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Original Article

Oxidative Stress and Metabolic Dysregulation in Psoriasis: Insights from Uric Acid and Nitric Oxide Levels @ Index Medical College, Indore, M.P.

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Abstract

Introduction: Psoriasis is a chronic autoimmune inflammatory skin disorder characterized by systemic inflammation and oxidative stress. Among the key biomarkers, uric acid (UA) and nitric oxide (NO) have emerged as critical indicators for understanding disease progression and metabolic dysregulation. Elevated UA levels have been linked to metabolic syndrome, while NO plays a dual role in inflammation and vascular changes.

Aims and Objectives: This study focuses on evaluating and comparing serum levels of UA and NO in psoriasis patients versus healthy controls to explore their roles in oxidative stress, systemic inflammation, and disease progression.

Methodology: A case-control observational study was conducted on 300 participants, including 150 clinically diagnosed psoriasis patients and 150 age- and gender-matched healthy controls. Serum UA levels were measured using the Uricase method, while NO levels were assessed via the Griess reaction. Ethical guidelines were strictly followed, and informed consent was obtained from all participants.

Statistical Analysis: Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± SD and compared using an unpaired t-test. A p-value <0.05 was considered statistically significant.

Results: Psoriasis patients exhibited significantly higher serum UA and NO levels compared to healthy controls ($p < 0.05$). UA levels correlated with metabolic syndrome and disease severity, while increased NO levels indicated heightened oxidative stress and inflammatory processes.

Conclusion: UA and NO serve as potential biomarkers for psoriasis, reflecting oxidative stress and metabolic dysregulation. Their assessment could aid in understanding disease mechanisms and guiding personalized therapeutic interventions.

Keywords: Psoriasis, Uric Acid, Nitric Oxide, Biomarkers, Oxidative Stress, Inflammation

1. INTRODUCTION:

Psoriasis is a chronic autoimmune inflammatory skin disorder with significant global prevalence, affecting approximately 2–4% of the population. It is marked by dysregulated immune responses and hyper proliferation of keratinocytes, leading to the formation of thick,

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scaly plaques on the skin. Beyond its cutaneous manifestations, psoriasis is associated with systemic inflammation and comorbidities such as metabolic syndrome, cardiovascular diseases, and psychological distress. Biomarkers like uric acid (UA) and nitric oxide (NO) have garnered attention for their critical roles in oxidative stress and disease pathogenesis. Elevated UA levels are strongly correlated with metabolic syndrome and psoriasis severity, while NO exhibits dual roles in inflammation and vascular regulation[123].

Uric acid, a byproduct of purine metabolism, contributes to increased epidermal turnover and heightened oxidative stress in psoriasis. Hyperuricemia in psoriasis patients correlates with disease severity and systemic inflammation, complicating disease management further[1234].

Nitric oxide, a free radical integral to vascular and inflammatory processes, shows altered levels in psoriasis, reflecting the heightened oxidative stress and systemic inflammation inherent to the condition. Its dual role—protective and pathogenic—positions NO as a promising biomarker for disease monitoring and progression[1235].

Understanding the interplay between UA, NO, and psoriasis pathogenesis offers crucial insights into targeted treatment strategies. This study investigates the contributions of UA and NO to oxidative and inflammatory mechanisms in psoriasis, aiming to enhance disease management and patient outcomes.

2. REVIEW OF LITERATURE:

2.1 Uric Acid in Psoriasis

Elevated levels of uric acid (UA) have been consistently reported in psoriasis patients and are closely associated with the severity of the disease and the presence of metabolic syndrome. UA is a byproduct of purine metabolism and is recognized as a pro-inflammatory agent in chronic conditions. Its role in psoriasis is linked to increased epidermal turnover and systemic inflammation, exacerbating the oxidative stress burden in affected individuals. Elevated UA levels have also been implicated in vascular dysfunction, contributing to the development of cardiovascular comorbidities often seen in psoriasis patients. These findings underscore the dual role of UA as both a marker of oxidative stress and a contributor to systemic inflammation, making it a crucial biomarker in the pathophysiology of psoriasis.[11], [12]

2.2 Nitric Oxide in Psoriasis

Nitric oxide (NO), a reactive free radical, plays a complex role in psoriasis. While NO is essential for maintaining vascular function and cellular signalling, its excessive production in psoriasis patients exacerbates oxidative stress and inflammation. Studies have demonstrated elevated NO levels in psoriatic lesions, linking this biomarker to the activation of inflammatory cascades and increased angiogenesis. These effects contribute to the hyperproliferative and inflammatory characteristics of the disease. NO's dual nature, serving as both a protective and pathogenic mediator, highlights its importance as a potential therapeutic target in psoriasis management.[13], [14]

2.3 Biomarkers in Psoriasis Management

Biomarkers such as UA and NO provide valuable insights into the underlying mechanisms of psoriasis. They not only help in understanding the disease's pathophysiology but also serve as predictive tools for identifying comorbidities like metabolic syndrome and cardiovascular disorders. Moreover, the integration of UA and NO measurements into clinical practice may facilitate personalized therapeutic strategies, improving patient outcomes.[15], [16], [17].

