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# Assessing Serum Biochemical Abnormalities in Rheumatoid Arthritis Patients: Implications for NSAID Treatment and Renal Function

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**Introduction:**

Renal failure-related mortality is significantly elevated among Rheumatoid Arthritis (RA) patients, with a documented prevalence of renal disease in approximately 72% of cases. The reported prevalence of kidney disease in RA varies widely, making its true prevalence uncertain. RA is associated with kidney disorders attributed to chronic inflammation and drug exposure. This study aims to explore serum biochemical abnormalities in RA, focusing on urea, creatinine, and erythrocyte sedimentation rate (ESR), particularly in response to NSAID treatment.

**Material and Methods:**

The study, conducted in Sambalpur City, included 180 volunteers categorized into three groups: Control (healthy individuals), Group I (RA patients), and Group II (RA patients using NSAIDs). Blood samples were collected for urea, creatinine, and ESR analysis. Data were presented as mean ± SD, and the significance of mean differences was assessed using the student's t-test.

**Results:**

Significant variations were observed in ESR, urea, and creatinine levels among the groups. ESR levels surged in RA patients, with NSAID use exhibiting a notable rise. Urea and creatinine levels increased in RA patients, showing a slight decrease after NSAID treatment. These alterations highlight distinct biochemical changes in RA patients and those using NSAIDs compared to the healthy Control Group.

**Discussion:**

The study illuminates the intricate links between Rheumatoid Arthritis (RA), renal health, and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Elevated Erythrocyte Sedimentation Rate (ESR), increased serum creatinine and urea levels in RA patients, and the potential renal impact of NSAIDs underscore the need for nuanced therapeutic approaches and vigilant monitoring in managing RA, shaping future research directions.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

**Conclusion:**

Findings underscore the need for vigilant monitoring and personalized therapeutic strategies in managing RA patients, particularly those undergoing NSAID treatment. This research lays a foundation for future investigations into tailored clinical interventions and a comprehensive understanding of the complexities of managing RA patients with renal implications.

**Keywords:** Rheumatoid Arthritis, NSAIDs, Renal Function, Serum Biochemical Abnormalities, Erythrocyte Sedimentation Rate, Urea, Creatinine.

## INTRODUCTION

Renal failure-related mortality is significantly higher among Rheumatoid Arthritis (RA) patients than in the general population, with documented renal disease in approximately 72% of RA patients at necropsy[1]. The reported prevalence of kidney disease in RA patients varies widely, ranging from 5% to 50% across diverse study designs, leaving the true prevalence uncertain[3,4].

RA is linked to various kidney disorders primarily attributed to chronic inflammation and drug-related exposure or toxicity[5]. The evolving treatment landscape for RA over time may influence the incidence of kidney disease. Previously prevalent agents like gold salts and d-penicillin, directly associated with proteinuria and kidney disease, have been replaced by newer treatments[6,7]. Cyclosporine therapy, previously linked to dose-dependent nephrotoxicity in RA patients, has become less prominent[8,9]. Recently, biologic agents, including tumor necrosis factor α inhibitors like etanercept, have emerged as effective treatments, yet case reports suggest a potential association with glomerulonephritis, underscoring the persistent link between kidney disease and RA treatment[10]. Additionally, the long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase 2 inhibitors is a recognized cause of kidney injury[11].

This study aims to ascertain the frequency of serum biochemical abnormalities in rheumatoid disease and elucidate some of the results obtained. Specifically, we analyze serum urea, serum creatinine, and erythrocyte sedimentation rate (ESR) in RA patients to:

(a) Investigate changes in the serum of RA patients on NSAIDs compared to RA patients without medication.

(b) Assess the impact of NSAIDs on the normalization of these biochemical profiles.

## MATERIAL AND METHODS

The study was conducted in Sambalpur City (Odisha) and included 180 volunteers aged 18-52, encompassing both genders. Participants were categorized into three groups: the Control group (comprising healthy males and females), Group I (consisting of Rheumatoid Arthritis (RA) patients), and Group II (comprising RA patients using non-steroidal anti-inflammatory drugs (NSAIDs)).

Blood samples were collected from the antecubital vein without venostasis for the analysis of various parameters. Serum samples were utilized for measuring urea and creatinine, while whole blood was employed for erythrocyte sedimentation rate (ESR) assessment. Diacetyl monoxime, Alkaline picrate, and Wintrobe methods were employed for estimating urea, creatinine, and ESR, respectively. Data are

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

presented as mean ± SD. The significance of mean differences between groups was determined using the student's t-test, and the probability distribution 'p' was assessed.

**Results**

A total of 180 students were enrolled in the study. The investigation into Erythrocyte Sedimentation Rate (ESR) levels among the three groups revealed significant variations.

