Acknowledgment:

This paper would not have been possible without the helpful guideline. I am especially indebted to Ahsan Habib Shimul Sir, Professor Department of Biotechnology & Genetic Engineering at Khulna University, who has been supportive of my career goals who worked actively to provide me with the protected academic time to pursue those goals. As my teacher and mentor, he has taught me more than I could ever give him credit for here. He has shown me by example what a good Nutritionist should be. Nobody has been more important to me in the pursuit of this project than the members of my family. I would like to thank my parents, whose love and guidance are with me in whatever I pursue. They are the ultimate role models to me.

Abstract:

Rheumatoid arthritis (RA) can lead to severe disability. Rheumatoid arthritis (RA) is a chronic systemic disease affecting joints as well as extra-articular structures and is the most common type of inflammatory arthritis worldwide. The enquiry of Rheumatoid Arthritis patient was done by well-organized surveillance. This literature review assessed the descriptive epidemiology, comorbidities and extra articular manifestations, functioning abilities and quality of life, and treatment patterns of RA patients. When comes patients profile of any disease , it indicates various features like patient demographics, duration of disease, nature of complications, food habit, family history, past history of patients, and treatment options. This review is confined to studies with small sample sizes, cross-sectional designs, and/or clinical settings that may not be representative of the entire population. There is a need for more robust studies, as conclusions for the entire RA population cannot be drawn from only the current observational studies. All of these data were beneficial for practical knowledge of Rheumatoid arthritis.

Keywords: Rheumatoid Arthritis, Patient profile, Practical knowledge, Surveillance.

Chapter -1

Introduction

1.1 Background of the study:

The Health care system in Bangladesh falls under the control of the Ministry of Health and Family Planning. The government is responsible for building health facilities in urban and rural areas. For example, in the late 1980's in Bangladesh, the rural health facilities that existed in the rural areas were mostly sub-district health centers, rural dispensaries and family welfare centers. Unfortunately, they were poorly administered. For example, a sub-district health center had only thirty hospital beds. Most of its services were useless because of staff problems like few medical professionals and because the hospitals had no support service. Urban health centers also had problems with inadequate medical supplies. In many urban centers today, health services are The Health care system in Bangladesh falls under the control of the Ministry of Health and Family Planning. The government is responsible for building health facilities in urban and rural areas. For example, in the late 1980's in Bangladesh, the rural health facilities that existed in the rural areas were mostly sub-district health centers, rural dispensaries and family welfare centers.
Unfortunately, they were poorly administered. For example, a sub-district health center had only thirty hospital beds. Most of its services were useless because of staff problems like few medical professionals and because the hospitals had no support service. Urban health centers also had problems with inadequate medical supplies. In many urban centers today, health services are (Aminul et al, 2017).

Arthritis and diseases of the joints have been plaguing mankind since ancient times. In around 1500 BC the Ebers Papyrus described a condition that is similar to rheumatoid arthritis. This is probably the first reference to this disease. Doctors don't know exactly what causes rheumatoid arthritis (Riekert et al, 2002). The condition is most likely triggered by a combination of factors including an abnormal autoimmune response, genetic susceptibility, and some environmental or biologic trigger such as a viral infection or hormonal changes. Rheumatoid arthritis is considered autoimmune disease. In autoimmune disorders, the body's immune system mistakenly attacks and destroys healthy cells and tissue (Sackett et al, 1997). Rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA) are three common types of inflammatory rheumatic diseases (IRD) associated with deformities and joint destruction. RA is the most frequent IRD, with a prevalence of 0.5% (Fausto et al, 2009). Patients with active RA have been shown to suffer deficits in health-related quality of life (HRQL) along a number of physical functioning and mental health dimensions (Menard et al, 2003). Furthermore, patients with RA who have significant

functional disability have a 3-fold increased risk of mortality compared with that of the general population; this risk is comparable with that of individuals of the general population in the highest quintile for systolic and diastolic blood pressure, cholesterol level, or pack-years of smoking.

AS is a systemic and IRD predominantly affecting the axial skeleton with sacroiliac joint involvement as its hallmark, causing decreased spinal mobility (Hayem et al, 1999). Similarly to other chronic diseases, AS can affect quality of life, morbidity, mortality, participation in paid and unpaid work and healthcare costs. Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease that is usually seronegative for rheumatoid factor, associated with psoriasis, and with a prevalence of 0.02–0.42% in the general population and 13.8–30% among patients with psoriasis 12. PsA is a heterogeneous condition with articular and extra-articular manifestations including a combination of peripheral arthritis, axial disease, enteritis, dactylitis, and skin and nail disease (Wagner et al, 1997).

The target of therapy for PsA is to reach a state of remission or, at least, minimal disease activity (MDA). For patients with PsA, the heterogeneity among disease manifestations as well as the need to validate outcome measures makes the definition of remission challenging .Clinical remission requires achieving disease quiescence in all disease domains. (Coates et al, 2010). Developed a composite outcome measure as a target of treatment for patients with PsA that encompasses most of the disease domains. These criteria for MDA were validated using interventional trial data. Recent studies have found that MDA could be a reliable target for antitumor necrosis factor alpha (anti-TNF) therapy (Falcini et al, 2000).

PsA has a high impact on the lives of patients. Patients with PsA experience significant disability and reduced quality of life, resulting from emotional distress and functional impairment associated with psoriatic skin lesions, as well as arthritis-related joint pain (Menard et al,2003).A prominent benefit of treatment with anti-TNF in PsA patients has been an improvement in patient-reported outcomes (PROs), including health-related quality of life .Recently Gosse, have developed and validated the PsA .Impact of Disease (PsAID) questionnaire which can be used to calculate a score reflecting the impact of PsA on the lives of patients(Ferdin et al, 2000).

Measures that assess outcomes in rheumatic diseases should not only capture the major domains of the disease, but also capture the vision of the patient for improvement in their overall health. The aim of this study was to determine the MDA rate in patients with PsA, to describe their

characteristics, and to evaluate the association between MDA and the impact of the disease as assessed by the PsAID questionnaire in routine clinical practice (Sauer et al, 1997).

PsA is an inflammatory peripheral and/or axial arthritis associated with psoriasis, usually seronegative for rheumatoid factor. In addition to the peripheral joint disease, patients with PsA have a debilitating skin disease, and up to 50% may also have spinal disease (Menard et al, 2005).Compared to RA and AS, there is less information about the burden of illness in PsA. Although considered a benign disease in the majority of cases given in previous reports or in population-based samples. Clinical cohort studies described PsA as a progressive, disabling disease, particularly when polyarticular peripheral arthritis is present. Thus, IRD represents a tremendous economic burden, not only for patients and their families, but also for society as a whole (Mesel et al, 2006).

The health-related quality of life (HRQL) is an important indicator of the burden of musculoskeletal disease. The Medical Outcome Study Short-Term 36 (SF-36) is the most used tool that evaluates HRQL as a subjective perception about psychological and physical limitations due to an underlying illness. The purpose of this study was to compare the HRQL scores among patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) and a selected sample of health people and determine their relationship with measures of clinical condition (Walter et al, 2009).

The endorsement of the ICF by the World Health Assembly (WHA) in May 2001 marks an important milestone in health services provision and research and especially in the field of rehabilitation (Antoni et al, 2005). Since the ICF has been developed in a worldwide, comprehensive consensus process over the last few years and was endorsed by the WHA as a member of the WHO Family of International Classifications, it is likely to become the generally accepted framework to describe functioning and health. The potential uses of the ICF are numerous. With the ICF, not only an etiologically neutral framework, but a globally-agreed-on language and a classification are available to describe functioning both on the individual and the population levels and from both the patient perspective and that of the health professionals. Therefore, the ICF provides a universal terminology to describe functioning and disability, which is applicable independent of a specific disease or health condition, etiology and pathogenesis, of the profession or specialization of the user, of time, place, culture, country, or health care system

(Tomus et al, 2009). The ICF can be used in clinical practice and rehabilitation to structure and to lead through, thus to facilitate the rehabilitation process. It can provide a standardized frame for rehabilitation understood as a problem solving process with its steps: assessment and goal setting, assignment, intervention, and evaluation .It can be used in teaching and education of 8 health professionals but also to aggregate information, e.g. for health reporting purposes, public health information systems and epidemiology to build the necessary evidence basis for individual clinical, population-based institutional, or political decisions .Also, the ICF is a useful tool for research, e.g. to select and to describe study populations, and also as a heuristic tool to clarify concepts, to generate and test hypotheses, or to explain health states. All member states of the WHO are now called upon to implement the ICF in multiple sectors that include, among other things health, education, insurance, labor, health-and-disability policy, statistics, etc. However, the ICF has to be tailored to suit these specific applications .In the clinical context, the main challenge is the length of the highly comprehensive classification with it's over 1400 categories. This comprehensiveness is a major advantage and strength of the ICF. But at the same time it is the major challenge to its practicability and feasibility (Michaela et al, 2008).

The concept of a "window of opportunity" for therapeutic intervention in rheumatoid arthritis was first hypothesized in the early 1990s. The hypothesis is based on the existence of a time frame within which there is a disproportionate response to therapy, resulting in long-term sustained benefits or more importantly the chance of "cure". It is an attractive approach to the management of a persistent, progressive, damaging, inflammatory disorder (Quinn, 2003).

1.2 Objectives:

- To examine the self-reported health status in patients with RA, AS, and PsA arthritis.
- To explore the associations between health status and age, and sex of the patients.
- To provide an update on the current knowledge of arthritis.