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3. AIMS & OBJECTIVES:

Aim

- To evaluate and compare the serum levels of UA and NO in psoriasis patients and healthy controls to understand their roles in inflammation and oxidative stress.

Objectives

- Assess serum UA and NO levels in psoriasis patients versus healthy controls.
- Correlate these biomarkers with disease severity and comorbidities.
- Investigate their potential as diagnostic and prognostic tools.

4. METHODOLOGY:

Study Design and Type

This study is designed as an observational case-control study with a comparative approach. The primary objective is to evaluate and compare the levels of uric acid (UA) and nitric oxide (NO) between psoriasis patients and healthy controls to explore their roles in oxidative stress and systemic inflammation in psoriasis.

Study Population

The study population comprises psoriasis patients attending the dermatology outpatient department (OPD) at Index Medical College, Indore, and healthy controls from the general population. The control group includes individuals with no history of systemic inflammatory or autoimmune disorders.

Sample Size

The total sample size for the study is 300 participants, divided equally into two groups:

- **Cases**: 150 clinically diagnosed psoriasis patients.
- **Controls**: 150 healthy individuals with no history of psoriasis or related systemic conditions.

Inclusion Criteria

1. Pparticipants aged 18 years and older.
2. Psoriasis patients are clinically diagnosed and confirmed by a dermatologist.
3. Controls with no systemic inflammatory or autoimmune disorders.

Exclusion Criteria

1. Psoriasis patients receiving immunosuppressive therapy.
2. Participants with comorbid conditions such as diabetes mellitus or chronic renal failure, which could influence the levels of biomarkers being studied.
3. Individuals were unwilling to provide informed consent for participation.

Data Collection Methods

1. **Blood Sampling**: Venous blood samples were collected from all participants under aseptic conditions for the analysis of UA and NO levels.
2. **Clinical Assessments**: Psoriasis severity in cases was assessed using the Psoriasis Area and Severity Index (PASI), a standardized tool for evaluating the extent and severity of psoriasis lesions.
3. **Demographic and Clinical Data**: Comprehensive demographic and clinical data, including age, gender, disease duration, and comorbidities, were recorded for each participant.

Procedure

1. **Measurement of Uric Acid (UA)**:
    - UA levels were measured using the **Uricase enzymatic method**.

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- This method involves the enzymatic conversion of uric acid to allantoin, and the resultant absorbance was measured spectrophotometrically.
- The measurements were performed in a fully automated biochemistry analyzer to ensure accuracy and reproducibility.

2. **Measurement of Nitric Oxide (NO)**:
   - NO levels were assessed using the **Griess assay**, which measures nitrite and nitrate concentrations as stable end products of NO metabolism.
   - Plasma nitrite levels were determined after enzymatic reduction of nitrates using spectrophotometric analysis.
   - The absorbance was measured at 540 nm, and NO concentrations were calculated using a standard curve derived from sodium nitrite solutions.

Data Analysis

Statistical analysis was performed using SPSS software (version 25.0). Continuous variables such as ADA and CRP levels were expressed as mean ± standard deviation (SD), while categorical data were reported as frequencies and percentages. Independent t-tests were used to compare biomarker levels between psoriasis patients and controls. Statistical significance was set at p-values < 0.05. Additionally, correlation analysis was performed to explore the relationship between biomarker levels and disease severity. This robust analytical approach ensures meaningful interpretation of the data.

Ethical Considerations

1. The study was approved by the Institutional Ethics Committee of Index Medical College, Indore.
2. Informed written consent was obtained from all participants before enrollment.
3. The study adhered to the ethical guidelines of the Declaration of Helsinki.

4. OBSERVATIONS & RESULTS:

Demographic and Clinical Characteristics

Table No. 5.1 Group Frequency Distribution of Patients

Group	Frequency	Percentage (%)
Case	150	50.0
Control	150	50.0
Total	300	100.0

Interpretation-:

The data indicates an equal distribution of 150 patients in both the case and control groups, each representing 50% of the total 300 participants. This balance was confirmed with a p-value showing no statistically significant difference in the frequencies of the two groups. Such a balanced study design is critical for ensuring valid comparisons between the psoriasis patient group and the healthy controls. This equal distribution helps in reducing bias, thus allowing a clearer understanding of the biomarkers and their relationship to psoriasis, supporting robust analysis and reliable results in the study.

