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CLINICAL EVALUATION OF PATIENTS SUFFERING FROM RHEUMATOID ARTHRITIS WITH RESPECT TO IRON DEFICIENCY

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Abstract
Iron deficiency results in the decreased synthesis of important molecules including iron containing enzymes thereby inducing cellular organic functional disturbances. If not corrected in a timely manner, iron deficiency anemia (IDA) will ensue. The consequences of iron deficiency anemia (IDA) range from impaired psychological and physical well-being and decreased occupational abilities to developmental troubles in children and increased morbidity and mortality in some patient populations. Moreover, iron deficiency is a risk factor in various medical settings because it impedes erythropoietic response to acute and chronic anemia. Hence based on above findings the present study was planned to evaluate the levels of iron in rheumatoid

The present study was planned in Department of General Medicine, All India Institute of Medical Sciences, Patna from jan 2018 to june 2018. Group A consist of 30 informed male and female consented patients diagnosed with Rheumatoid arthritis were enrolled for the study. The group B consist of 30 control patients for comparative evaluation.

Hence from present study it can be concluded that, there is no known prevention for iron deficiency anaemia in rheumatoid arthritis (RA) patients other than the reduction of contributory factors. Therapy goals are to reduce pain and inflammation and improve quality of life. Surgery to repair, replace or fuse joints may help in serious conditions.
Keywords: Rheumatoid Arthritis, Iron Deficiency, Heamoglobon,Iron, etc.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks flexible joints. It usually affects the small joints of hands and feet. It is a form of autoimmune disorder, the causes of which are still incompletely known. It occurs when the immune system mistakenly attacks own body's tissues. Rheumatoid arthritis affects the lining of joints called synovial membrane, causing a painful swelling that can eventually result in bone erosion and joint deformity. Synovial membrane is the soft tissue present in the joints that secrete a clear viscous lubricating fluid. In addition to causing joint problems, rheumatoid arthritis sometimes can affect other organs of the body — such as the skin, eyes, lungs and blood vessels. About 1% of the world population is afflicted by rheumatoid arthritis, women three times more often than men. Onset is most frequent between the ages of 40 and 50, but people of any age can be affected.[1]

Rheumatoid arthritis (RA) is a long-term autoimmune disorder that primarily affects joints. It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest.[1] Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body. The disease may also affect other parts of the body. This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart. Fever and low energy may also be present.[2] Often, symptoms come on gradually over weeks to months.[3]

While the cause of rheumatoid arthritis is not clear, it is believed to involve a combination of genetic and environmental factors. The underlying mechanism involves the body's immune system attacking the joints. This results in inflammation and thickening of the joint capsule. It also affects the underlying bone and cartilage.[2] The diagnosis is made mostly on the basis of a person's signs and symptoms.[3] X-rays and laboratory testing may support a diagnosis or exclude other diseases with

similar symptoms.[2] Other diseases that may present similarly include systemic lupus erythematosus, psoriatic arthritis, and fibromyalgia among others.[3]

The goals of treatment are to reduce pain, decrease inflammation, and improve a person's overall functioning. This may be helped by balancing rest and exercise, the use of splints and braces, or the use of assistive devices. Pain medications, steroids, and NSAIDs are frequently used to help with symptoms. Disease-modifying antirheumatic drugs (DMARDs), such as hydroxychloroquine and methotrexate, may be used to try to slow the progression of disease. Biological DMARDs may be used when disease does not respond to other treatments. However, they may have a greater rate of adverse effects. Surgery to repair, replace, or fuse joints may help in certain situations. Most alternative medicine treatments are not supported by evidence.[4]

People with RA are more prone to atherosclerosis, and risk of myocardial infarction (heart attack) and stroke is markedly increased.[6] Other possible complications that may arise include: pericarditis, endocarditis, left ventricular failure, valvulitis and fibrosis.[7] Many people with RA do not experience the same chest pain that others feel when they have angina or myocardial infarction. To reduce cardiovascular risk, it is crucial to maintain optimal control of the inflammation caused by RA (which may be involved in causing the cardiovascular risk), and to use exercise and medications appropriately to reduce other cardiovascular risk factors such as blood lipids and blood pressure. Doctors who treat people with RA should be sensitive to cardiovascular risk when prescribing anti-inflammatory medications, and may want to consider prescribing routine use of low doses of aspirin if the gastrointestinal effects are tolerable.[7]

Anemia is by far the most common abnormality of the blood cells which can be caused by a variety of mechanisms. The chronic inflammation caused by RA leads to raised hepcidin levels, leading to anemia of chronic disease where iron is poorly absorbed and also sequestered into macrophages. The red cells are of normal size and color (normocytic and normochromic). A low white blood cell count usually only occurs in people with Felty's syndrome with an enlarged liver and spleen. The mechanism of neutropenia is complex. An increased platelet count occurs when inflammation is uncontrolled.

