلمي المتعلق بدراسة معرفة العلاقة بين معدل ترسيب كريات الدم الحمراء وبروتين سي في مرضى التهاب المفاصل

إلطاف عبد الله صديق البشير

بعد أن شرح لي بأنه لا يترتب عليه أي أذى جسدي أو نفسي واعلم أن المشاركة فـــي هـــذا البحث لن تؤثر بأي حال من الأحوال في الرعاية الطبية التي أتلقاها كما أنه يحق لي بـــدون إبداء أسباب الانسحاب من هذا البحث في أي مرحلة من مراحله.

البحث بإشراف:

د.محمد عثمان علي

التوقيع: ----------

التاريخ:----------