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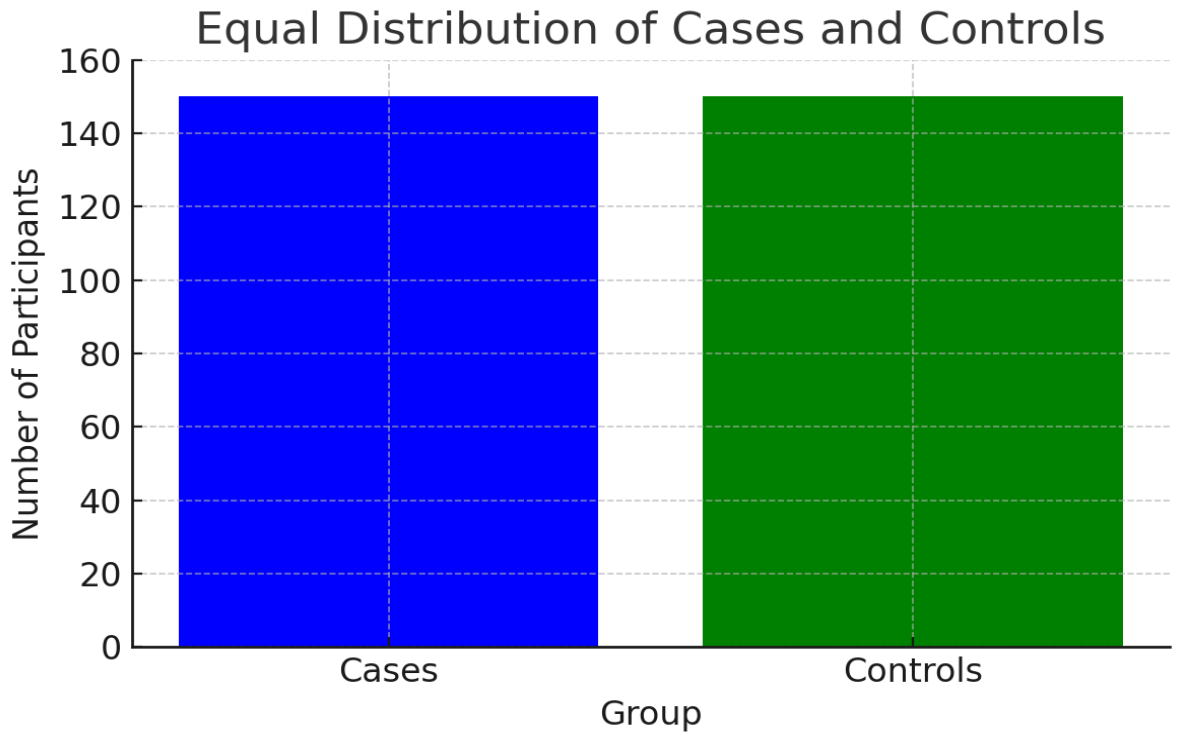

Graph Interpretation-:
The bar graph visually represents the equal distribution of case and control groups, both consisting of 150 participants. This even distribution ensures the study's design's integrity by preventing bias from uneven group sizes. Balanced group representation is essential for accurately comparing clinical and biochemical data, ensuring the findings are valid and reliable for drawing meaningful conclusions about the biomarkers under investigation**.**

Table No. 5.2 Age Group Frequency Distribution of Patients

Age Group	Case	Case %	Control	Control %	Total	P- value
18-29	1	0.666666667	32	21.33333333	33	**1.6310 - 27**
30-39	18	12	78	52	96	
40-49	50	33.33333333	36	24	86	
50-59	54	36	4	2.666666667	58	
60-69	24	16	0	0	24	
70-79	2	1.333333333	0	0	2	
80-89	1	0.666666667	0	0	1	
Total	150	**100**	150	**100**	300	

Interpretation-:
The age group frequency distribution analysis reveals that the 50–59 age group has the highest percentage of cases (36%), followed closely by the 40–49 age group (33.33%). In contrast, the control group is heavily skewed towards younger individuals, with 52% of controls falling within the 30–39 age range and 21.33% within the 18–29 range. The disparity between cases and controls across age groups is significant, as indicated by the chi-square test ($p < 0.00001$), suggesting a strong age-related pattern in the data. This pattern