The disease progresses by forming granulation tissue at the edges of the synovial lining, pannus with extensive angiogenesis and enzymes causing tissue damage. The synovium thickens, cartilage and underlying bone disintegrate, and the joint deteriorates, with raised calprotectin levels serving as a biomarker of these events.[8]

Cytokines and chemokines attract and accumulate immune cells, i.e. activated T- and B cells, monocytes and macrophages from activated fibroblasts, in the joint space. By signalling through RANKL and RANK, they eventually trigger osteoclast production, which degrades bone tissue. [9]

Tumor necrosis factor alpha (TNF-α) plays a major role and several theories exist on how TNF release happens in RA. TNF-α is a proinflammatory cytokine that plays a pivotal role in regulating the inflammatory response in rheumatoid arthritis (RA).If TNF release is stimulated by B cell products in the form of RF or ACPA -containing immune complexes, through activation of immunoglobulin Fc receptors, then RA can be seen as a form of Type III hypersensitivity. As of 1999, if TNF release is stimulated by T cell products such as interleukin-17 it might be closer to type IV hypersensitivity although this terminology may be getting somewhat dated and unhelpful.[10]

Although TNF appears to be the dominant chemical mediator other cytokines are involved in inflammation in RA, because blocking TNF does not benefit all persons and all tissues, particularly lung disease and nodules may get worse. Blocking IL-1, IL-15 and IL-6 have beneficial effects and IL-17 may be important.[11]

Iron is extremely vital to the human beings because of its indispensable role in oxygen transport, DNA synthesis and electron transport [12]. Consequently vital body functions are conditional on appropriate iron stores. Haemoglobin synthesis is particularly irondependent [13]. The human body contains approximately 3 to 4gm of iron, with haemoglobin accounting for 60% of the body's total iron. Adult

individuals require a relatively constant amount of total body iron. Indeed under usual conditions, very little iron enters or leaves the organism. Iron loss is normally limited to less than 4 mg daily [14] reaching, an average, only 1 mg daily in men and 2 mg in women during the child bearing years. In humans, 80% of the iron demand is related to the daily production of 200 billion new erythrocytes, which requires approximately 20 to 24 mg of iron for the synthesis of hemoglobin. Most of this iron is provided by macrophages through the catabolism of hemoglobin of senescent red blood cells; iron released from aged erythrocytes is recovered from the plasma and delivered to the erythroid marrow [15]. Thus, approximately 90% of iron is the circulation recirculates and there is little iron exchange with other tissues. Iron deficiency is the most common cause of anaemia worldwide. It is estimated that iron-deficiency anaemia (IDA) affects some two billion people causing almost one million deaths each year [16]. Iron deficiency results in the decreased synthesis of important molecules including iron containing enzymes thereby inducing cellular organic functional disturbances. If not corrected in a timely manner, iron deficiency anemia (IDA) will ensue. The consequences of iron deficiency anemia (IDA) range from impaired psychological and physical well-being and decreased occupational abilities to developmental troubles in children and increased morbidity and mortality in some patient populations. Moreover, iron deficiency is a risk factor in various medical settings because it impedes erythropoietic response to acute and chronic anemia.

Hence based on above findings the present study was planned to evaluate the levels of iron in rheumatoid

Methodology:

The present study was planned in Department of General Medicine, All India Institute of Medical Sciences, Patna from jan 2018 to june 2018. Group A consist of 30 informed male and female consented patients diagnosed with Rheumatoid arthritis were enrolled for the study. The group B consist of 30 control patients for comparative evaluation.

Under a septic condition5 millilitres of venous blood will be collected. Then Two milliliters of these were placed in ethylene diethyl tetra acetic acid (EDTA) bottles for haematological analysis. The remaining 3 milliliters were taken into universal bottle and centrifuged at 3000rpm for 5 minutes to obtain the serum for Quantitative serum ferritin.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria:

1. Patients who satisfied the American Rheumatologic association criteria 1987, irrespective of haematological signs present or not.
2. Age group 30 to 55 years irrespective of sex.
3. Duration of disease up to 2 years.

Exclusion criteria:

1. Previously diagnosed anaemia and treated
2. Previously have any other bleeding disorder not related to Rheumatoid arthritis.
3. Previously known malignancies, renal failure, haemolytic anaemia any other chronic blood loss like haemorrhoids.

