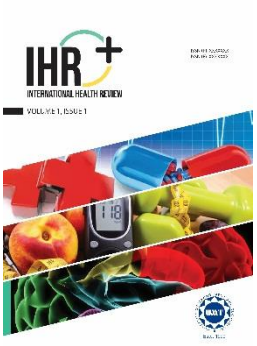

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Article: **Therapeutic Role of Glucosamine Sulphate Among patients with Rheumatoid Arthritis**

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# Therapeutic Role of Glucosamine Sulphate Among Patients with Rheumatoid Arthritis

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## Abstract

*Rheumatoid Arthritis (RA) is a fatal disease. At present, the prevalence of rheumatoid arthritis (RA) in human beings is approximately 1%. Glucosamine (2-amino-2-deoxy-D-glucose) is a naturally occurring amino-monosaccharide in the human body. It is present abundantly in the cartilage and the connective tissue of human beings. It also originates from glucose in almost every human tissue. The purpose of this research is to evaluate the effect of glucosamine sulphate supplements in patients with rheumatoid arthritis to assess it as a treatment for RA. This study was completed in the duration of 2 months using a randomized control trial study method. Ninety individuals (men and women) participated in this research. The data was collected from Azhar Orthopedics Clinic and Mayo Hospital in Lahore. The sample population was divided into group I, II & III, with 30 patients in each group. Group I was given 500 mg glucosamine sulphate/day, group II was given 1000 mg/day for two months, and group III was a controlled group (it was not supplemented with glucosamine sulphate). To conduct an ESR test, a blood sample was taken from the study population on day 0, 30, and 60. The ESR test readings of the individuals were statistically evaluated to assess the anti-arthritic effect of the glucosamine sulphate supplement. The readings were also used to evaluate a more effective dose of the supplement ranging between 500mg and 1000mg. The results indicated that glucosamine sulphate supplements significantly reduced the ESR levels in patients with rheumatoid arthritis. Furthermore, group I and group II exhibited significant results ($p<0.001$), indicating a reduction in the ESR levels. Therefore, it was determined that glucosamine sulphate*

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*supplementation does exhibit an anti-arthritic effect on rheumatoid arthritis patients.*

**Keywords:** anti-arthritic, cartilage, ESR**,** glucosamine sulphate, rheumatoid arthritis

## Introduction

Rheumatoid Arthritis (RA) is an inflammatory disorder which affects the joints in the human. Its pathophysiology stems from hyperactive immune system towards its own cells. Its clinical characteristics include joint swelling, fever, weight loss, fatigue, anaemia, and crippling pain. Chronic inflammation triggers the production of those enzymes that gradually digest adjacent tissues [1], this causes swelling in the synovial tissue and leads to excessive production of the synovial fluid. RA affects 0.24% of the people worldwide, although men are less affected than women [2]. The prevalence of RA is 0.14% in Karachi and 0.55% in northern areas of Pakistan. A study [3] showed that out of the 63 patients, 28% patients had joint deformities. It also showed that females are more prone to joint deformities and related diseases than males (18 males and 45 females). A similar trend has also been reported by other researchers from Pakistan [4].

Glucosamine is a biochemical naturally present in the human body, it is also an important structural component of the cartilage system. It is a member of the glycosaminoglycan (GAG) family that is present in the cartilage matrix and synovial fluid [5]. It has two types, namely glucosamine hydrochloride and glucosamine sulphate. Glucosamine Sulphate is a naturally occurring chemical in the human body. It produces a variety of chemicals involved in building tendons, cartilage, ligaments, and other thick fluids that cushion the joints in the human body. This fluid is important because it acts as a cushion for joints, protecting them from harm caused by a sudden jerk [6]. Glucosamine sulphate acts as an essential substrate, formulates a healthy joint matrix, and stimulates the biosynthesis of GAGs. The primary role of this biochemical is to halt or reverse joint degeneration. Furthermore, it also stimulates the production and synthesis of hyaluronic acid in the backbone which is necessary for the formation of proteoglycans present in the structural matrix of joints.

