

RENAL EXCRETORY RESPONSE AT HIGH ALTITUDE

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SUMMARY

This study was carried out to demonstrate changes in renal excretory system in response to acute ascent. Twenty four hours sampling was done at Rawalpindi before start, 12 hours after reaching Khunjrab, 72 hours after stay at Khunjrab and the last sample was collected after returning back to Rawalpindi. Changes in the urinary pH, 24 hours urinary volume, 24 hours urinary excretion of potassium, sodium, calcium, phosphate, oxalate, protein, uric acid and creatinine were measured. We came to the conclusion that the changes were highly significant between the two places. These changes returned to pre-ascent level after reaching back to Rawalpindi. There was no statistically significant changes in other variables. Thus we conclude that there is no permanent demonstrable changes in the renal excretory system in response to acute ascent and stay for few days at high altitude.

INTRODUCTION

High altitude has not been defined precisely. Most of the individuals develop clinical, physiological and biochemical changes above 3000 m. However, there are individual variations and some people develop signs and symptoms of high altitude sickness at altitudes as low as 2000 m.¹ Others have defined high altitude arbitrarily as elevation above 2500 m.² Although most of the unwanted effects of high altitude are due to hypoxia but additional deterioration also results from cold, dehydration, solar and even ionizing radiation. However, this additional deterioration can be prevented by proper clothing and shelter. Only hypoxia is unavoidable until and unless supplementary oxygen is available.³ Like other organs of the body, kidneys also respond to hypoxia. It has been demonstrated that hypoxia may activate the renal nerves^{4,5} and increase secretion of hormones^{6,7} and thus the renal

function is affected. Acute severe hypoxia decreases the glomerular filtration rate and renal blood flow in rats resulting in severe renal ischaemia.^{8,9} Changes in renal function have been studied mostly in animals like rats and rabbits. These animals were subjected to simulated high altitude and it was demonstrated that the urine output, plasma and urinary electrolytes and renal hemodynamics were not significantly affected in hypoxic rats.¹⁰ There are various studies from abroad showing effect of high altitude on renal function under different condition.^{11,12} The northern areas of Pakistan have high mountains and peaks like Nanga Parbat and Rakaposhi and mountaineers from all over the world visit this area. No effort has been ever made to demonstrate the effects of acute ascent to high altitude on renal excretory function in this part of the world. Therefore the present project was designed to study the response of renal excretory system to high altitude in human beings.

MATERIAL AND METHODS

Twelve normal adult subjects were included in this study. The age of the subjects ranged from 19-47 years. They were not suffering from any obvious debilitating disease and were normotensive. The first 24 hours urinary sampling was collected at Rawalpindi. On the next day, the subjects were transported to Gilgit (height: 4700 feet) by road. The team had a rest for a one night Gilgit and on day 2 morning ascended a height of 9000 feet from Gilgit (4700 feet) to the camp at Khunjrab (14600 feet) in 10 hours by road.

Diet:

Subjects were on normal diet. They had free access to food and water and did not have any special preference for proteins and salts.

Sampling:

First 24 hours urinary sampling was done at Rawalpindi and labelled as R-I. Second 24 hours urinary sampling was done on the second day on reaching Khunjrab and was labelled as K-I. Third sampling was done on Day-IV at Khunjrab and labelled as K-II. Last 24 hours urinary sampling was done on Day-II after reaching back Rawalpindi and labelled as R-II.

24 hours urinary volume of each subject was measured and 10 ml of the sample was preserved in liquid nitrogen and transported to the Pathology Department, Postgraduate Medical Institute, Lahore and the following variables were calculated.

- i Urinary pH.
- ii 24 hours urinary volume.
- iii. 24 hours urinary excretion of potassium, sodium, calcium, phosphate, oxalate, protein, uric acid and creatinine.

Statistical analysis

Help of statistician was taken and statistical analysis was done by applying "student's test".