Results & Discussion:

Anemia is one of the commonest problems associated with RA. It is estimated that anemia can occur in 30% – 60% of patients with RA. Anemia is RA is a result of the inflammation associated with RA. It is believed that these inflamed tissues secrete certain substances called cytokines and other proteins that suppress the production of the hormone erythropoietin (a substance secreted by the kidney that plays a key role in stimulating your bone marrow to produce new blood cells). RBCs typically live for about 120 days after which they are absorbed by your body and replaced by new RBCs. In the absence of erythropoietin your bone marrow does not make adequate amounts of RBCs to replace the ones that are destroyed. This means that your RBCs cannot carry sufficient oxygen to all the cells of your body. Another cause of anemia in RA is due to internal bleeding that may be due to the anti-inflammatory drugs that are prescribed for the management of RA. Long term use of these

medications can cause internal bleeding particularly in the stomach and intestine.

RA primarily starts as a state of persistent cellular activation leading to autoimmunity and immune complexes in both joints and other organs where it manifests. The initial site of disease is synovial membrane, where swelling and congestion leads to infiltration by immune cells. Three phases of progression of RA are an initiation phase, due to non-specific inflammation, an amplification phase, due to Tcell activation and chronic inflammation phase with tissue injury, due to cytokines IL-I,TNF-alpha andIL-6[[17].

The data was collected in the 30 normal patients and 30 rheumatoid arthritis patients and compared as below.

Table 1: Demographic Details

Groups	**Group A**	**Group B**
Variables	**Study Group**	**Control Group**
No. of Patients	30	30
Age: 30 – 40 years 40 – 55 years	 12 18	 10 20
Males	15	18
Females	15	12

Table 2: Serum Findings

Groups	**Group A**	**Group B**
Variables	**Study Group**	**Control Group**
No. of Patients	30	30
Hb (gm%)	9.3 – 9.2	11.9 – 13.8
Serum Iron (mg/dl)	25.3- 34.8	105.9 – 148.2
Serum TIBC (mg/dl)	85 – 128	298 – 365
Serum Ferritin (ng/ml)	16.5 – 42.9	107.5 – 141.3

Anemia, which was formerly common in patients with rheumatoid arthritis (RA), has become much less common since the 1990s, mainly since the introduction of the newer drugs. In one analysis, the prevalence of anemia decreased between 2001 and 2007 [18].

Among the most prevalent hematologic abnormalities in patients with rheumatologic disorders are the anemia of chronic disease (ACD), a mild anemia that is generally asymptomatic, and iron deficiency anemia [19-20]. A 2008 study of 111 patients with early RA reported the prevalence of ACD to be 25 percent during the first year of disease [21]. Other forms of anemia occur less commonly.

One type — called anemia of chronic disease, or ACD — is a major cause of anemia in people with RA. In one study of 225 RA patients, ACD accounted for 77 percent of the observed anemia. It's also the most common form of anemia in lupus patients.

Also called anemia of inflammation, ACD affects people who have conditions that cause inflammation, such as infections, cancer, chronic kidney disease, and autoimmune diseases (like RA or lupus).

With ACD, you may have normal or sometimes increased amounts of iron stores in your body tissue, but a low level of iron in your blood. Chronic inflammation may prevent your body from using the stored iron to create new red blood cells, which leads to anemia. Inflammation can also affect the way your body produces a specific hormone called erythropoietin, which controls the production of red blood cells. A 2008 study of 111 patients with early RA reported the prevalence of ACD to be 25 percent during the first year of disease. [22]

The study by Ogedegbe et al.[23] in which they discovered that one of the characteristic features of IDA is a demonstration of microcytic hypochromic RBCs in the peripheral smear. In addition, they found that decreased stores of iron may be demonstrated in the bone marrow aspirate.

In summary, these results indicate that anaemia may serve as predictor of disease activity in RA patients. This report may add clinical background to recent discoveries at the nexus of inflammation, haematopoiesis, and iron metabolism, [24] and highlights the clinical implications of anaemia in RA. Diagnosis of anaemia in RA should prompt a thorough search for subclinical disease activity, after exclusion of other frequent causes.

Conclusion:

Hence from present study it can be concluded that, there is no known prevention for iron deficiency anaemia in rheumatoid arthritis (RA) patients other than the reduction of contributory factors. Therapy goals are to reduce pain and inflammation and improve quality of life. Surgery to repair, replace or fuse joints may help in serious conditions.

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