Glucosamine is available in the United States (US) drug stores as a nutritional supplement. NIH conducted a Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) to test its effectiveness as a treatment for knee pain [7]. The results concluded that a dose of 1500 mg glucosamine (500 mg, thrice a day) with 1200 mg of chondroitin (400 mg, thrice a day) acted as a painkiller for patients suffering from moderate to mild pain; however, these doses are not effective for the treatment of rheumatoid arthritis (RA) in patients with mild pain subset.

Setnikar explored the utilization of glucosamine for the treatment of anti-inflammatory diseases [8]. He evaluated the effectiveness of glucosamine for the treatment of Kaolin arthritis and adjuvant arthritis in rats using sponge and croton oil granuloma models. The results expressed an anti-inflammatory activity by Glucosamine. Glucosamine has a higher therapeutic margin than indomethacin, even though its impact is 50-300 times lower. Indomethacin's toxicity is also 1000 to 4000 times higher.

The mechanisms of glucosamine's anti-inflammatory activity are substantially different from those of non-steroidal anti-inflammatory drugs (NSAIDs), which act primarily through the inhibition of cyclooxygenases.

Chondroitin Sulphates (CS) are additional substrates that are used for the formation of a healthy joint matrix. Their constituents are either absorbed, intact, or broken during joint formation. Many clinical pieces of evidence support the fact that chondroitin sulphates are useful for the treatment of joint disease since they act as symptomatic slow-acting drugs (SYSADOAs). The use of glucosamine sulphates and chondroitin sulphates for the treatment of degenerative joint disease is receiving more attention recently. It is an extremely popular supplementation protocol in arthritic conditions of the joints since they are partially absorbed by the joints and relieve pain by slowing the rate of joint and cartilage loss and destruction [9]. Hence, glucosamine and chondroitin sulphates are useful for the treatment of rheumatoid arthritis (RA); however. there is little to no clinical evidence and research to support this claim.

This research is a novel study since it examined the efficacy of glucosamine sulphate in the treatment of rheumatoid arthritis (RA) within the population of Lahore, Pakistan. The data was collected from male and

female subjects ranging between the ages of 20 and 60. It investigated the efficacy of glucosamine sulphates. It also determined the doses necessary for the treatment of RA. This research provided clinical evidence of glucosamine sulphate's effectiveness against minor cartilage loss and rheumatoid arthritis. Our hypothesis tested the positive therapeutic effect of glucosamine sulphate, which can be used to control and reduce joint inflammation in patients with rheumatoid arthritis (RA). There were two main objectives of this research. First, we aimed to diagnose the anti-arthritic effect of glucosamine sulphate on patients with rheumatoid arthritis (if any). Second, we determined the dose of glucosamine sulphate necessary to treat patients with rheumatoid arthritis (RA).

## Materials and Methods

### Study Design

The study utilized a randomized controlled trial (RCT) which is an open-labelled study design. Three groups were included in this trial. Group I and group II were given glucosamine sulphate as a nutritional supplement [9], whereas group III served as control. A follow-up study was conducted on the three groups to see the difference between the outcomes.

### Study Location

The data was collected from Mayo Hospital, Lahore. Mayo Hospital is one of the oldest hospitals in Pakistan., It is even older than Pakistan itself since it was founded in Lahore in 1871. Mayo Hospital is affiliated with King Edward Medical University, which is a prestigious institute in South Asia. The entire write up and planning of the research was done in NUR International University (NIU), Lahore. It is located in the middle of Lahore and provides treatment at a very low cost to the admitted patients as per government policy.

