

## URINARY HYDROXY PROLINE IN PATIENTS OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS- A COMPARATIVE STUDY

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### ABSTRACT

**Introduction:** Hydroxyproline is present almost entirely in collagen. Bone tissue pathologies are reflected in the metabolism of hydroxyproline as are articular connective tissue pathology. Hence the study was conducted to compare the levels of hydroxy proline in urine of patients of Rheumatoid arthritis and osteoarthritis to study if hydroxy proline urinary values can be used for differentiating the two conditions. **Materials and Methods** 25 normal healthy volunteers working in Gandhi Medical College participated in the study to form the control group. Study includes 50 cases of arthritis. Cases are divided into two groups. Group I includes 25 cases of established rheumatoid arthritis patients and Group II includes 25 cases of established osteoarthritis. Both control and study group persons were

advised to have collagen free diet for two days. Hydroxy proline and creatinine are estimated in 24 hrs urine sample in control and study groups. **Results:** There is a statistically significant increase in hydroxy proline excretion in group I when compared to control group. ( $p < 0.05$ ). Hydroxyproline excretion is more in Group II when compared to control group but there is no statistical significance. ( $p > 0.05$ ). Excretion of hydroxyproline in group I cases is more than in Group II cases ( $p < 0.05$ ). There is a significant increase in urinary hydroxyproline:creatinine ratio in Group I when compared to group II ( $p < 0.05$ ). No significant change is observed in urinary hydroxyproline:creatinine ratio levels between control group and Group II. **Discussion:** Hydroxy proline is present only in collagen and to a little extent in elastin. Its quantity therefore reflects the synthesis and breakdown of collagen or one of its precursors. Though it is focal, in cases of Rheumatoid arthritis collagen degeneration is sufficiently large in magnitude to increase the excretion of hydroxy proline in urine. In osteoarthritis no collagen is involved hence there is no significant increase in

excretion of hydroxyproline. **Conclusion:** In the present study there is increase in excretion of hydroxyproline and increase in urine hydroxyl proline /urine creatinine ratio in cases of rheumatoid arthritis when compared to osteoarthritis cases.

**KEYWORDS:** Rheumatoid arthritis, Osteoarthritis, Urine Hydroxyproline.

## INTRODUCTION

The Amino acid hydroxy proline constitutes approximately 13% of collagen<sup>[1,2]</sup> and 1 to 2 % of elastin. It is present in no other protein of the body. For this reason, the determination of hydroxy proline has been utilized for the estimation of collagen in various animal tissues, and in the fibrinoid material of the subcutaneous nodule of rheumatoid arthritis.<sup>[3]</sup> Because hydroxy proline is present almost entirely in collagen, it was felt that if there were a significant deviation from normal in the metabolism of collagen or an increase in degradation of this protein in patients with collagen diseases, these changes might be reflected by increased levels of excretion of this amino acid in urine.

Degradation of collagen releases free hydroxyproline which is excreted in urine.<sup>[4]</sup> Modifications in urinary hydroxyproline concentrations were studied in various collagen degradation diseases. A significant increase in hydroxyprolinuria was found in both men and women with Paget's disease in all age groups considered. Significant increases were found in men with the same pathologies. Rheumatoid arthritis also increased urinary hydroxyproline in both males and females. It therefore seems that bone tissue pathologies are reflected in the metabolism of hydroxyproline as are articular connective tissue pathology strictly related to it. Hence the study was conducted to compare the levels of hydroxy proline in urine of patients of Rheumatoid arthritis and osteoarthritis to study if hydroxy proline urinary values can be used for differentiating the two conditions.

## MATERIALS AND METHODS

25 normal healthy volunteers working in Gandhi Medical College participated in the study to form the control group. These persons are excluded from collagen related diseases i.e persons with acute infection, renal disease, arthritis, recent fractures, on steroid medication and other collagen vascular diseases. None of them were diabetic nor hypertensive and were in the age group of 30-60 yrs.

Study includes 50 cases of arthritis. Cases are divided into two groups. Group I includes 25 cases of established rheumatoid arthritis patients admitted or attended out patient clinics of

orthopaedics department of Gandhi Hospital Secunderabad. Group II includes 25 cases of established osteo arthritis admitted or attended op in Gandhi hospital. All the patients are diagnosed based on radiological evidences. The patients in both Groups were in the age group of 35 to 60 yrs.