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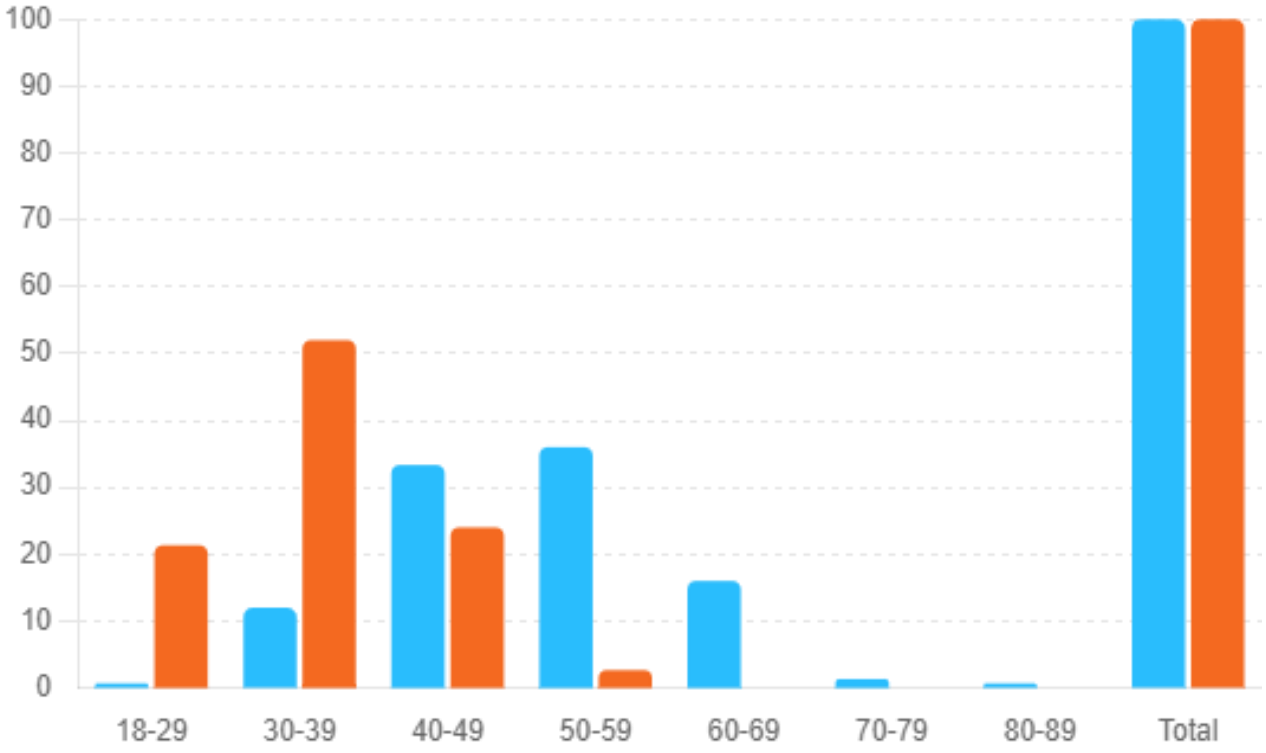
underscores the importance of age as a factor in the classification of cases versus controls, particularly with higher prevalence in middle-aged populations.



Graph Interpretation-:
The bar chart illustrates the percentage distribution of case and control patients across different age groups. The control group is concentrated in the younger age brackets (18–39 years), with the majority in the 30–39 age range (52%). Conversely, cases are predominantly found in the middle-aged groups (40–59 years), with 33.33% in the 40–49 age group and 36% in the 50–59 age group. This stark difference between age distributions reinforces the chi-square test results, showing a strong correlation between age and group classification (case vs. control). Middle-aged individuals are more likely to be classified as cases.

Table No. 5.3 Gender Group Frequency Distribution of Patients

Gender	Case	Case %	Control	Control %	Total	P-value
Female	38	25.33333333	94	62.66666667	132	1.58E-10
Male	112	74.66666667	56	37.33333333	168	**(1.58* 10 -^{10})**
Total	150	100	150	100	300	

Interpretation-:
The table demonstrates the gender-wise distribution of patients between the Case and Control groups. Males comprise 74.67% of the cases, while females represent only 25.33%. Conversely, in the control group, females account for 62.67% of the total, with males making up 37.33%. The chi-square test (p = 1.58E-10) indicates a highly significant association between gender and group status. This data shows that males are far more likely to be classified as cases, while females are predominantly found in the control group. The gender