### Study Population

The study population consisted only of those participants which were diagnosed with rheumatoid arthritis (RA). The targeted population included patients between the age of 20 and 60. Overall 90 patients with Rheumatoid Arthritis (RA) were included in the study since they were available at Outpatients Department (OPD). These patients were divided into three groups, namely I, II, and III. Each group consisted of 30 individuals. Group

I was given 500 mg glucosamine sulphate/day, while group II was given 1000 mg glucosamine sulphate/day. Group III was the control group and was not supplemented with glucosamine sulphate dose. The doses were extrapolated from previously conducted studies, which used these amounts and concluded with solid results. The intervention study was completed in 2 months. Blood samples were taken to determine the supplement's effect on patients with rheumatoid arthritis (RA).

## Sampling Technique

The study utilized a non-probability convenience sampling technique. All the participants of the study were diagnosed with rheumatoid arthritis and were between the age of 20 to 60. According to the diagnostic ACR 2010 criteria and only patients with prescribed medications, individuals below the age of 20 and above 60 were excluded. Also individuals with thyroid disease and dyslipidemia were eliminated from this study.

## Sample Size

The sample size consisted of 90 patients. There were three groups, namely group A, and group B (intervention) and group C (controlled). A sample size of 90 patients was selected using a 5% significance level, 90% confidence interval, 0.35 clinically acceptable margin, and 1.22 pooled standard deviation.

## Biochemical Analysis

Standard Westergren method was initially used to check the ESR mm/hr before the trial on day 0 and after the trial on day 30 and 60. This was done because raised erythrocyte sedimentation rate (ESR) is an indicator of rheumatoid arthritis (RA). ESR is a non-specific screening test that is used to measure the presence of inflammation in the human body. It reflects the increase in plasma immune-globulins and fibrinogens. Red blood cells tend to rapidly settle down in the case of any disease. ESR changes in case of any change in the shape of red blood cells in the blood.

For the evaluation of ESR, anti-coagulated blood is kept inside a narrow vertical tube The red blood cells settle down and separate from plasma due to gravity's influence. The amount of plasma present at the top of the column after one hour (mm/hr) is measured using two methods, namely the Westergren method and the Wintrobe method. Each method shows or

produces slightly different results; however, the Westergren method is mostly used in laboratories.

Westergren Method

The Westergren method requires 2 ml venous blood in a test tube containing 0.5 ml sodium citrate. It should not be stored for more than 2 hours at room temperature or 6 hours at 4 Celsius. In the Westergren-Kartz tube, the blood was drawn up to the 200 mm mark and placed in a vertical position for at least an hour at room temperature. The distance of fall of erythrocytes in 1 hour is the result of ESR. The distance is expressed as millimetres.

Ethical Approval

Institutional Review Board letter was signed from the Institutional Review Board (IRB) department of NIU, Lahore.

Informed Consent

Written consent was taken from all participants and their information was ensured as confidential. A consent letter was signed by all the patients participating in the study.

## Statistical Analysis

The data was entered and analyzed in SPSS version 25 and a descriptive analysis was performed on all the variables. Categorical variables were presented in the form of frequency and percentages; whereas, quantitative variables were presented in form of the mean (SD). ANOVA test was used to conduct a group comparison between quantitative variables such as age and erythrocyte sedimentation rate (ESR). Chi-square test was applied to see the association between categorical variables such as gender, pain, stiffness, and movement of all participants within three study groups (group I, group II, and group III). Friedman was applied to conduct a within group comparison between erythrocyte sedimentation rate (ESR) values at different time points (Pre, Post 1, and Post 2). P-value was less than 0.05 and was considered significant.