1.3 Limitations of the study:

During the time of the study some difficulties and challenges were faced which were addressed and mitigated properly to ensure most accuracy. These are-

- There were limitations of logistic support to correctly gather and manipulate data.
- The information in few cases could not provide the relevant data due to unconsciousness and conventional thinking.
- There was a problem of communication due to severely environment of the area.
- Many respondents did not agree to spend some time for their interview and felt disturbed during survey time.
- Respondents were not willing to give personal informational related to their lifestyle especially about family history and education.
- The respondents were initially confused about the intention and of the study.
- Few respondents felt ashamed.

1.4 Statement of the Problem:

Arthritis and related musculoskeletal conditions are the leading cause of disability in the United States, making them a significant public health issue. More than 7 million Americans report limitation of activity due to arthritis and there is a significantly higher rate of no leisure‐time physical activity among people with arthritis as compared with the general population. Prolonged inactivity can result in much of the morbidity attributed to arthritis problems such as fatigue, reduced joint flexibility and muscle strength, loss of independence, poor endurance and overall fitness, and depression. Inactivity also increases the risk for comorbid conditions, such as coronary heart disease, diabetes, and osteoporosis. On the other hand, several randomized, controlled trials have shown that people with arthritis who participate in appropriate land‐based or aquatic exercise programs can experience significant improvements in their physical and psychosocial status without exacerbating their disease. Based on such evidence, the Surgeon General's report on physical activity and health concluded that people with osteoarthritis (OA) and rheumatoid arthritis (RA) can improve their pain and function by participating in regular moderate aerobic or resistance training exercise programs. In the past, patients with arthritis were often cautioned against exercising, however, the current American College of Rheumatology guidelines for OA management include exercise as a mainstay of treatment. The Arthritis Foundation has developed 2 physical activity programs, the AFAP and the PACE program, that have been evaluated in different settings and appear to provide some positive benefits to participants. Unfortunately, these programs are not widely utilized, reaching less than 1% of people with arthritis (Arthritis Foundation, unpublished data).

Chapter – 02

Literature Review

2.1 Definition of Arthritis:

Arthritis is the swelling and tenderness of one or more of your joints. Inherently, it is not just a single disease rather a collection of medical problems collectively termed as “Arthritis. The main symptoms of arthritis are joint pain and stiffness, which typically worsen with age (Sullivan et al, 2014). The most common types of arthritis are osteoarthritis and rheumatoid arthritis. Nearly 47 million adults and 300,000 children suffer in the US alone. The disease can incapacitate permanently if proper treatments are not provided in time. Globally, it imposes a huge financial burden through wage loss along with the cost of medications (Mitra et al, 2013). Arthritis is inflammation or degeneration of one or more joints. A joint is the area where 2 bones meet. Inflammation of a joint usually accompanied by pain, swelling, and stiffness, resulting from infection, trauma, degenerative changes, metabolic disturbances, or other causes. It occurs in various forms, such as bacterial arthritis, osteoarthritis, or rheumatoid arthritis (Bishop et al, 2014)

2.2Types of Arthritis:

Rheumatoid arthritis (RA) is characterized by asymmetrical distribution of joint inflammation in conjunction with ongoing pain, as well as in-creased pain during movement and light pressure to the articular margin of the joint (Keefe et al, 2001). Pain associated with RA can occur spontaneously or can be evoked by gentle stimulation of the joint when it is moved within its normal working range (Martin et al, 2001). Furthermore, pain and tender-ness are not only present in joints directly affected but also in surrounding, apparently normal, tissues. Referred pain syndromes may also occur. The magnitude of symptoms may not necessarily correlate with the severity of the under lying disease and symptoms may persist even when disease exacerbations have apparently settled (Bradley et al, 2001).

By nature, arthritis is versatile. The few common ones are-

1. Osteo-arthritis (OA)
2. Rheumatoid Arthritis (RA)
3. Gout
4. Ankylosing Spondylitis (AS)
5. Lupus arthritis (LA)
6. Infectious arthritis (IA)
7. Juvenile arthritis (JA)
8. Psoritic arthritis (PA)
9. Fibromyalgia.

Most of the outbreaks are seen for OA, RA and gout or to a certain extent AS, whereas the remaining others are less frequent (Mitra et al, 2013).

2.2.1 Osteo-arthritis (OA):

In case of Osteo-arthrities, cartilage undergoes a slow damage because of stiffness which is developed by losing the elasticity. This is the reason it no longer can act as a proper shock absorber. Ligaments face stretching that initiates the pain due to gradual erosion and the bones start rubbing with each other adding agony and suffering (Mitsuyama et al, 2007). The symptoms advances slowly initially but gets worsen with time causing inflammation and creating more harm to the joint (Thorn et al, 2007). Patients feel pain during and after the joint- movement which usually occurs waking up at the morning. In most cases a common indication is the development of stiffness. Progression of the disease happens with age and patients lose flexibility and feel irritating sensation while flexing the joints and along with its progression,. As a symptom, hard lumps or bone spikes appear at the joints under attack via knees, hands, hips or spines (Kean et al, 2004).

2.2.2 Rheumatoid arthritis (RA):

This is a widely known autoimmune and inflammatory disease, which means that our immune system attacks healthy cells in our body by mistake, causing inflammation (painful swelling) in the affected parts of the body) producing stiffness, swelling, pain and deformity at the later stage It occurs three times more within the women than men at ages ranging from 40 – 60 but rarely, children are the victims (Campbel et al, 2009). The affected joints are arms, fingers, wrists, knees or legs. The joints are swollen due to inflammation thus felt stiffness especially after waking up at

morning and when touched, patients feel tenderness showing red or puffy colors at the affected areas and they also often feel tired and experience weight losses. The disease can strike at several places simultaneously spreading from smaller to the larger joints; like wrists, ankles and feet to elbows, knees, hips, necks or shoulders (Mitra et al, 2013).

2.2.3 Gout:

Gout is a common form of inflammatory arthritis that is very painful and caused by is caused by a condition known as hyperuricemia, where there is too much uric acid in the body. Hyperuricemia does not always cause gout (Edwards et al, 2009). Gout flares start suddenly and can last days or weeks. These flares are followed by long periods of remission weeks, months, or years without symptoms before another flare begins. Gout usually occurs in only one joint at a time. It is often found in the big toe. Along with the big toe, joints that are commonly affected are the lesser toe joints, the ankle, and the knee. Symptoms of gout include intense pain, swelling, redness and heat. There is no cure for gout, but you can effectively treat and manage the condition with medication and self-management strategies (Jaakkola et al, 2006).

2.2.4 Ankylosing Spondylitis (AS):

It is also called an inflammatory autoimmune disease of the spinal joints or between spine and pelvis (Prakash et al, 1984).The inflamed joints perpetrate excruciating pain which increases with time. Along that course, spine experiences stiffness due to the fusion of bones. However the exact cause remains unidentified, suspicion points it to be genetic. More male gets affected by the disease than the female and it often starts at the ages of 20 – 40 (Calin et al, 1999).The pain and stiffness becomes severe at night or morning but subsides during the day with start of physical activities and the disease onsets at the sacroiliac (spine and pelvis) joints and afterward affects the other places also. Patients lose mobility of the lower spine and cannot expand chest properly for taking a full breath. The other associated symptoms are; swelling of the eye, pain in the hip, heel or other joints accompanied with low level fever, loss of appetite and weight loss (Garrett et al, 1994).

2.2.5 Lupus arthritis (LA):

It is a systemic autoimmune disorder affecting nearly 1.5 million people in the US alone. Almost 90% of the lupus patients suffer from joint and muscle pain and about 35% ofthem bear LA. The disease produces pain and swelling of the joints accompanied by morning stiffness and occasionally fluid accumulates at the swelled joints. Besides serious damages, LA creates deformities and discomforts but does not attack neck or spine and mostly affected areas are- fingers, wrists, knees, feet, toes, elbows and hands. LA has a symmetrical effect, for example, attacking identical joints on both sides of the body (Mitra et al, 2013).

2.2.6 Infectious arthritis (IA):

IA arises due to infection inside the synovial caused by bacteria, fungi or viruses. The infection spreads through circulation later affecting the joints. If patients already suffering from any arthritis, they would be prone to it which then synergizes the sufferings further. It might be the cause why patients with arthritis often become the prey to infection thus worsening the situation more. The symptoms are pain, swelling, inflammation of the joints followed by frequent fever; often starts with an injury. The areas falls under attack are knee, ankle, shoulder, wrist, elbow, finger etc. But IA affects single joint only (Quartana et al, 2009).

2.2.7 Juvenile arthritis (JA):

Obviously, patients involved are the child. And the symptoms involve occasional evening fever, poor appetite, weight loss followed by rashes on the arms and legs. The patients frequently limp and experience sore at the wrist, finger or knee and the joints appear larger due to swelling. The sufferings include pain and stiffness at the neck or hips. The frequent development of anemia is also detected (Stanish et al, 2010).