Both control and study group persons were advised to have collagen free diet for two days i.e less meat, fish, jelly, candy or ice cream and 24hrs urine sample was collected with toluene as preservative.

Urinary hydroxy proline was determined by modified Neuman and Logan method<sup>[5]</sup> and urinary creatinine is measured by jaffes method . Fasting serum is also collected in all the groups and controls and serum Alkaline phosphatase and serum calcium are measured using kit method and o- cresolphthaline method respectively.

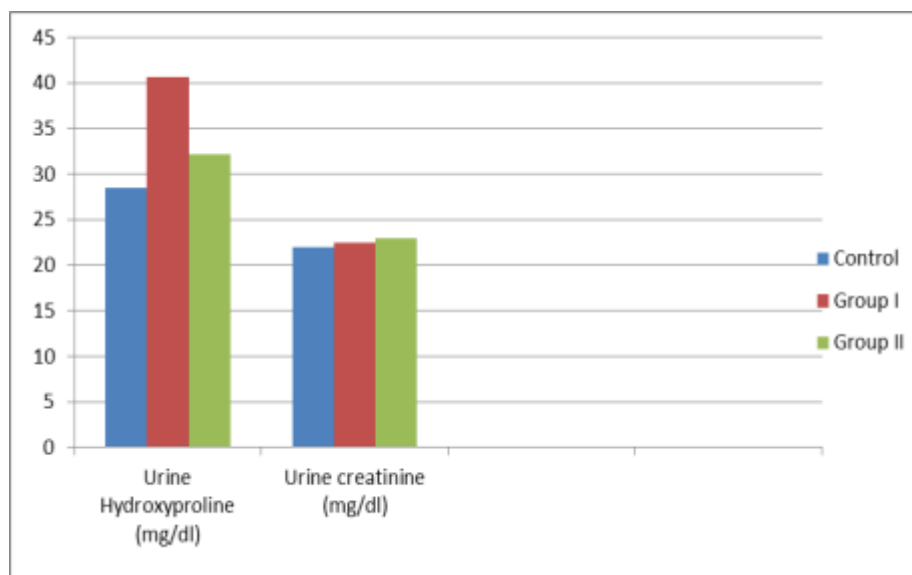
## RESULTS

Hydroxy proline and creatinine are estimated in 24 hrs urine sample in control and study groups. The mean hydroxyproline excreted in control group (n=25) is 28.5 mg/dl. Mean hydroxyproline excreted in Group I (n=25) is 40.6 mg/dl hrs and the mean value in Group II (n=25) is 32.1 mg/dl. The mean values are compared by student t –test in all the three groups. There is a statistically significant increase in hydroxy proline excretion in group I when compared to control group.(p<0.05) . Hydroxyproline excretion is more in Group II when compared to control group but there is no statistical significance. (p>0.05). Excretion of hydroxyproline in group I cases is more than in Group II cases (p<0.05). (Table-1).

The mean urinary creatinine excreted in control, group-I and in Group II are 21.92 mg/dl, 22.5 mg/dl and 22.92mg/dl respectively. In all the groups ratio between urinary hydroxyl proline and urinary creatinine are calculated. Urin HP / Urin Creatinine ratio in controls is 1.3 (Range 0.6-2.2) . In group I the ratio is 1.8 (0.9-