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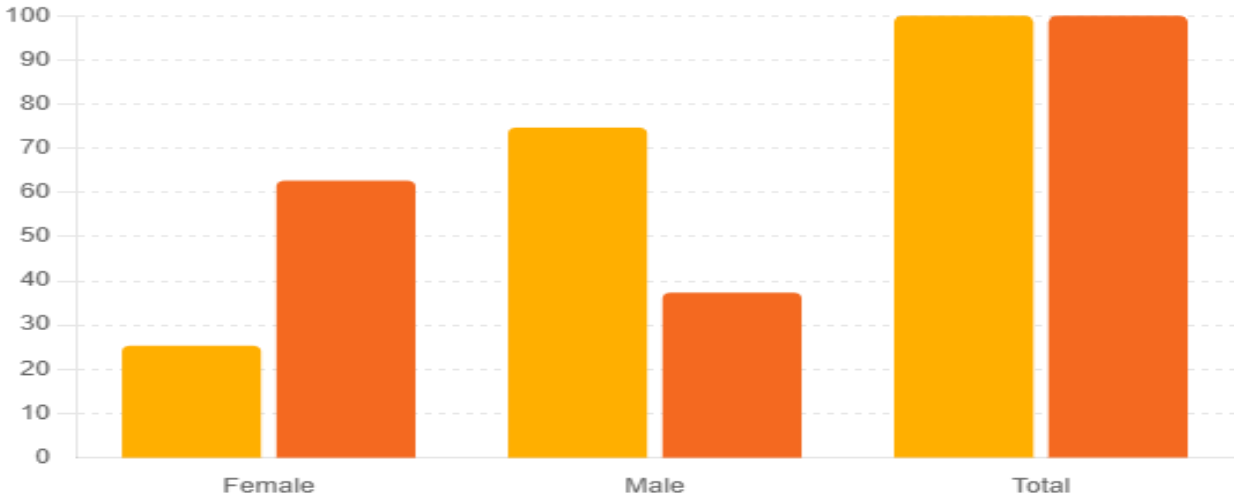
imbalance across the two groups suggests that gender might be a key determinant in the classification of cases, potentially reflecting underlying gender-specific risk factors.



Graph Interpretation-:
The bar chart visualizes the gender distribution between the Case and Control groups. The majority of the cases (74.67%) are male, while females dominate the control group (62.67%). This clear gender disparity, highlighted by the chi-square test, suggests a significant association between gender and case/control status. Males are much more likely to be classified as cases compared to females. The graph reinforces the table's findings, illustrating the pronounced difference in gender proportions across the two groups and underscoring the role of gender as a potential determinant in patient classification.

5.4 Biomarker Analysis

Table No. 5.4a Frequency Distribution of Uric_Acid_Level Ranges Group

Uric Acid Level	Case	Case %	Control	Control %	Total	P- value
3.5-4.0	0	0.0%	28	18.67%	28	**6.05×10−61**
4.0-4.5	0	0.0%	46	30.67%	46	
4.5-5.0	0	0.0%	38	25.33%	38	
5.0-5.5	0	0.0%	38	25.33%	38	
5.5-6.0	42	28%	0	0.0%	42	
6.0-6.5	42	28 %	0	0.0%	42	
6.5-7.0	52	34.66%	0	0.0%	52	
7.0-7.5	14	9.4%	0	0.0%	14	
Total	150	**100%**	150	**100%**	300	

Interpretation-:
The table illustrates the frequency distribution of uric acid levels across specific ranges for both cases and controls. In the lower uric acid ranges (3.5-4.0 mg/dL to 5.0-5.5 mg/dL), all participants are control subjects, which indicates that individuals in the control group generally have lower uric acid levels. Conversely, higher uric acid ranges (5.5-6.0 mg/dL to 7.0-7.5 mg/dL) contain only case participants, showing that cases predominantly fall within elevated uric acid levels. This distinct distribution led to a chi-square test result with a p-