**Table 1 Effect on NSAIDs on ESR in RA Patients**

| PARTICULARS | CONTROL GROUP | GROUP -I | GROUP –II |
|---|---|---|---|
| Sample size | 60 | 60 | 60 |
| Mean | 12.7 | 48.3 | 31.2 |
| ± S.D | 0.445 | 1.533 | 1.34 |
| % INC | - | 276.1% | 149.3% |
| % DEC | - | - | - |
| t- value | - | 29.2 | 18.1 |
| p- value | - | <0.001 | <0.001 |

In the Control Group, the mean ESR was 12.7 mg/dl, while in Group-I (Rheumatoid Arthritis patients), it surged to 48.3 mg/dl, marking a substantial 276.1% increase. Group-II, consisting of Rheumatoid Arthritis patients using NSAIDs, exhibited a mean ESR of 31.2 mg/dl, indicating a notable 149.3% rise compared to the control. Statistical analysis confirmed these differences, with t-values of 29.2 ($p < 0.001$) for Group-I and 18.1 ($p < 0.001$) for Group-II.

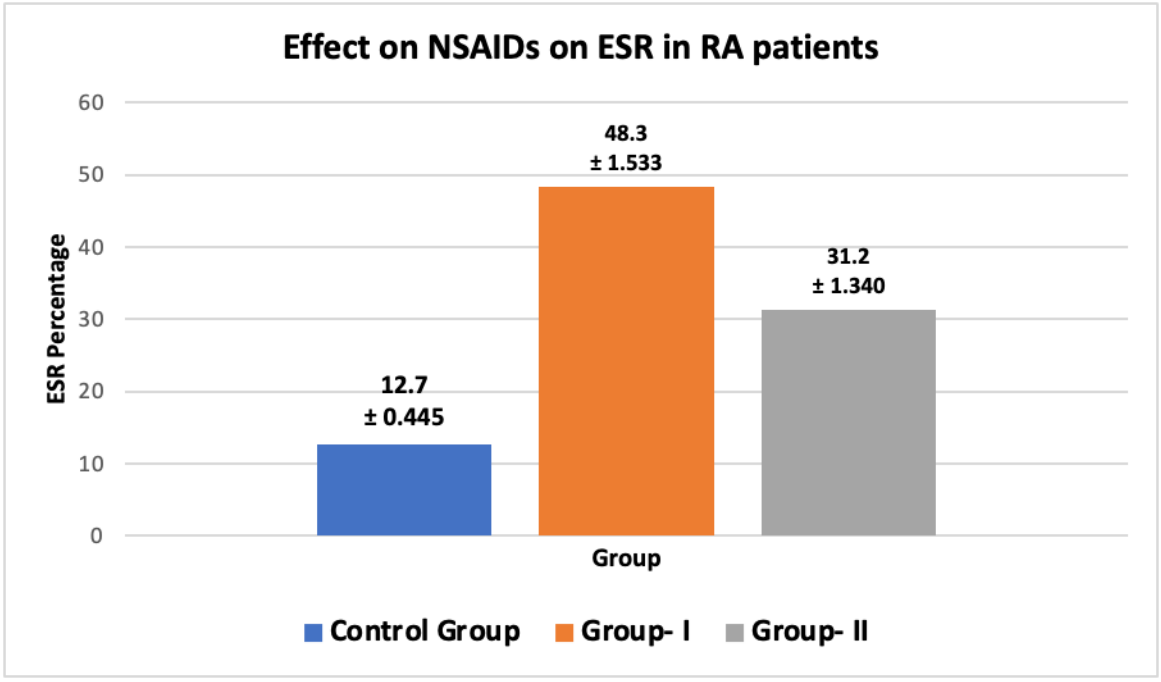


**Figure 1 Effect on NSAIDs on ESR in RA Patients**

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

The investigation extended to urea levels, where the Control Group showed a mean concentration of 17 mg/dl.

**Table 2 Effect on NSAIDs on Urea in RA Patients**

| PARTICULARS | CONTROL GROUP | GROUP -I | GROUP –I |
|---|---|---|---|
| Sample size | 60 | 60 | 60 |
| Mean | 17 | 35.1 | 28.8 |
| ± S.D | 2.25 | 0.814 | 0.978 |
| % INC | - | 112.2% | 45.4% |
| % DEC | - | - | - |
| t- value | - | 11.72 | 6.224 |
| p- value | - | <0.01 | <0.01 |

In Group-I, urea levels significantly rose to 35.1 mg/dl, reflecting a substantial 112.2% increase. Group-II exhibited a mean urea concentration of 28.8 mg/dl, indicating a noticeable 45.4% increase relative to the control. Statistical analysis confirmed these differences, with t-values of 11.72 ($p < 0.01$) for Group-I and 6.224 ($p < 0.01$) for Group-II.