2.2.8 Psoriatic arthritis (PA):

Psoriatic arthritis is a form of arthritis that affects some people who have psoriasis which is a condition that features red patches of skin topped with silvery scales. Psoriatic arthritis occurs when body's immune system begins to attack healthy cells and tissue. The abnormal immune response causes inflammation in joints as well as overproduction of skin cells where both genetic and environmental factors play a role as many people with psoriatic arthritis have a family history

of either psoriasis or psoriatic arthritis and researchers have discovered certain genetic markers that appear to be associated with psoriatic arthritis. At the same time Physical trauma or something in the environment such as a viral or bacterial infection may trigger psoriatic arthritis in people with an inherited tendency. Most people develop psoriasis first and are later diagnosed with psoriatic arthritis, but the joint problems can sometimes begin before skin patches appear. People who have pitted, deformed nails are especially likely to develop psoriatic arthritis and it occurs most often in adults between the ages of 30 and 50 although anyone can develop psoriatic arthritis complications Joint pain, stiffness and swelling are the main signs and symptoms of psoriatic arthritis and they can affect any part of the body, including fingertips and spine, and can range from relatively mild to severe. In both psoriasis and psoriatic arthritis, disease flares may alternate with periods of remission. No cure for psoriatic arthritis exists, so the focus is on controlling symptoms and preventing damage to the joints and without treatment, psoriatic arthritis may be disabling (Dean et al, 1998).

A small percentage of people with psoriatic arthritis develop arthritis mutilans - a severe, painful and disabling form of the disease. Over time, arthritis mutilans destroys the small bones in the hands, especially the fingers, leading to permanent deformity and disability. People who have psoriatic arthritis sometimes also develop eye problems such as pinkeye (conjunctivitis) or uveitis, which can cause painful, reddened eyes and blurred vision. They are also at higher risk of cardiovascular disease (Maureen et al, 2010).

2.2.9 Fibromyalgia:

This disease is defined as a disorder originated due to musculoskeletal pain along with the fatigue. Many believe that it over-amplifies the pain sensation in comparison to normal perception. And often psychological stress, physical trauma or infection may initiate the disorder. Survey indicates that women are the major victims than men. A significant section of patients suffering from fibromyalgia also show the tension headaches, irritable bowel syndrome, anxiety and depression. As the disease runs in the families so there is a good possibility of genetic mutations involved in it. In many cases post-traumatic stress disorders or those suffering from RA tend to help develop the disease (Arnold et al, 2004)

2.3 Risk Factors:

There are 100 different forms of arthritis with each having its own set of causes and risk factors. The most common types include osteoarthritis, rheumatoid arthritis, and gout. Determining the cause of arthritis can be difficult since multiple, overlapping factors typically contribute to its development but the possible causes of arthritis include age- and lifestyle-related wear and tear, infections, injuries, and autoimmune conditions.

2.3.1 Common Causes:

With each of the major types of arthritis, there are different causes and risk factors, but these are the ones most often at play (Bowman et al, 2005).

2.3.1.1 Older Age:

Older age is a major factor in arthritis as cartilage becomes increasingly brittle over time and has less capacity to repair itself and the development of osteoarthritis is typically seen to begin between the ages of 40 and 50, although it can start earlier in other forms of the disorder. Arthritis can strike at any age, including in children. While more common in older adults, symptoms should be assessed in all age groups (Elwee et al, 2014).

2.3.1.2 Injury:

Previous joint damage can cause irregularities in the normal, smooth joint surface. Prior injury certainly plays a part in the development of arthritis of the wrist, where the complex bone and cartilage structure can be easily compromised by impact or compression. Another example is arthritis caused by a tibia plateau fracture, where a broken area of bone enters the cartilage of the knee joint (Elwee et al, 2004).

2.3.1.3 Autoimmune Factors:

Rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, and lupus are among the types of inflammatory arthritis in which the immune system attacks own tissues. However what causes this to happen is unclear, it can be due to several factors, including genetic predisposition, infections, or environmental exposures (Smyth et al, 2004).

2.3.1.4 Genetics:

Genetics plays a key role the development of certain types of arthritis, although the association is still not fully understood. A family history can suggest an increased risk depending on the type of arthritis involved e.g. approximately 40% of patients with psoriasis or psoriatic arthritis have family members who have one of these conditions (Smyth et al, 2004).

Certain forms of rheumatoid arthritis are linked to genetic markers known as HLA-B27 and HLA-DR4. Variants in other genes may also contribute, including:

- STAT4, a gene that plays an important role in the regulation and activation of the immune response.
- TRAF1 and C5, two genes associated with chronic inflammation.
- PTPN22, a gene associated with both the development and progression of rheumatoid arthritis.

Gout, which is defined by a problem with the production and elimination of uric acid, is also influenced by genetics. Hereditary hyperuricemia, caused by SLC2A9 and SLC22A12 mutations, is one condition which impairs the excretion of uric acid by the kidneys.

The influence of genetics in developing osteoarthritis is still being explored. A review found differences in heritability depending on which joint was affected. It was most influential for spinal arthritis (70%) and hip arthritis (60%), and less so for that of the knee (40%). Osteoarthritis seems to be influenced by several gene variants and having more of them at the same time adds to risk (Casanova et al, 2004).

2.3.1.5 Lifestyle Risk Factors:

There are things you do that can increase your risk of some forms of arthritis and might worsen the effects of other types. Importantly, the stress you place our joints today can lead to the development of arthritis later (Cooper et al, 2004).

2.3.1.5.1 Obesity:

Obesity is a factor as it directly contributes to the stress a joint can be placed under which is especially true for hip and knee joints, where excessive weight have a direct impact and cause inflammation that causes the gradual deterioration of joint tissues. People who are overweight or obese are more likely to get knee osteoarthritis than people who are not overweight. Excess weight can also make knee osteoarthritis worse. Extra weight puts more stress on joints, particularly weight-bearing joints like the hips and knees (Cua et al, 2004).

2.3.1.5.2 Occupational Hazards:

Jobs and activities involving manual labor or repetitive motion can lead to joint damage and arthritis. Even minor repetitive movements like pulling a lever or pushing a cart can cause deterioration of bone and joint cartilage over a period of years. As such, protective measures are often put in place to minimize damage caused by heavy lifting and activities that demand the constant flexion and extension of a joint. Occupations that involve repetitive knee bending and squatting are associated with osteoarthritis of the knee (Naik et al, 2004).

2.3.1.5.3 Sports:

High-level sports activity may lead to arthritis if it involves blunt force impact or results in damage to a bone or joint. This happens in contact sports, but also those that place persistent impact stress on a joint, such as long-distance running.

On the flip side, moderate, routine exercise can minimize the symptoms or development of arthritis as the muscular structure gets bolstered around a joint, giving it support (Bouladoux et al, 2004).

2.3.1.5.4 Sports:

Cigarette smoking increases the risk of the development of rheumatoid arthritis. It can also worsen the condition and cause other medical problems. Cigarette smoking increases a person's risk of developing rheumatoid arthritis (RA) and can make the disease worse. It can also cause other medical problems. Smoking can also make it more difficult to stay physically active, which is an important part of managing RA and other types of arthritis (Linehan et al, 2008).

2.3.1.5.5 Foods and Medications:

In the case of gout, certain foods and medications can increase the level of uric acid, which can then cause a gout flare. Certain foods should be avoided including beer and foods high in purine (Harrison et al, 2009).

2.3.1.6 Infection:

Certain infections around the joint, whether bacterial or viral leads to the deterioration of cartilage or the formation of skin lesions that penetrate the joint and synovial membrane. People who experience a joint infection (septic joint), multiple episodes of gout, or recurrent staph infection around a joint have a higher risk of developing arthritis. Many microbial agents can infect joints and potentially cause the development of various forms of arthritis (Wilhelm et al, 2007). Osteoarthritis, rheumatoid arthritis, and fibromyalgia are more common in women, while gout is more common in men. The reasons for this difference in risk are unclear.

2.4 Current practices for Arthritis management and prevention :

2.4.1 Prevention of Arthritis:

Risk levels differ among individuals, but there are several areas which can help to lower the risk:

- **Weight:** Losing weight is a great way to lower risk as research has strongly supported a connection between weight loss and lower risk of osteoarthritis.
- **Exercise:** Not only exercise can help to lose weight more quickly, the strength it can add to the muscles can go a long way to preventing arthritis. Muscles support joint health, and exercises that are simultaneously light on the joints such as biking and swimming, for instance are great for strengthening muscle without putting too much pressure on joints.
- **Hot and cold:** Both as a complement to exercise and on its own, using ice and heat treatments for any minor joint can help relieve pain and swelling.
- **Treat injuries:** A person experiencing a joint injury is at a higher risk of arthritis. One should take more precautions when exercising—stretch longer, and use proper equipment.

- **Walking devices:** For people trying to limit joint pain, things like canes and walkers can be valuable. They make daily tasks easier while taking pressure off the joints.
- **Diet:** A good diet will help one lose weight, and there are some nutrients (Omega-3 fatty acids, vitamin D) that may reduce the risk (Quinones et al, 2004).

2.4.2 Management of Arthritis:

For those who do develop it, there are several treatment methods available. These range from medications to surgery, and some people have found success with massage and other forms of alternative medicine. If a person is demonstrating early signs of arthritis or experiencing joint pain, he should speak to his doctor about treatment and prevention options. Exciting new treatments for arthritis are-

Classically, anti-inflammatory medication in the form of pills or gels applied directly to a joint has been the mainstay of treatment. A cortisone injection into the joint was reserved for more painful cases of arthritis.

While both those treatment options still have an important role to play in certain cases, neither focuses on preserving or decreasing the wear-and-tear on the joint. In fact, recent studies have shown that repetitive injections of cortisone actually erode cartilage, despite its anti-inflammatory effect.

Today, therapies have evolved past simply taking pills to decrease inflammation. However, early evaluation by skilled clinicians is still key to combating the many factors in arthritis.

Modern treatments involve a holistic, team-based approach, including physician, kinesiologist and physiotherapist, which focuses on the underlying causes of the disability and strategies for joint preservation (Brophy et al, 2000).