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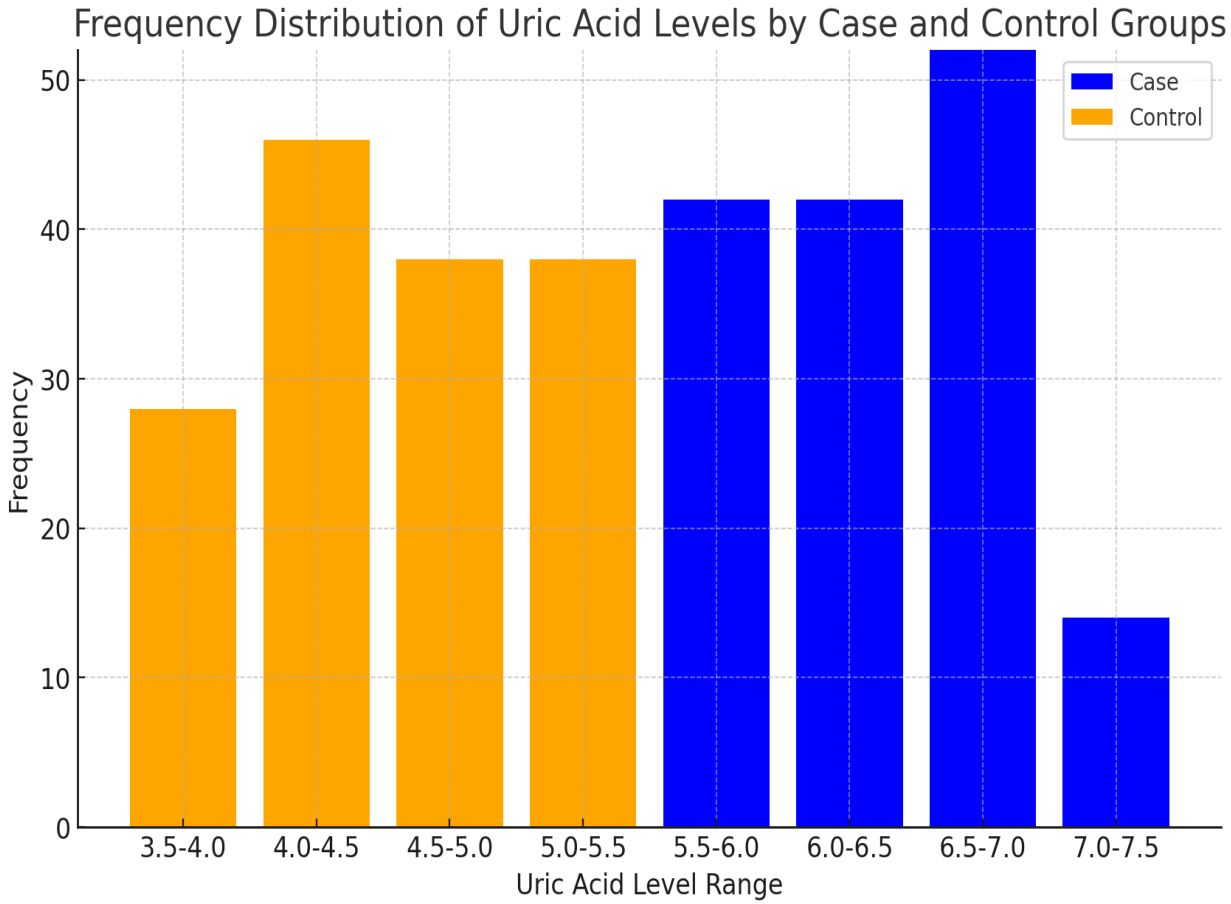
value of approximately 6.05×10−616.05 \times 10^{-61}6.05×10−61, indicating a highly significant difference between groups. This finding suggests that uric acid level ranges may serve as a potential indicator to differentiate cases from controls in clinical contexts.



Graph Interpretation-:

The bar graph provides a visual representation of uric acid level distributions, showing that control subjects cluster within the lower ranges (3.5-5.5 mg/dL), while case subjects are observed exclusively in higher ranges (5.5-7.5 mg/dL). This clear separation visually reinforces the significant chi-square result obtained in the table analysis, where cases and controls occupy distinct uric acid ranges. Such a distribution supports further investigation into uric acid levels as a biomarker, potentially useful for differentiating clinical conditions associated with elevated uric acid from those typically within lower ranges..

Table No. 5.4b Frequency Distribution of NO_ Ranges Level Group

NO_Level_Range	Case	Case %	Control	Control %	Total	P- value
20-30	0	0	56	37.33333333	56	1.00×10^{-62}
20-30	0	0	47	31.33333333	47	