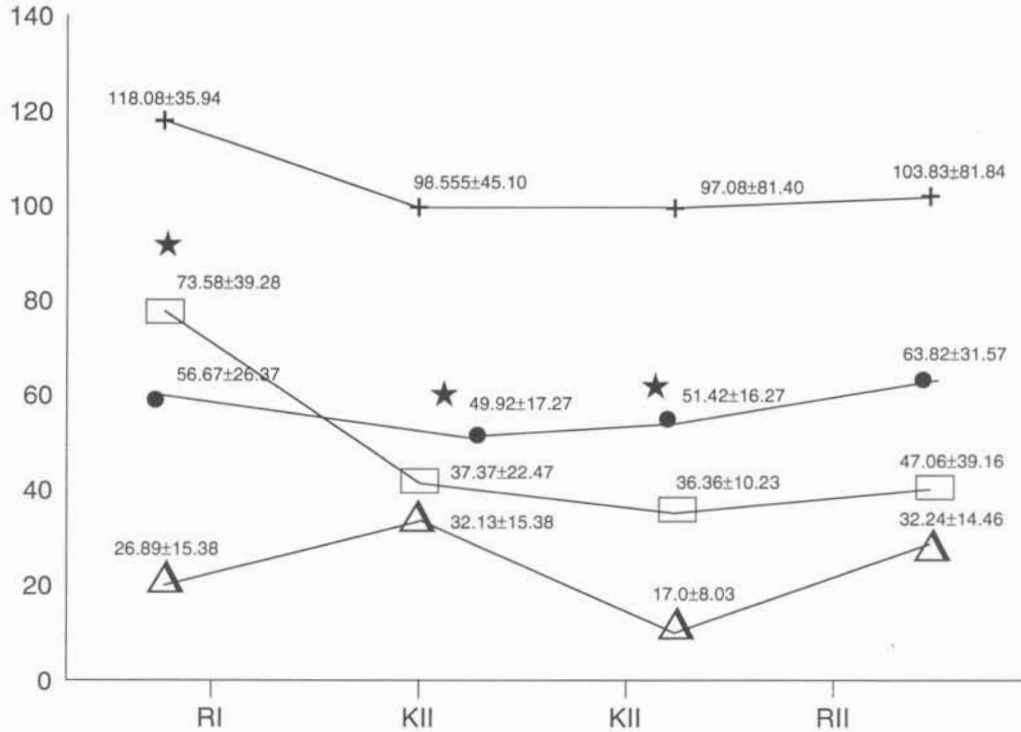
RESULTS

These were as follows:-

- i. 24 hours urinary volume:- Mean \pm S.D. of 24 hours urinary volume at R-I was 735.0 ± 255.61 ml and it dropped to 473.0 ± 136.67 ml at K-I and the difference was statistically significant. Then it gradually increased to 1538.9 ± 168.95 ml at K-II but the difference was still statistically significant. On reaching back to Rawalpindi (R-II), the mean \pm S.D. of 24 hours urinary volume was 700.00 ± 240.24 ml and the difference was statistically not significant from the pre ascent value.
- ii. Urinary pH:- Mean \pm S.D. of urinary pH at R-I was 5.55 ± 0.34 , and increased to 6.0 ± 0.58 at K-I and the difference was statistically significant. Then it gradually decreased to 5.59 ± 0.58 at K-II and the difference from R-I was statistically not significant. On reaching back to Rawalpindi (R-II), mean \pm S.D of urinary pH was 5.50 ± 0.35 and the difference from R-I was statistically not significant.
- iii. Urinary 24 hours potassium excretion:- Mean S.D. of urinary potassium excretion at R-I, K-I K-II were 56.67 ± 26.37 , 49.92 ± 17.27 , $\pm 51.42 \pm 16.27$ and 63.82 ± 31.57 mg respectively and the difference at different altitudes was statistically not significant (Fig-I).
- iv. 24 Hours Urinary Sodium Excretion:- Mean S.D. of 24 hours urinary sodium excretion at R-I, K-I, K-II and R-II were 118.08 ± 35.94 , 98.55 ± 45.10 , 97.08 ± 81.40 and 103.40 ± 81.84 mg respectively and the difference at different altitudes was statistically not significant (Fig-I).

Fig. I = Mean \pm S.D. of 24 Hours Urinary Excretion (mg) of

Sodium = + Oxalate = \triangle
 Potassium = \bullet Calcium = \square



RI = At Rawalpindi before ascent
 KI = on day I at Khunjrab
 KII = on day II at Khunjrab
 RII = on day II after reaching back Rawalpindi
 ★ = Statistically Significant