- **Hyaluronic acid injections** are examples of treatments that may have some joint-preserving power. These injections are jelly-like substances that mimic the fluid already in our joints and act as a sort-of lubricant allowing for better range of motion and a decrease in pain – kind-of like putting WD-40 on a rusty hinge. One or two relatively painless yearly injections can produce excellent results for those with mild to moderate arthritis.

- **Platelet rich plasma (prp) therapy** is a more novel and cutting-edge arthritis treatment. PRP is an all-natural therapy that has gained an immense amount of interest in recent years as the techniques of using this therapy have improved. It first attracted attention when Tiger Woods used it to improve his knee joints and tennis elbow about 15 years ago.

PRP therapy involves harnessing the healing power of your own blood by concentrating platelets and growth factors into a syringe and then injecting it back into the body. This has been shown to help heal and rejuvenate the tissue that is exposed to the plasma concentration. In the case of arthritis, PRP affects the joint cartilage that is being eroded (Blake et al, 2012).

Although used throughout the United States and by professional sports programs extensively, PRP has been used minimally in Canada. Research continues to build for this exciting therapy that's now showing good evidence for more widespread use. We have begun to offer this therapy at the Cope man Healthcare Centre in Calgary, with plans to expand to other centers (Helmickey et al, 2012).

To be most effective, the options discussed should be employed earlier, when arthritis of the joint is of mild to moderate severity. Waiting too long to treat your arthritis may result in treatment methods not having any effect due to the overwhelming cartilage erosion and pain generated when bone contacts bone (Brophy et al, 2012).

If someone is feeling pain in his joints, he should seek the advice of a well-versed healthcare provider who can discuss which options are right for him (Blake et al, 2012).

2.5The global prevalence of Arthritis:

Studies performed by Helmick et al identifies that in the US alone > 21 % adults or ~ 46.4 million are diagnosed to be currently suffering from the arthritis. Further as reported in 2008, approximately 1.3 million of the US population have the RA which is somewhat less than that estimated (2.1 million) in 1995. The study also indicates that AS sufferer ranges from 0.6 to 2.4 million whereas the LA affects 161,000 to 322,000. In case of JA, the value is ~ 294,000. The study also shows that ~ 27 million of the US population possesses clinical OA which is up from 21

million compared to the year 1995. Regarding other kinds, about 5.0 million have Fibromyalgia and ~ 3.0 million carries the gout (up from 1995 which was 2.1 million). (Helmick et al, 2008).

A Canadian study in recent decade shows that in general, ~ 15% of the overall population suffers from any kind of arthritis. Among the victims, 48.8% are male and 51.2% are the female. The difference is claimed significant which is supported by other studies pointing the problem more toward females. The study further indicates that within the Canadian nationals, white Europeans / Caucasians bear a higher percentage (19.7%) than the Asians (5.5%) or other ethnic categories (8.8%, including Africans & other non-Caucasians). Several relating studies convince also that the Asian race have lower incidences of any arthritis irrespective of their age, sex or education level. In US, concerning the ethnicity, no exact consensus has been reached concretely but a few studies reflect that there is a distinguishable role regarding some forms of arthritis. For example as an average estimate, the incidence of RA is seen somewhat higher within the Hispanics community (Helmick et al, 2008).

In previous decades, arthritis is estimated to be the 40th leading cause of non-fatal burden. In the last decade just before changing of the century, it has been accounted that about 0.7% of the total years people lived with disability (YLD). In next decade, just RA alone is considered to be the 31st leading cause of YLD globally and that percentage (0.7%) increases to greater than >1% (Mitra et al, 2013).

The hip joints OA are more prevalent within Caucasians than in Asians, particularly comparing to the Japanese (Inoue et al. 2001). Studies performed in nineties covering up the last three decades indicate that among developing Asian nations the prevalence of RA is just about the same as for Western nations (0.75%) whereas in the case of India or Pakistan it is somewhat less, about 0.55% . The value is even remarkably low (0.4%) for China and Indonesia including both urban and rural population. Interestingly, in rural African nations RA is considerably low whereas it is extremely high in Jamaica (2%) and Latin American nations (1.5%). The ecological factors or genetic variations are suspected to be largely responsible behind these differences. A number of studies show that the frequency of RA or its severity is somewhat less within Asians and West Africans. Studies conducted in the US with worldwide focus on RA alone showed that the prevalence is much higher in Europe and North America than in any developing nations. The data from India or Pakistan remains questionable. In some studies it has been reported that no real difference exists when compared with the West-European nations. The genetic profile associated with RA is uniform

for 0.55%. The value is even remarkably low (0.4%) for China and Indonesia including both urban and rural population. Interestingly, in rural African nations RA is considerably low whereas it is extremely high in Jamaica (2%) and Latin American nations (1.5%).The ecological factors or genetic variations are suspected to be largely responsible behind these differences. A number of studies show that the frequency of RA or its severity is somewhat less within Asians and West Africans. Studies conducted in the US with worldwide focus on RA alone showed that the prevalence is much higher in Europe and North America than in any developing nations. Following the New York criteria, the prevalence of AS in Dutch population was seen 0.24% whereas the value for HLA-B27 is noted to be 0.1%. Surprisingly only a limited number among the AS sufferers corresponds to HLA-B27 positive. In Asian region the average prevalence of OA is 0.11% which is almost equal to that of Chinese, Thai and average Caucasians but not for the Japanese who bears a significantly lower rate due to low prevalence of HLA-B27 antigen.

The middle-east Arab population shows a higher rate of AS compared to the south Asians. Further the diversity of HLA-B27 antigen regarding the subtypes is identified when Indonesian Chinese (HLA – B2704) are compared with the natives (HLA –B2705). The prevalence of AS in rural Indian population is 0.09% (Mitra et al, 2013).

Chapter – 03

Methods and Methodology

3.1 Study planning:

To give a comparative scenario, the present study was conducted in rural of Khulna district. Three villages were selected for the study. Shially, Goyara & Doba were purposively selected for the study purpose. Therefore, as a resident of Khulna district and due to some convenient reason of being a native researcher like all of the rural areas are located under Khulna district and familiarity with the language and cultural practices of local people.

3.2 Nature and Research design of the Study:

The study was descriptive in nature. Descriptive studies generally attempts to specify the present situation of the respondents and how it is happened. The study tried to find out the arthritis patients and their physical condition of rural the people. The study was conducted through using survey research design to deal with the physical condition of the rural people & their food habit. Particularly, survey research has a greater importance in collecting greater body of data within a short time as well as its wider applicability in various dimensions.

3.3 Sampling Procedure and Sample Size:

It is not possible to survey each household due to various limitations. For this study the sample is randomly selected from the population. The sampling is the fundamental to all the statistical techniques and statistical analysis. Sampling is indispensable technique of behavioral research, the research work cannot be undertaken without use of sampling. The study of the total population is not possible and it also impractical. The study comprised of 150 arthritis patients of 16-80 years.

3.4 Techniques of Data Collection:

In this study survey method was followed and an interview schedule and case study method was made on the basis of unit of analysis and objectives of the research topic, in which contained both open and close ended items. These were primary data, which were collected from the field through face to face interview.

3.5 Data processing and statistical analysis:

During the field work, information of respondents was written on the copies. After field work, data was input in the Microsoft excel for calculating the data and kaleida Graph was used for making graph. The obtained data were analyzed with the use of statistical methods, including Pearson's Chi-square test of independence (data in rows and columns of contingency tables, degree of freedom ≥ 1)

Chapter -04

Result and Discussion

❖ Result:

The results and implications of this survey shed light on many of the challenges RA patients face throughout their treatment. From facing unknown or misdiagnoses to feeling overwhelming levels of anxiety, fear, and confusion, there is nothing "easy" about navigating the world of rheumatoid arthritis and its extra-articular manifestations. In total, 150 patients with RA participated in this survey. Many of the free response questions required participants to elaborate on particular survey questions, allowing for a detailed description of their personal experiences. The results of the survey depict the need for additional research and acknowledgment of the extensive effects of this disease.

Question no.1: what is your gender?

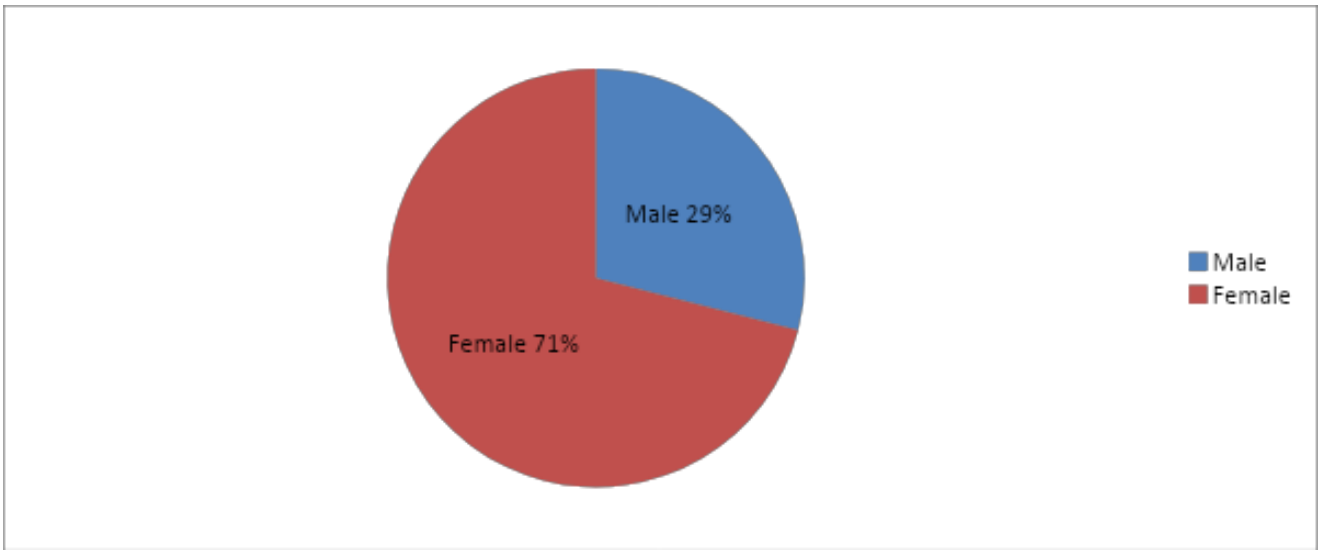

Figure 1

Question no.2: what is your age?