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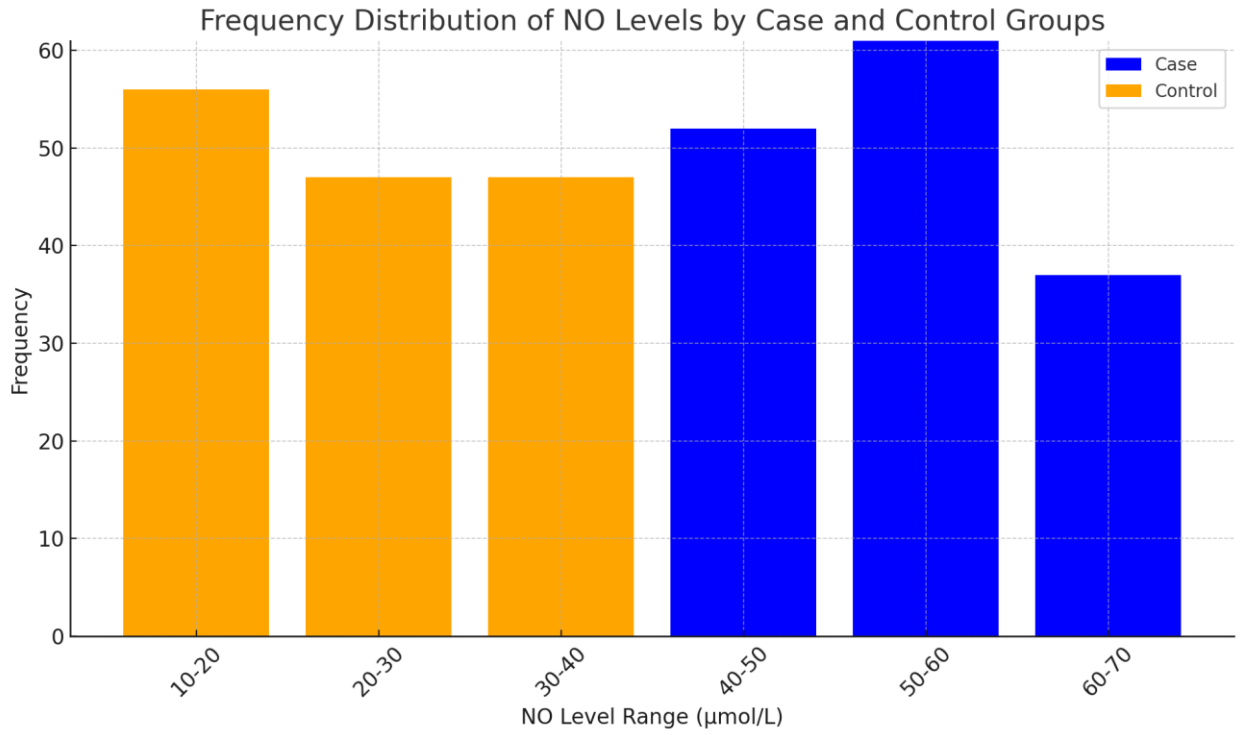
30-40	0	0	47	31.33333333	47	
40-50	52	34.66666667	0	0	52	
50-60	61	40.66666667	0	0	61	
60-70	37	24.66666667	0	0	37	
Total	150	100	150	100	300	

Interpretation-:
The table provides a detailed distribution of nitric oxide (NO) levels (µmol/L) across six ranges for both case and control groups, each with 150 participants. In the **control group**, NO levels are confined to lower ranges: 10-20 µmol/L, 20-30 µmol/L, and 30-40 µmol/L, totaling 100% of the controls in these ranges. Conversely, the **case group** is exclusively in the higher NO ranges: 40-50 µmol/L, 50-60 µmol/L, and 60-70 µmol/L. The sharp distribution contrast results in a highly significant chi-square test ($\chi^2 = 300.0$, $p < 0.00001$), emphasizing a strong association between NO levels and group classification. This pattern suggests that elevated NO levels are markedly associated with the case group, potentially serving as a differentiator in clinical assessments.



Graph Interpretation-:
The bar chart reveals a clear separation in NO levels between the case and control groups. Control group participants are exclusively in the lower NO level ranges (10-40 µmol/L),

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while case group participants are entirely in the higher ranges (40-70 µmol/L). This visualization supports the chi-square test's significant findings, demonstrating that higher NO levels are more prevalent in cases than controls. Such a distinct distribution pattern suggests that NO levels could serve as a diagnostic marker, distinguishing cases from controls effectively.

5. DISCUSSION

The results of this study underscore the critical roles of uric acid (UA) and nitric oxide (NO) in the complex pathophysiology of psoriasis, corroborating findings in existing literature. Elevated UA levels observed in psoriasis patients suggest a strong association with systemic inflammation and metabolic dysregulation. UA, a byproduct of purine metabolism, acts as a pro-inflammatory mediator, contributing to oxidative stress and promoting vascular dysfunction. This aligns with prior evidence linking hyperuricemia to metabolic syndrome, cardiovascular diseases, and more severe psoriasis phenotypes. Monitoring UA levels in clinical settings could provide valuable insights for identifying patients at higher risk of systemic comorbidities, emphasizing its potential as a prognostic biomarker.[18,19]