**Table-1: (2.5). In group II it is 1.4 (0.6-2.3). (Table-1).**

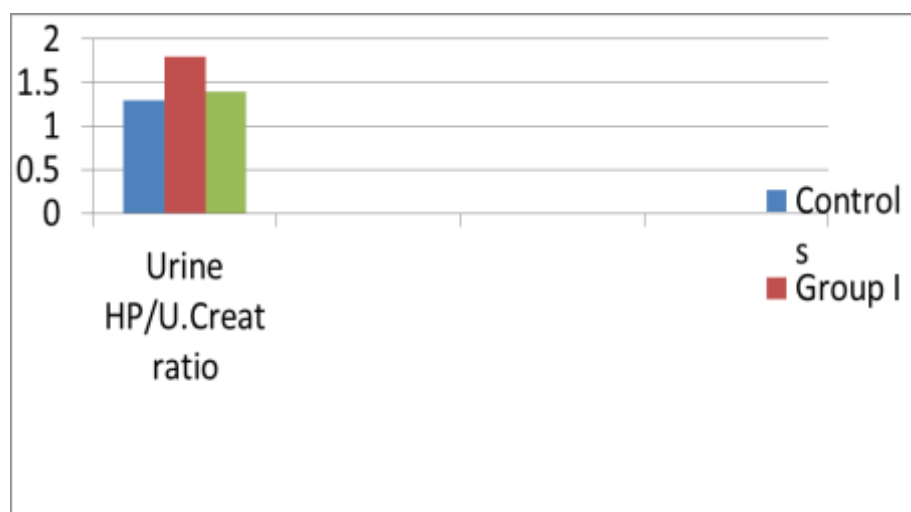
Parameter	Control group (n=25)	Group I (n=25) Rheumatoid arthritis cases	Group II (n=25) Osteoarthritis cases
24 hrs Urine Hydroxyproline	28.5 mg/dl	40.6 mg/dl*	32.1 mg/dl
24 hrs Creatinine	21.92 mg/dl,	22.5 mg/dl	22.92mg/dl
Urin HP / Urin Creatinine ratio	1.3 (Range 0.6-2.2)	1.8 (0.9-2.5).	1.4 (0.6-2.3).



**Urinary Hydroxyproline and Urine creatine levels in controls and study groups Fig-1**

In all the groups ratio between urinary hydroxyl proline and urinary creatinine are calculated. Urin HP / Urin Creatinine ratio in controls is 1.3 (Range 0.6-2.2). In group I the ratio is 1.8 (0.9-2.5). In group II it is 1.4 (0.6-2.3). (Table-1)

A comparison of urinary hydroxy proline creatinine ratio is made between control and groupI, and GroupII. In group I Cases there is a significant increase in urinary hydroxy proline creatinine ratio 1.8 range ( 0.9-2.5) when compared to control group 1.3 (0.6 -2.2) ( $p < 0.01$ ). A comparison is made between group I and Group II. There is a significant increase in urinary hydroxyprolinecreatinine ratio in GroupI when compared to group II ( $p < 0.05$ ). No significant change is observed in urinaryhydroxyprolinecreatinine ratio levels between control group and GroupII. ( Fig-2)



**Urine Hydroxyproline/Urine Creatinine Ratio in control and study groups Fig-2**

## DISCUSSION

Hydroxy proline is present only in collagen and to a little extent in elastin. So the bound hydroxy proline of urine represents a peptide which is present in the collagen molecule. It's quantity therefore reflects the synthesis and breakdown of collagen or one of its precursors.

Here median values in patients with Rheumatoid arthritis are higher than in control group whereas the median values in patients with osteoarthritis are lower than in control group.

Previous studies are indicating that the lesions of the connective tissue in the rheumatic diseases and in hypersensitivity states are relatively focal in character.<sup>[6,7,8,9]</sup> Alteration of collagen fibers in tissue lesions of collagen diseases were studied which have shown different results,<sup>[10,11,12,13]</sup> Though it is focal in cases of Rheumatoid arthritis collagen degeneration is sufficiently large in magnitude to increase the excretion of hydroxy proline in urine.

In cases of osteoarthritis there is no significant change in excretion of hydroxyl proline when compared to controls as collagen degradation is seen but is to a little extent and there is a decrease in proteoglycan content within cartilage. The breakdown products from the cartilage are released into the synovial space and the cells lining the joint remove them, thus less products of cartilage collagen are released into blood circulation.<sup>[14,15]</sup>

## CONCLUSION

In the present study there is increase in excretion of hydroxyproline and increase in urine hydroxyl proline /urine creatinine ratio in cases of rheumatoid arthritis when compared to osteoarthritis cases. Hence estimation of urinary hydroxyl proline alone or urine hydroxyl

proline/urine creatinine ratio may be used as a marker for differentiating between rheumatoid arthritis and osteoarthritis cases.

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