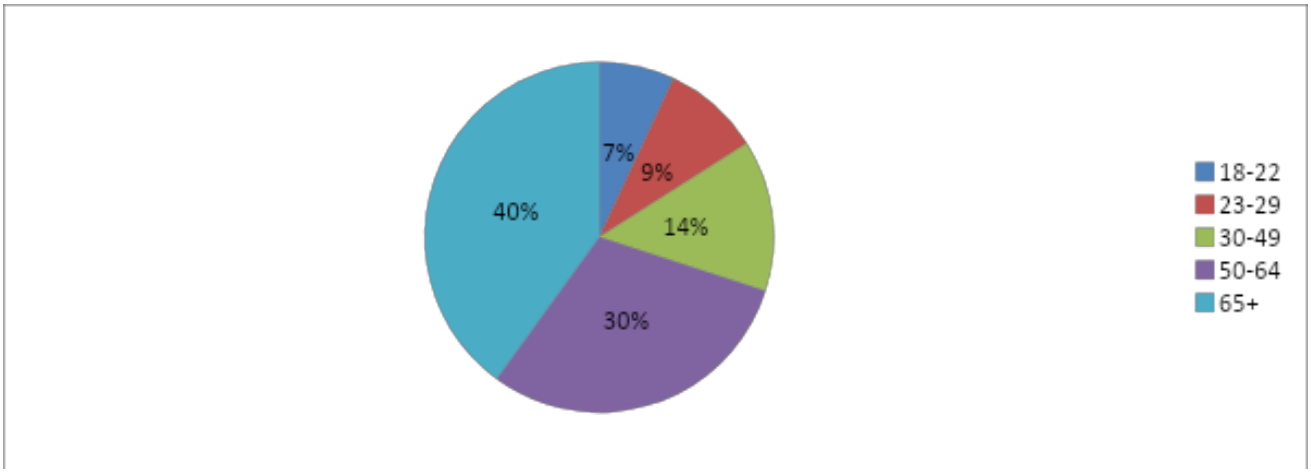

Figure 2

Question no.3: How old were you when you were first diagnosed with Rheumatoid Arthritis?

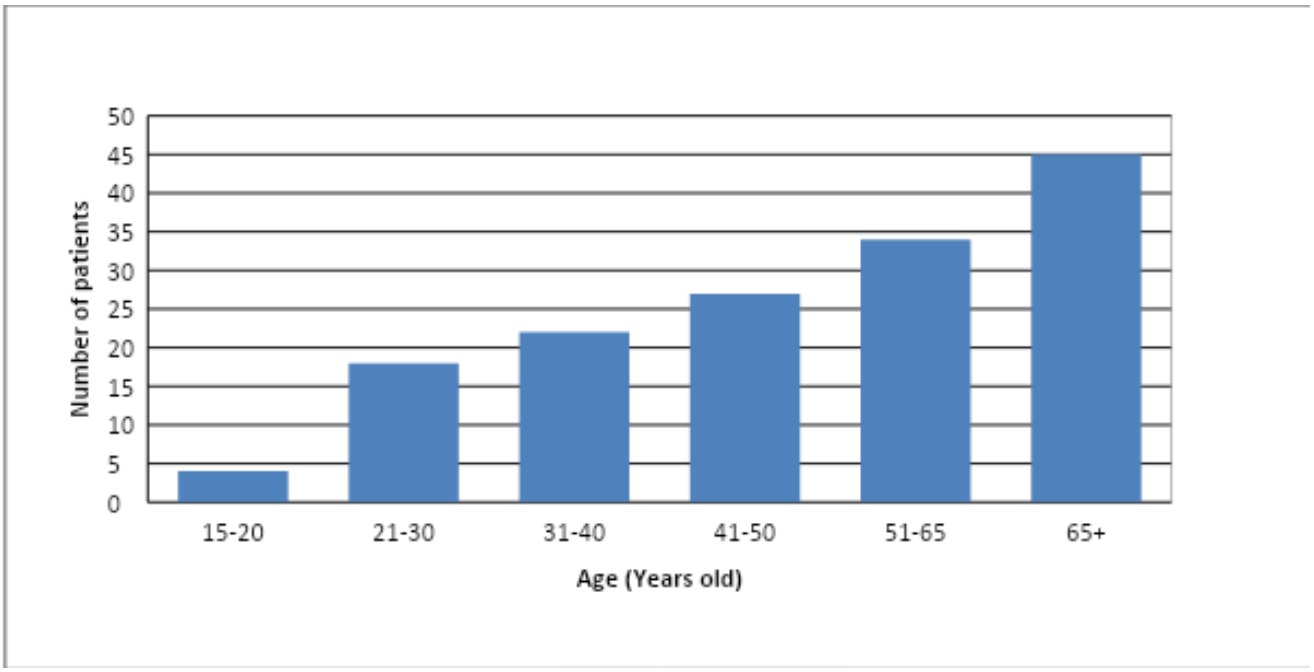

Figure 3

Question no.4: Were you diagnosed immediately after your symptoms first appeared?

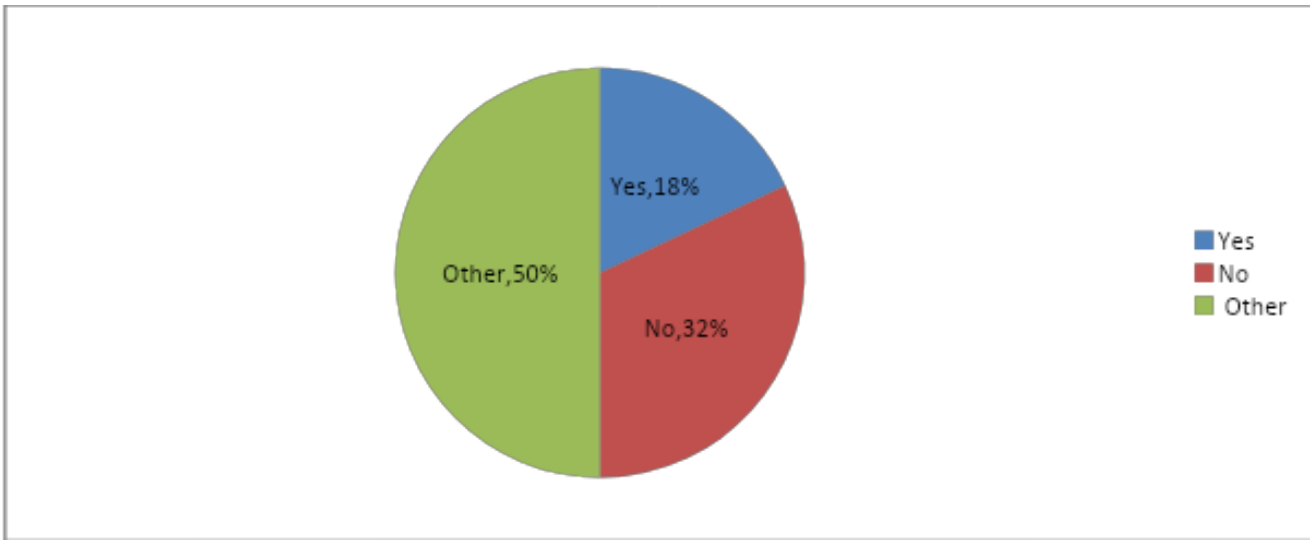

Figure 4

"Other" Responses

- I started noticing differences in my daily fatigue levels but thought I was just overworking myself.
- Once I stepped back from a few responsibilities and the fatigue continued I made an appointment with my doctor.
- I had been exceptionally sore for a long while.
- No, I was just diagnosed recently.
- Shortly after.
- Yes, but took 6 months to get into a Rheumatologist.
- Soon after, my knees and lower joints really blew up.
- I wasn't sure what was wrong until the symptoms got really bad.
- I had been having symptoms for a while, but I didn't realize their severity.
- I was misdiagnosed.

Question no.5: What type of Rheumatoid Arthritis were you diagnosed with?