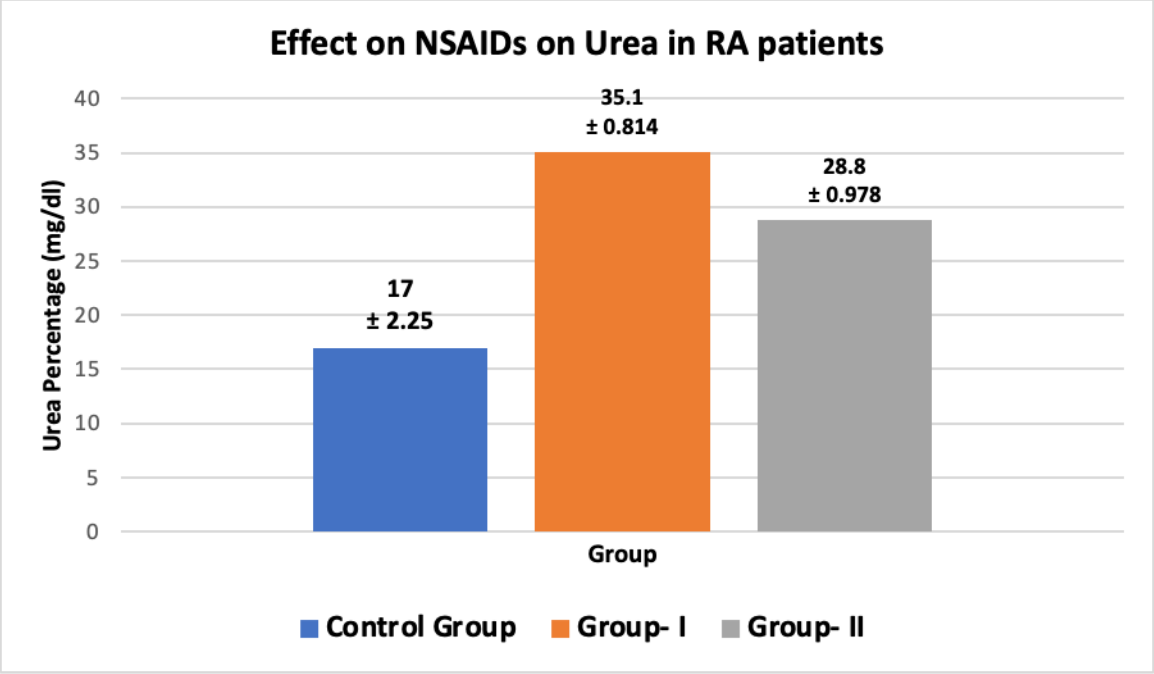


**Figure 2 Effect on NSAIDs on Urea in RA Patients**

Regarding creatinine levels, the Control Group displayed a mean of 0.44 mg/dl. In Group-I, creatinine levels increased significantly to 1.5 mg/dl, marking a 155.2% rise.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

**Table 3 Effect on NSAIDs on Creatinine in RA Patients**

| PARTICULARS | CONTROL GROUP | GROUP -I | GROUP –II |
|---|---|---|---|
| Sample size | 60 | 60 | 60 |
| Mean | .44 | 1.5 | 1.4 |
| ± S.D | .048 | .091 | .037 |
| % INC | - | 155.2% | 134.1% |
| % DEC | - | - | - |
| t- value | - | 13.4 | 26.7 |
| p- value | - | <0.001 | <0.001 |

Group-II exhibited a mean creatinine level of 1.4 mg/dl, signifying a substantial 134.1% increase compared to the control. Statistical analysis confirmed these differences, with t-values of 13.4 ($p < 0.001$) for Group-I and 26.7 ($p < 0.001$) for Group-II. Overall, the results highlight distinct alterations in ESR, urea, and creatinine levels in Rheumatoid Arthritis patients and those using NSAIDs compared to the healthy Control Group.