## Results and Discussion

### Demographics of Age and Gender

**Table 1.** The Mean Age of the Patients with Rheumatoid Arthritis

| Groups (n=30 in each group) | Mean Age (yr.) | Standard Deviations | Total | P-value |
|---|---|---|---|---|
| Group I (Glucosamine Sulphate 500mg) | 37.47 | 7.128 | 36.84 | 0.002 |
| Group II (Glucosamine Sulphate 1000mg) | 33.43 | 5.710 | | |
| Group III (Placebo) | 39.63 | 7.346 | | |

(Patients between the age of 20 – 60 years were included in the study). P<0.05

ANOVA

**Table 2.** Gender Distribution between Groups I, Ii & Iii

| Gender | Groups (n=30 in each group) | | | Total | P-value |
|---|---|---|---|---|---|
| | Group I (500mg) | Group II (1000mg) | Group III (Placebo) | | |
| Male | 9(10%) | 10(10%) | 15(16%) | 34(37.8%) | 0.231 |
| Female | 21(23%) | 20(22%) | 15(16%) | 56(62,2%) | |
| Total | 30(33%) | 30(33%) | 30(33%) | 90(100%) | |

Chi square method was used to analyze the difference between gender groups. (P > 0.05)

### Effect of Glucosamine Sulphate on Esr Mm/Hr at Different Durations

**Table 3.** Erythrocyte Sedimentation Rate (Esr) Mm/Hr Readings On 0 Day

| | Groups | ESR (mm/hr.) at 0 day | Total | P-value |
|---|---|---|---|---|
| Glucosamine sulphate/day | Group I (500mg/day) | 38.27±5.23 | 36.28±5.54 | 0.004 |
| | Group II (1000mg/day) | 36.83±5.55 | | |
| | Group III (Placebo) | 33.73±4.99 | | |

All the variables are presented in form of Mean±SD. (P<0.05)

**Table 4.** Erythrocyte Sedimentation Rate (Esr) Mm/Hr Readings On 30th Day

| | Groups | ESR (mm/hr.) at 30th day | Total | P-value |
|---|---|---|---|---|
| Glucosamine sulphate/day | Group I (500mg/day) | 36.50±5.03 | 34.57±5.42 | 0.054 |
| | Group II (1000mg/day) | 33.47±5.83 | | |
| | Group III (Placebo) | 33.73±4.99 | | |

All the variables are presented in form of Mean±SD. P<0.05

**Table 5.** Erythrocyte Sedimentation Rate (Esr) Mm/Hr Readings on 60th Day

| | Groups | ESR (mm/hr.) at 30th day | Total | P-value |
|---|---|---|---|---|
| Glucosamine sulphate/day | Group I (500mg/day) | 34.93±4.82 | 32.97±5.72 | .003 |
| | Group II (1000mg/day) | 30.23±6.33 | | |
| | Group III (Placebo) | 33.73±4.99 | | |

All the variables are presented in form of Mean±SD. P<0.05

## Effect of Glucosamine Sulphate (Gs) with Different Doses on the Study Groups

**Table 6.** Effects of Doses 500 Mg & 1000 Mg between Group I & Group Ii

| Group | Erythrocyte Sedimentation Rate(ESR) (mm/hr.) | | | P-value* |
|---|---|---|---|---|
| | Pre (0 day) | Post I (30th day) | Post II (60th day) | |
| Group I (Glucosamine Sulphate 500mg) | 38.27±5.22 | 36.50±5.03 | 34.93±4.82 | 0.000 |

| | | | | |
|---|---|---|---|---|
| Group II (Glucosamine Sulphate 1000mg) | 36.83±5.54 | 33.47±5.83 | 30.23±6.33 | 0.000 |
| Group III (Placebo) | 33.73±4.99 | 33.73±4.99 | 33.73±4.99 | NA |

All the variables are presented in form of Mean±SD P< 0.001

## Effect of Glucosamine Sulphate on Rheumatoid Arthritis Patients (Self-Assessment) as Reflected by Reduction in Disease Symptoms

**Table 7.** Self-Assessment of Rheumatoid Arthritis Patients about their Pain

| | Response | Participants In Groups | | | P-Value |
|---|---|---|---|---|---|
| | | Group I (500mg/day) | Group II (1000mg/day) | Group III (placebo) | |
| Pain | Improved | 24(26.7%) | 28(31.1%) | 0(0.0%) | 0.0001 |
| | Not Improved | 6(6-7%) | 2(2.2%) | 30(33.3%) | |