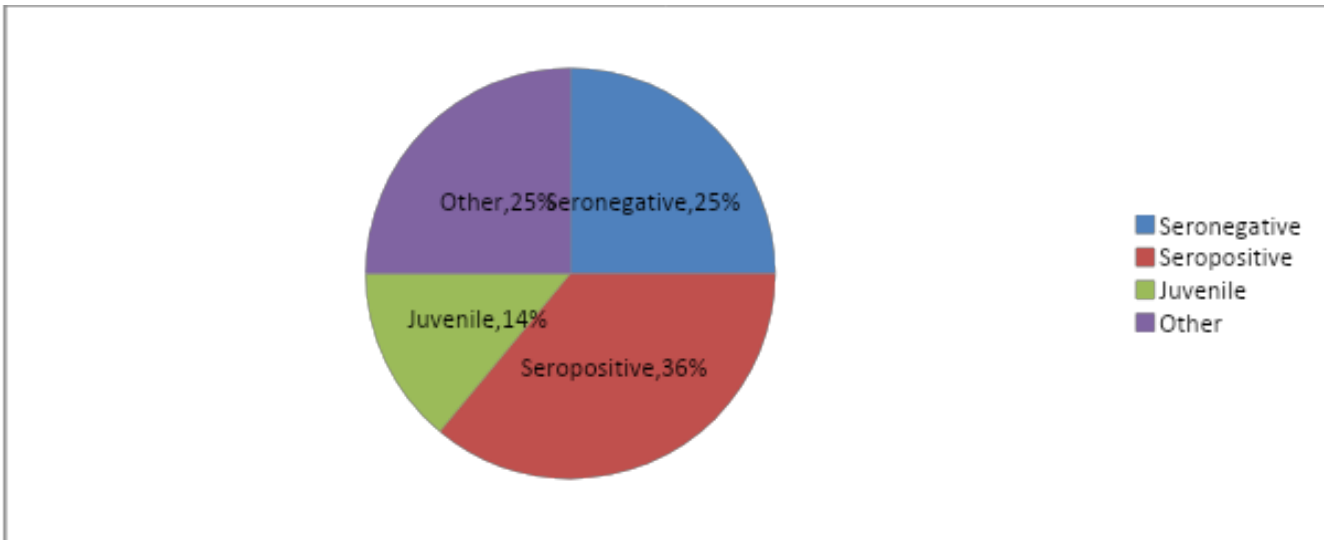

Figure 5

"Other" Responses

- Unknown.
- I was diagnosed with Lupus.
- Unsure.
- Tested positive for RF and ACPA.
- Unknown.
- Dr. never specified.
- Ankylosing Spondylitis.

Question 6- How did this diagnosis make you feel?

Participant Responses-

- It didn't affect my feelings until I was about 15 years old because it made me quit all my sports.
- Scared.
- Ambiguous
- Worried an unsure of how to best deal with it.
- Very scared, nervous, somewhat relieved to know what was wrong.
- Concerned.

- I didn't think it was Lupus. I had to wait a long time to see a Rheumatologist before I got the proper diagnosis.
- I didn't know RA was an autoimmune disease.
- Confused.
- A little anxious, but my doctor helped me to feel better about it.
- Worried, but glad to know I wasn't going crazy.
- Concerned, but I knew where my fatigue was coming from.
- Annoyed as I have always been very active.
- Confused since my blood tests were not positive**.**

Questions 7- What did your initial treatment plan entail?

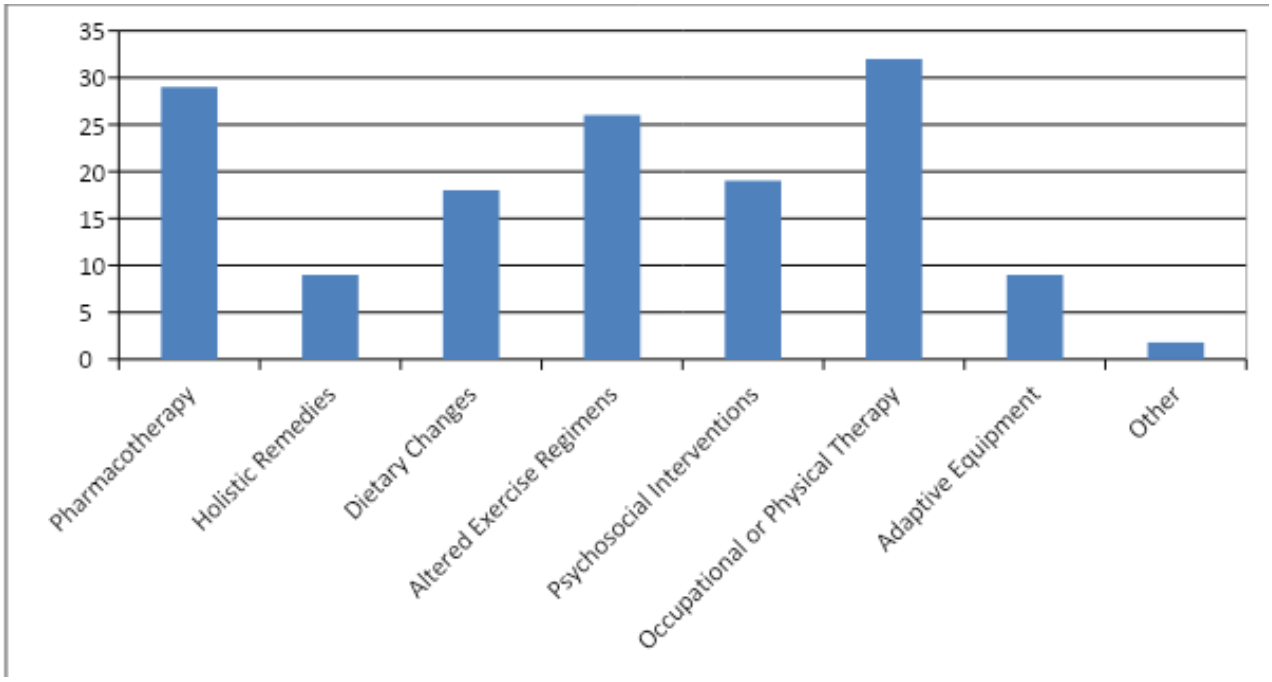

Figure 6

"Other" Responses

- Methotrexate.
- Cortisone injection under full sedation in both knees and ankles.
- 18 Ecotrin aspirin a day.

Question 8 - Have you changed the course of your treatment during the duration of your diagnosis? Why or why not?

Participant Responses

- Yes, I have changed drugs several times.
- Yes. Many times. Sometimes due to something not working effectively and other timed due to allergies.
- Yes, because I had knees the size of softballs which made me paralyzed for a short time
- Added an additional drug.
- I have added in some dietary changes to try to reduce inflammation. I have added some natural ant inflammatory supplements to my routine.
- Yes, I have tried different drugs and exercise during flare ups. My OT has really focused on helping me with small daily tasks that I am embarrassed to ask for help with like buttons, cutting food etc.
- Yes, as it started to make my joints deteriorate, I had shoulder replacement surgery, have changed my exercise habits and have changed medications.
- Yes, different therapies, different medication.
- Yes, wasn't seeing any change from the medications.
- Yes, I began receiving cortisone injections and they have worked quite well.
- Yes, I've changed medications.
- Yes, I am deeply involved with the treatment of Rheumatoid Arthritis. I have changed medications many times and have developed my won remedies.
- Yes, I was taking methotrexate but found it to negatively affect my lungs.
- Yes, I like to keep up-to-date on different DIY treatments along with non-steroidal medications.

Question 9– What have you found to be the most effective in regard to your treatment plans?

Participant Responses

- Fish oil supplements.
- My medications.
- The addition of Humira actually put me in remission for two years a few years ago.
- Methotrexate.
- Medical cannabis and swimming.
- Combination of all of the previous methods (meds, massage and acupuncture, exercise helps as well but I haven't been good at maintaining just because of time constraints, not arthritis).
- Lifestyle Changes.
- Naproxen.
- Humeria or Enbrel.
- Celebrex.
- Therapy.

Question 10-Have you ever discussed how your Rheumatoid Arthritis diagnosis might affect you personally or socially with your primary care physician?

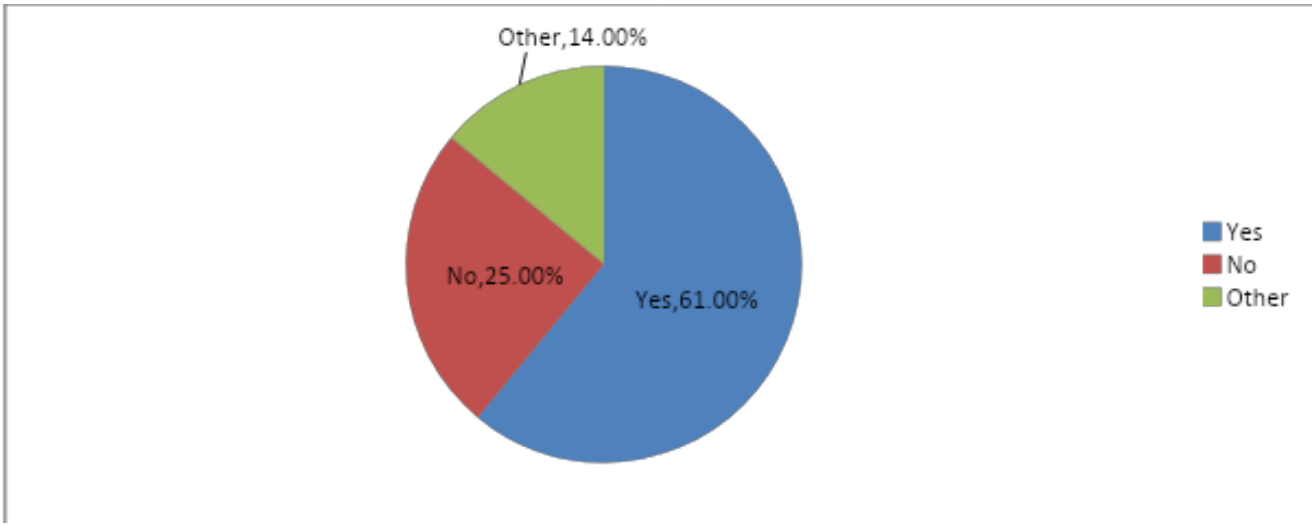

Figure 7

"**Other" Responses**

- Yes, but there weren't many avenues to explore with other people Briefly, after proper diagnosis by my Rheumatologist.
- Has little speech to discuss a determination of this possibility.
- My rheumatologist recommended I join the Arthritis Foundation fb page and I've been able to share my experiences with others and vice versa.