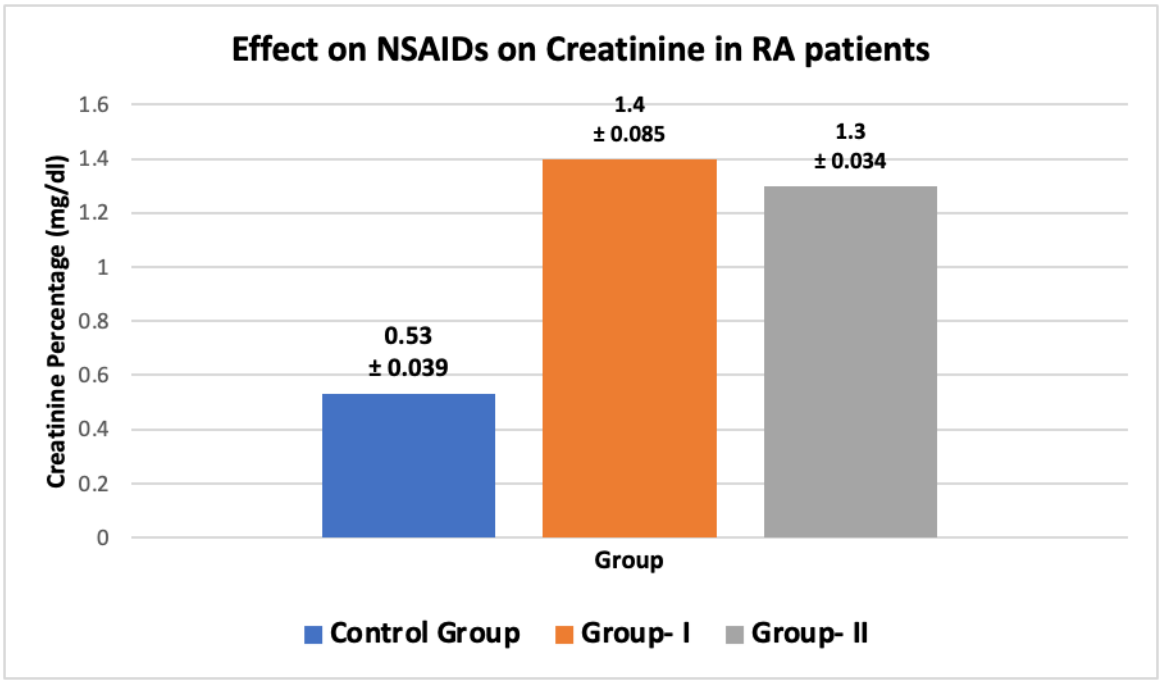


**Figure 3 Effect on NSAIDs on Creatinine in RA Patients**

**Discussion:**

We conducted a study to investigate the impact of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) on renal function in patients with Rheumatoid Arthritis (RA), given the frequent and prolonged use of NSAIDs in managing this common inflammatory rheumatic disorder. It is noteworthy that renal disease directly attributed to RA is an exceedingly rare occurrence. Studies by Bjarrason et al. demonstrated that NSAIDs could induce intestinal inflammation in individuals with rheumatic diseases, potentially leading

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to blood and protein loss from the gastrointestinal tract. This underscores the need to examine the effects of NSAIDs on various organ systems, including the kidneys [12,13].

The elevation of erythrocyte sedimentation rate (ESR) is indicative of inflammation in the body. High ESR levels are commonly associated with RA, serving as a clinical marker for disease activity. Carlson et al. and Barland P., Lipstein E. emphasized the significance of ESR as a marker of disease activity in rheumatoid arthritis, showing a strong association with clinical indicators such as disability score and swollen joints. Our study aligns with these findings, revealing a statistically significant increase in ESR levels among RA patients[14,15].

Serum creatinine, a widely used marker of renal function, was examined in our study. We observed increased levels of serum creatinine and serum urea in RA patients, with a slight decrease after NSAID treatment, although the reduction was not statistically significant. This finding is consistent with the research by Fried E. Silverstein et al., which compared gastrointestinal toxicity with Celecoxib versus traditional NSAIDs for osteoarthritis and rheumatoid arthritis. Their study demonstrated a lower incidence of renal adverse effects, including increased creatinine, in patients receiving Celecoxib compared to NSAIDs [16-20].

Moreover, a comprehensive investigation into renal comorbidity in patients with rheumatic diseases by Anders and Vielhauer indicated a significant overlap between RA and renal disease. Elevated serum creatinine values were found in a substantial proportion of prevalent RA patients, emphasizing the complex interplay between antirheumatic drugs, chronic inflammatory processes, and primary disease manifestations.

The potential for NSAIDs, including cyclooxygenase-2 inhibitors, to cause acute deterioration of renal function is well-established. Renal blood flow is reliant on renal prostaglandin synthesis, and NSAIDs can disrupt this process. Our study contributes to the growing body of evidence highlighting the intricate relationship between NSAID use, RA, and renal function, emphasizing the need for vigilant monitoring and personalized therapeutic approaches in managing RA patients.

**Conclusion:**

In summary, our investigation delved into the intricate interplay between Rheumatoid Arthritis (RA), renal function, and the impact of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Renal failure-related mortality is notably higher in RA patients, with kidney disease documented in a significant proportion of cases. The prevalence of kidney disease in RA varies widely, emphasizing the need for a comprehensive understanding of its implications.

This study contributes valuable insights into the biochemical alterations associated with RA and NSAID treatment, shedding light on the complexities of this medical landscape. The findings provide a foundation for future research and tailored clinical interventions, acknowledging the need for vigilant monitoring and personalized therapeutic strategies in the management of RA patients.

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ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

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