Chi Square

**Table 8.** Self-Assessment of Rheumatoid Arthritis Patients about their Stiffness

| | Response | Group | | | P-Value |
|---|---|---|---|---|---|
| | | I | II | III | |
| Stiffness | Improved | 16(17%) | 23(25%) | 0(0%) | 0.0001 |
| | Not Improved | 14(15%) | 7(7%) | 30(33%) | |

Chi Square

**Table 9.** Self-Assessment of Rheumatoid Arthritis Patients about their Body Movements

| | Response | Group | | | P-Value |
|---|---|---|---|---|---|
| | | I | II | III | |
| Body Movements | Improved | 20(22.2%) | 24(26.7%) | 0(0%) | 0.0001 |
| | Not Improved | 10(11.1%) | 6(6.7%) | 30(33%) | |

Chi Square

## Conclusion

Groups I and II were uncontrolled, but group III was controlled. Although group I (500 mg/day) experienced an anti-arthritic effect, group II (1000 mg/day) had more distinguishable outcomes. It was determined that glucosamine sulphate slows the course of rheumatoid arthritis (RA) by lowering the ESR levels of patients. These findings suggest that glucosamine sulphate can help RA patients reduce pain and stiffness, which improves their physical activity.

### Limitations and Suggestions

1. Due to the COVID-19 pandemic, it was difficult to collect study samples. It was also extremely difficult to commute from one place to another.
2. The large sample should be taken for more genuine results
3. Large scale clinical trials are suggested for future studies.

It should also be mentioned that due to the pandemic, it was really difficult to gather participants since everyone was paranoid due to fear and phobia of COVID-19.

## References

[1] Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumaticdrugs: 2016update. *Ann Rheumatic Dis*. 2017;76(6):960-77. http://dx.doi.org/10.1136/annrheumdis-2016-210715

[2] Leakey JE, Ali AA, Babb AR, et al. Subchronic toxicity evaluation of glucosamine and glucosamine in combination with chondroitin sulfate in obese Zucker rats. *ToxicolAppl Pharma*. 2021;412:115371. https://doi.org/10.1016/j.taap.2020.115371

[3] Munir MAA, Aziz M, Mahboob A. Frequency of Rheumatoid Factor Positivity in Patients of Rheumatoid Arthritis Report of 95 cases from Lahore, Pakistan. *J Fatima Jinnah Med Uni*. 2013;7(4):1-5.

[4] Vasiliadis HS, Tsikopoulos K.Glucosamine and chondroitin for the treatment of osteoarthritis. *World J Orthop*. 2017;8(1):1-8.

[5] Reginster JYL, Bruyere O, Cooper C. Different glucosamine sulphate products generate different outcomes on osteoarthritis symptoms. *Annals Rheumatic Dis*. 2018;77(7):e39-e39.

[6] National Center for Complementary and Alternative Medicine, National Institutes of Health. The NIH glucosamine/chondroitin arthritis intervention trial (GAIT). *J Pain Palliative Care Pharma*. 2008;*22*(1):39-43.

[7] Setnikar I, Pacini MA, Revel L. Antiarthritic effects of glucosamine sulfate studied in animal models. *Arzneimittel-forschung*. 1991;41(5):542-5.

[8] Zhu X, Sang L, Wu D, Rong J, Jiang L. Effectiveness and safety of glucosamine and chondroitin for the treatment of osteoarthritis: a meta-analysis of randomized controlled trials. *J Orthop Surgery Res*. 2018;13(1):170-180.

[9] Way WK, Gibson KG, Breite AG. Determination of glucosamine in nutritional supplements by reversed-phase ion-pairing HPLC. *J Liquid Chroma Related Technol*, 2000;*23*(18):2861-2871.