Question 11– Do you currently feel your Rheumatoid Arthritis symptoms are under control?

Responses to "other" option

- Somewhat. I feel my symptoms could probably be better.
- Yes, the do have flare-up's every to often but I know how to control them.
- Occasional flare ups from time to time.

❖ Discussion

Rheumatoid arthritis name alone is misleading and confusing to many of those who are diagnosed at young ages. The word “arthritis” generally implies aging and the subsequent deterioration of the bones and joints. While inflammation, fatigue, and destruction of the joints are all major effects of RA, its systemic impact on the body is what makes it notably unique and is what differentiates it from other forms of arthritis. The results of this survey demonstrate the complexity of this disease and its profound impact on each patient as it takes on a chronic state within the body.

The respondent demographics aligned with national RA statistics. The majority of participants were female and 82% identified. The 150 respondents ranged in ages from 18 to over 65 years old, and while varying ages of initial diagnoses of RA were reported, the age ranges of 41-50 and 51-65 were the most common (see Figure 3). A possible explanation for this is the fact that 45% of participants fell between ages 60-65 and had likely been diagnosed in early to middle- adulthood (see Figure 2).

In regard to the diagnoses of RA, the results of the literature review examined how obtaining a formal diagnosis by a rheumatologist or primary physician can be a long and frustrating process. For instance, for those patients who do not produce blood samples with positive ACPA and RF factors, the diagnosing procedure is based solely upon the clinical phenotypic observance of the distal joints. The literature review also revealed that many other organ involvements, including that of the heart, lungs, and larynx, may be indicative of the presence of RA without any swelling of the distal joints. This information suggests that patients may be suffering from the onset of RA symptoms without visible inflammation of the joints. Participants in this survey were asked to reveal if they had been diagnosed immediately after first noticing their symptoms and the type of RA they were diagnosed with. Alarmingly, 50% of participants answered “no” to being immediately diagnosed, while 32% answered “other”. Responses within the “other” option included answers ranging from patients being misdiagnosed, not realizing the extent of their symptoms, or not being able to make an appointment with a rheumatologist for 6 months. Likewise, when asked the type of RA they were diagnosed with, 36% of participants reported being diagnosed with seropositive RA, 25% seronegative RA, 14% juvenile RA, and 25% reported “other”. Similar to the previous “other” responses, participants who elaborated in this section reported answers ranging from not knowing their diagnosis, being misdiagnosed with Lupus, to their doctor never even specifying to them the type of RA their diagnosis entailed. This information

is distressing considering that similar to many other chronic diseases, treatment intervention of RA is most effective when the disease is detected accurately and early in its progression (Mota et al, 2013). In addition, the fact that at least three participants did not know what type of RA they were diagnosed with is incredibly unsettling. For treatment to be effective, the patient must understand the full context of their diagnosis.

Similarly, the survey results disclosed pertinent information concerning the emotional and psychological toll of RA. When asked how their diagnosis made the participants feel, some participants reported feelings of worry, concern, anxiety, and confusion. While few expressed relief in knowing where their pain, fatigue, and symptoms were coming from, the overwhelming majority responded otherwise. From the results of the literature review, it was expected for some of the participants to not understand their diagnosis. When a young and seemingly healthy 30- year-old is told they have "arthritis," it would be surprising if they were not confused. This is precisely why professionals should integrate the education of RA and its differentiation from other forms of arthritis into their practice.

Along with this idea, Figure 15 depicts participant responses to whether or not they had ever discussed how their RA diagnosis might affect them personally or socially with a physician. 61% of participants responded "yes," 25% "no," and 14% responded "other." Among the "other" responses, one participant stated, 'Yes, but there weren't many avenues to explore with other people. These results signify that while it is apt that 61% of patients had discussed with their doctors how their diagnosis might affect them personally or socially, the extent to what actions were taken after this discussion is unknown. Because the prevalence of major depressive disorder is so high amongst RA patients, this conversation between patient and doctor should be routine.

This and the availability of more information regarding a patient's diagnosis should be available to mitigate feelings of confusion and worry after the initial diagnosis is made.

Some information related to patient perspectives regarding their treatment plans and how these plans have changed throughout their disease. The results shown in Figure 6 depict that over 28 patients reported pharmacotherapy as being included in their initial treatment plans. This survey question allowed participants to answer more than one treatment plan; participants may likely have chosen a multitude of answers to this particular question. Every treatment option available for this question was utilized; however, dietary changes, psychosocial interventions, and the use of adaptive equipment were each only reported as being included by some participants. Some

participants answered “other” and each elaborative response within the “other” option included the pharmacotherapy use of methotrexate, cortisone injection, and aspirin (see Figure 6). While these results confirm medicine to be the ‘go-to’ option for initial RA treatment plans amongst the participants, the widespread utilization of non-pharmacological options gives insight towards where the future of RA treatment may be headed. Even if drug treatment is effective in slowing the progression of disease or in alleviating patient symptoms, a patient’s quality of life may still be adversely affected. An overwhelming amount of research highlighted in the literature review revealed the positive effects of a comprehensive and holistic approach to the treatment of RA **(**Cunningham et al, 2013).

Furthermore, when asked how many of the participants had changed the course of their treatment plans since their initial diagnoses, maximum participant reported that they had changed medications, while others stated that they had experimented with various self-treatments or home remedies. Markedly, participant responses to what they felt had been the most effective element of their treatment plans varied immensely. Among the vast amount of answers claiming medication to be the most efficacious, methotrexate, cortisone injections, and Humira were among the most popular.

Humira, while not included in the literature review, is a type of medication called a biologic. Biologics are special forms of DMARDS that are often prescribed when a conventional DMARD is not effective (Biologics, n.d.**)**. Along with this, many responses attested to the benefits of being active and consistent with daily lifestyle routines.

Namely, it is noteworthy to consider the vast number of patients who reported a combination of treatments as being the most effective. While not overly popular among participant responses, some patients reported the use of medical cannabis and THC oil as being the most effective treatment modalit. Because the benefits of medical cannabis and THC oil are not empirically researched to the extent of other medications and treatments, it is not well known how their use will impact RA patients over time. Nevertheless, the first-ever cannabis-based medical trial for the treatment of pain in RA was conducted in 2005; its results are worthy of further research. In a study of 75 patients, the researchers concluded that cannabis-based medicine produced “a significant analgesic effect and disease activity was significantly suppressed” (Blake et al, 2005). While information and support concerning the use of cannabis in its many forms are new and forthcoming, its efficacy in reducing pain amongst RA patients is favorable for larger research.

Among participant responses considering what they felt to be least effective in treating their symptoms, maintaining exercise regimens, dietary changes, and attending therapy were three of the most popular responses. A few respondents reported the use of non-steroidal medications to be ineffective, while one respondent stated the side effects of steroids as being a hindrance to their treatment plan. Because most non-pharmacological approaches entail major changes to the lifestyle, it is understandable why so many of the participants feel these are the least effective or most difficult to attain. Changing one's diet or maintaining an exercise regimen can be incredibly difficult for healthy adults, let alone for those who are suffering from extreme pain, fatigue, and inflammation. While the efficacy of these regimens is well known and supported, their implementation may be easier on paper than in one's actual lifestyle.

While this may be the case, the effort put in by the participants of this study to try different treatment approaches should not be overlooked.

To conclude the survey, respondents were asked to compare their pain at the time of the survey compared to when they were first diagnosed. The final survey questions were designed to ask the participants to reflect on their journeys with RA and to reveal any activities they could no longer pursue due to their symptoms. While some respondents revealed that they could still pursue all their activities, the majority of responses revealed that the participants could either no longer do certain activities at all, or at least not to the extent that they were once able to. Activities like running or hiking were popular amongst the responses, likely due to the severe impact of these exercises on the lower joints. Other activities, such as sewing, which require fine motor movements, were also common responses. Interestingly, compared to when the participants were first diagnosed, 25% of participants stated they had "no pain," 32% had "mild pain," 39% had "moderate pain," 4% had "severe pain" and 0% reported "worse pain". Because the majority of patients reported to not be experiencing levels of 'severe pain,' it can be inferred that their treatment plans are contributing to the improvement of their symptoms. Similarly, 75% of patients reported "yes" to their RA symptoms currently being under control, while only 7% reported "no" and 18% reported "other". Among the "other" responses, a few patients felt that their symptoms were only "somewhat" controlled, while others seemed to be able to manage their pain but were concerned about symptomatic flare-ups.

With the vast number of patients reporting that their RA symptoms are under control, there is something to be said about the efficacy of their treatment plans. Yet, at the same time, this survey highlights the struggles faced by many RA patients when it comes to finalizing a treatment plan,

maintaining new regimens, and dealing with the emotional toll that an RA diagnosis can bring. The need for comprehensive and personalized inter professional teams is integral for the treatment of this complex disease.