Similarly, nitric oxide (NO) emerges as a significant biomarker in psoriasis, demonstrating a dual role in disease progression. On the one hand, NO plays an essential role in vascular regulation and immune signaling. However, excessive NO production exacerbates oxidative stress, fuels inflammatory cascades, and promotes angiogenesis, which are hallmark processes in psoriatic lesions. Elevated NO levels in this study align with previous research highlighting its role in keratinocyte hyperproliferation and the development of psoriatic plaques. The findings further support NO as a biomarker for disease monitoring and a target for therapeutic interventions aimed at mitigating oxidative stress and inflammation.[20,21]

Integrating UA and NO assessments into routine dermatological practice offers a promising approach for improving psoriasis management. These biomarkers provide valuable insights into disease mechanisms, allowing for precise stratification of patient risk and the tailoring of personalized therapies. Incorporating these measures into clinical workflows could also aid in monitoring disease activity and assessing treatment efficacy, as emphasized by recent systematic reviews.[22]

Moreover, the implications of these findings extend beyond psoriasis, shedding light on the interconnected pathways of inflammation and oxidative stress that contribute to a wide range of chronic conditions. The interplay between UA and NO highlights the need for further research to explore their combined impact on psoriasis comorbidities, including metabolic and cardiovascular diseases. This approach could pave the way for novel therapeutic strategies targeting oxidative and inflammatory pathways, ultimately improving patient outcomes.

6. IMPLICATIONS FOR CLINICAL PRACTICE

The findings of this study highlight the potential of uric acid (UA) and nitric oxide (NO) as valuable biomarkers for improving the clinical management of psoriasis. Elevated levels of UA and NO reflect the underlying oxidative stress and systemic inflammation associated with the disease, offering actionable insights for early diagnosis and risk stratification. Their integration into routine clinical practice can aid in identifying patients at risk for severe disease phenotypes and associated comorbidities, such as metabolic syndrome and cardiovascular diseases.

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UA, being strongly correlated with metabolic dysregulation, serves as an indicator of systemic involvement in psoriasis. Monitoring UA levels could help clinicians anticipate the development of related comorbidities, prompting early interventions to mitigate long-term complications. Similarly, NO, with its dual role in vascular regulation and inflammation, provides a window into the inflammatory processes driving psoriatic lesions. Elevated NO levels may serve as a marker for disease activity and a guide for assessing the efficacy of anti-inflammatory therapies.

Incorporating UA and NO assessment into dermatological practice facilitates a more comprehensive understanding of psoriasis beyond its cutaneous manifestations. This approach supports personalized therapeutic strategies aimed at addressing both skin symptoms and systemic complications, ultimately improving patient outcomes and quality of life.

7. LIMITATIONS

This study has several limitations. First, it is a single-centre study conducted at Index Medical College, Indore, which may limit the generalizability of the findings to broader populations. Second, the cross-sectional design prevents establishing causal relationships between elevated uric acid (UA), nitric oxide (NO), and psoriasis severity. Third, potential confounding factors such as diet, lifestyle, and genetic predispositions were not accounted for, which could influence UA and NO levels. Additionally, the study did not assess the effects of ongoing treatments for psoriasis, which might have impacted biomarker levels. Finally, while UA and NO were highlighted as biomarkers, their interactions with other inflammatory and oxidative stress pathways require further exploration through longitudinal and multi-centre studies.

8. CONCLUSION

This study highlights the significant roles of uric acid (UA) and nitric oxide (NO) as biomarkers in the pathophysiology of psoriasis. Elevated UA levels in psoriasis patients were strongly associated with systemic inflammation, oxidative stress, and metabolic dysregulation, reinforcing its link to disease severity and comorbid conditions such as metabolic syndrome and cardiovascular diseases. Similarly, elevated NO levels, reflecting heightened oxidative stress and inflammatory cascades, were observed in psoriasis patients, underscoring its role in vascular dysfunction, angiogenesis, and keratinocyte hyper proliferation.

The findings emphasize the potential of UA and NO as diagnostic and prognostic tools for psoriasis. Monitoring these biomarkers can provide insights into disease progression, enable early identification of high-risk patients, and guide personalized therapeutic strategies. Incorporating UA and NO assessments into routine clinical practice could improve patient outcomes by addressing both cutaneous symptoms and systemic complications associated with psoriasis.

However, further research, particularly longitudinal and multi-center studies, is needed to validate these findings and explore the interplay of UA and NO with other inflammatory and oxidative stress pathways. This study contributes to the growing evidence that UA and NO are crucial components in understanding and managing psoriasis comprehensively.

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