Chapter- 05

Conclusion

The treatment for rheumatoid arthritis is variable and especially complex due to its manifestations in the non-articular systems of the body. While it was once considered to strictly be a disease affecting the synovial linings of the distal joints, the overtly systemic impact of RA on all major systems of the body is becoming more realized by professionals due to the insights of recent research. While the pathogenesis and pathophysiology of the disease are still not well-understood, the implication for how genetic and environmental risk factors may exacerbate the mechanisms of the disease is central to the current work.

Because RA can show symptoms in the body without the clinical phenotypic observation of swelling in the distal joints, the results of the literature review reveal the urgent need for physicians and rheumatologists to explore non-articular patient symptoms with the insight that these symptoms could indicate the early presence of rheumatoid arthritis. Observance of the early indicators of disease activity present in the larynx, lungs, heart, and vascular systems could be transformative in the detection of RA. With knowledge of how the early detection of this disease can impact a patient's long-term prognosis (Hiedari et al, 2013), it is inherent for professionals to recognize the importance of patient symptoms that go beyond pain, fatigue, and joint inflammation.

The optimism demonstrated by the participants of this survey towards the exploration of non-pharmacological treatment options for RA indicates the need for further research regarding the efficacy of these treatment options. While the medical treatment of RA will surely continue to improve with time, it is in the best interest of all RA patients to understand the full range of available treatment options. Likewise, the results of the literature review and patient survey affirm the struggles many RA patients experience in treating, managing, understanding, and accepting their disease.

The overall findings of this literature review and patient study point towards adopting a holistic, multifaceted, and inter professional approach towards the treatment and chronic evaluation of rheumatoid arthritis.. By increasing awareness of the fundamental and unparalleled components of this disease, there is hope that future research will be directed towards expanding treatment options and improving the experiences and wellbeing of those who are affected and impacted by rheumatoid arthritis.

Reference

1.Arnold, L. M., Hudson, J. I., Hess, E. V., Ware, A. E., Fritz, D. A., Auchenbach, M. B., ... & Keck Jr, P. E. (2004). Family study of fibromyalgia. Arthritis & Rheumatism, 50(3), 944-952.

2.Calin, A., Brophy, S., & Blake, D. (1999). Impact of sex on inheritance of ankylosing spondylitis: a cohort study. The Lancet, 354(9191), 1687-1690.

3.Garrett, S., Jenkinson, T., Kennedy, L. G., Whitelock, H., Gaisford, P., & Calin, A. (1994). A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. The Journal of rheumatology, 21(12), 2286-2291.

4.Helmick, C. G., Felson, D. T., Lawrence, R. C., Gabriel, S., Hirsch, R., Kwoh, C. K., ... & Pillemer, S. R. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part I. Arthritis & Rheumatism, 58(1), 15-25.

5.https://medlineplus.gov/ankylosingspondylitis.html#:~:text=Ankylosing%20spondylitis%20is%20a%20type,and%20more%20severe%20in%20men.

6.https://www.cdc.gov/arthritis/basics/rheumatoid-arthritis.html

7. Gladman DD, Antoni C, Mease P, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis. 2005;64 Suppl 2:ii14–7.

8.https://www.mayoclinic.org/diseasesconditions/osteoarthritis/symptomscauses/syc20351925#:~:text=Osteoarthritis%20is%20the%20most%20common,%2C%20knees%2C%20hips%20and%20spine.

9. Sato T, Ozawa T, Kikuchi M, et al. A case of progressive systemic sclerosis associated with mutilans-type arthropathy and suspected Felty's syndrome. Ryumachi. 1990;30:53–9.

10.Inoue, K., Hukuda, S., Fardellon, P., Yang, Z. Q., Nakai, M., Katayama, K., ... & Catteddu, I. (2001). Prevalence of large‐joint osteoarthritis in Asian and Caucasian skeletal populations. Rheumatology, 40(1), 70-73.

11.Jaakkola, E., Herzberg, I., Laiho, K., Barnardo, M. C., Pointon, J. J., Kauppi, M., ... & Brown, M. A. (2006). Finnish HLA studies confirm the increased risk conferred by HLA-B27 homozygosity in ankylosing spondylitis. Annals of the rheumatic diseases, 65(6), 775-780.

12.Kean, W. F., Kean, R., & Buchanan, W. W. (2004). Osteoarthritis: symptoms, signs and source of pain. Inflammopharmacology, 12(1), 3-31.

13.Lawrence, R. C., Felson, D. T., Helmick, C. G., Arnold, L. M., Choi, H., Deyo, R. A., ... & Jordan, J. M. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part II. Arthritis & Rheumatism, 58(1), 26-35.

14.Mitra, S. P. (2013). Arthritis: Classifications, Nature & Cause–A review. Am J Biopharmacol Biochem Life Sci, 2(3), 1-25.

15.Mitsuyama, H., Healey, R. M., Terkeltaub, R. A., Coutts, R. D., & Amiel, D. (2007). Calcification of human articular knee cartilage is primarily an effect of aging rather than osteoarthritis. Osteoarthritis and cartilage, 15(5), 559-565.

16.Prakash, S., Mehra, N. K., Bhargava, S. N. E. H., Vaidya, M. C., & Malaviya, A. N. (1984). Ankylosing spondylitis in North India: a clinical and immunogenetic study. Annals of the rheumatic diseases, 43(3), 381-385.

17.https://www.google.com/search?client=firefox-b-d&q=arthritis+definition# C. Shiel Jr., MD, FACP, FACR

18.Calin, A., Brophy, S., & Blake, D. (1999). Impact of sex on inheritance of ankylosing spondylitis: a cohort study. The Lancet, 354(9191), 1687-1690.

19.Garrett, S., Jenkinson, T., Kennedy, L. G., Whitelock, H., Gaisford, P., & Calin, A. (1994). A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. The Journal of rheumatology, 21(12), 2286-2291.

20.Helmick, C. G., Felson, D. T., Lawrence, R. C., Gabriel, S., Hirsch, R., Kwoh, C. K., ... & Pillemer, S. R. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part I. Arthritis & Rheumatism, 58(1), 15-25.

21.https://www.mayoclinic.org/diseases-conditions/arthritis/symptoms-causes/syc-20350772,

https://www.mayoclinic.org/diseases-conditions/osteoarthritis/symptoms-causes

22.Ferucci, E. D., Templin, D. W., & Lanier, A. P. (2005). Rheumatoid arthritis in American Indians and Alaska natives: A review of the literature. Seminars in Arthritis and Rheumatism, 34(4), 662–667. doi: 10.1016/j.semarthrit.2004.08.003.

23.Heidari, B. (2011). Rheumatoid arthritis: early diagnosis and treatment outcomes. Caspian Journal of Internal Medicine, 2(1), 161–170.

24.Cunningham, N. R., & Kashikar-Zuck, S. (2013). Nonpharmacological treatment of pain in rheumatic diseases and other musculoskeletal pain conditions. Current rheumatology reports, 15(2), 306. https://doi.org/10.1007/s11926-012-0306-y.

25.Blake, D. R., Robson, P., Ho, M., Jubb, R. W., & Mccabe, C. S. (2005). Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid.

26.Gibofsky, A. (2012). Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. The American journal of managed care, 18(13 Suppl), S295- 302.

27.Boilard, E., Nigrovic, P. A., Larabee, K., Watts, G. F., Coblyn, J. S., Weinblatt, M. E., ... & Lee, D. M. (2010). Platelets amplify inflammation in arthritis via collagendependent microparticle production. Science, 327(5965), 580-583.

28.Nikolaus, S., Bode, C., Taal, E., & M. A. F. J. Van De Laar. (2010). New insights into the experience of fatigue among patients with rheumatoid arthritis: a qualitative study. Annals of the Rheumatic Diseases, 69(5), 895–897. doi: 10.1136/ard.2009.118067.

29.Gary S. Firestein,2003, Evolving concepts of rheumatoid arthritis, 30.Freeman, J. (2018, October 27). RA treatment costs: What are the costs of RA medications and surgery? Rheumatoid Arthritis Support Network

30. Hayem G, Chazerain P, Combe B, Elias A, Haim T, Nicaise P, Benali K, Eliaou JF, Kahn MF, Sany J, Meyer O: Anti-Sa antibody is an accurate diagnostic and prognostic marker in adult rheumatoid arthritis. J Rheumatol. 1999, 26: 7-13.

31.Fausto Salaaffi, Marina Carrotti ,Stefania Gasparini, Michele Introcia & Walter Grassi .2009. The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. Open Access,1-18.

32.Rubén Queiro, Juan D.Cañete, Carlos Montilla, Miguel Abad, María Montoro, Susana Gómez, Ana Cábez & on behalf of the MAAPS study group. 2017. Minimal disease activity and impact of disease in psoriatic arthritis: a Spanish cross-sectional multicenter study. Springer link. 1-12.

33.Vorgelegt von ,Michaela Coenen.2008. Developing a method to validate the WHO ICF Core Sets from the patient perspective: rheumatoid arthritis as a case in point, Springer link.

34.Michele L. Boutough.2003. Arthritis Foundation community‐based physical activity programs: Effectiveness and implementation issues. Wiley Online Libray.

35.Robert F. Meenan MD, MPH, Paul M.Gertman ,MD . John H, Mason MA, 1980, Measuring health status in arthritis, Wiley Online Libray.

36.James F. Fries, Patricia Spitz, R. Guy Kraines, and Halsted R. Holman, 1980, Measurement of patient outcome in arthritis, Wiley Online Libray.

37.henri A Ménard, Elvy Lapointe, Moulay D Rochdi & Zhi J Zhou Arthritis Research & Therapy **volume 2**, Article number: 429 (2000)