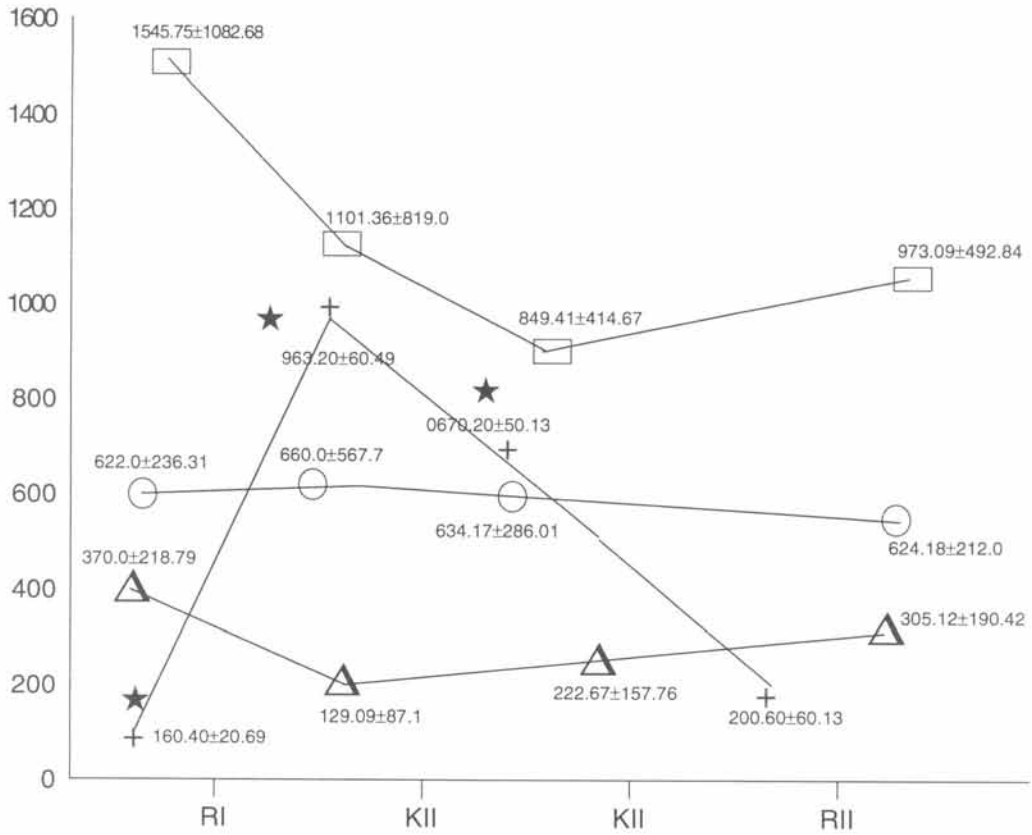
v. 24 Hours Urinary Phosphate Excretion:- Mean \pm S.D. of 24 hours urinary calcium excretion at R-I was $73.58 \pm 39 \pm 28$ mg and dropped to 37.37 ± 22.47 mg at K-I and the difference was statistically significant. At K-II it was 36.36 ± 19.23 mg and the excretion increased to 47.06 ± 39.16 mg at R-II and the difference with the pre ascent (R-I) value

was statistically not significant (Fig-II).

vi. 24 Hours Urinary Calcium Excretion:- Mean \pm SD of urinary phosphate excretion at R-I, K-I, K-II and R-II were 370.0 ± 218.79 , 129.09 ± 97.0 , 222.67 ± 157.76 and 305.12 ± 190.42 mg respectively and the difference at different altitudes was statistically not significant (Fig-II).

Fig. II = Mean \pm S.D. of 24 Hours Urinary Excretion (mg) of

Protein = + Phosphate = \triangle
 Uric Acid = \circ Creatinine = \square



RI = At Rawalpindi before ascent
 KI = on day I at Khunjrab
 KII = on day II at Khunjrab
 RII = on day II after reaching back Rawalpindi
 ★ = Statistically Significant

vii. 24 Hours Urinary Oxalate Excretion:-
 Mean \pm S.D. of urinary oxalate excretion at R-I, K-I, K-II and R-II were 26.89 \pm 15.38, 32.13 \pm 15.76, 17.0 \pm 8.03 and 32.24 \pm 14.46 mg respectively and the difference at different altitudes was statistically not significant (Fig-I).

viii. 24 Hours Urinary Protein Excretion:-
 Mean \pm S.D. of urinary protein excretion at R-I was 166.40 \pm 20.69 mg and increased to 963.20 \pm 60.49 mg and the difference was statistically significant. At K-II, it dropped to 670.20 \pm 50.13 mg and the difference was still statis-

tically significant as compared to R-I. At R-II, it further dropped and reached to 200.60 ± 60.13 mg and difference with R-I was statistically not significant (Fig-II).

- ix. 24 Hours Urinary Uric Acid Excretion:- Mean \pm S.D of urinary uric acid excretion at R-I, K-I, K-II and R-II were 622.0 ± 236.31 , 660.0 ± 567.7 , 634.17 ± 286.01 and 624.18 ± 212.0 mg respectively and there was no statistically significant difference at difference altitudes (Fig-II).
- x. 24 Hours Urinary Creatinine Excretion:- Mean \pm S.D. of urinary creatinine excretion at R-I, K-I, K-II and R-II were 1545.75 ± 1082.68 , 1101.36 ± 819.0 , 849.41 ± 414.47 and 973.09 ± 492.84 mg respectively and the difference at different altitude was statistically not significant (Fig-II).

DISCUSSION

Renal response to high altitude has not been studied previously in this region and no account is available on the subject. About a decade ago Khan¹³ had reviewed the subject and discussed various changes in renal function in response to high altitude.

There was statistically significant drop in urine output which normalized after reaching back to the baseline. This has already been shown by our previous study.¹⁴ It has been demonstrated by various studies in animals that mild degree of hypoxia induces polyuria and severe hypoxia induces oliguria.¹⁵ Therefore, decreased urine output in our study can be due to severe hypoxia as well as decreased fluid intake. Moreover, it has been demonstrated that the subjects who develop oliguria at high altitude are more likely to develop acute mountain sickness.¹⁶ Although no possible explanation has been given but the version was seconded by our own observations that the subjects who have decreased urine

output also developed signs and symptoms of acute mountain sickness.

There was statistically significant increase in urinary pH in response to acute ascent but it was still in the normal physiological range. By staying at high altitude the urinary pH decrease. Breathlessness is the most predominant symptom observed in unacclimatized subjects. This hyperventilation leads to respiratory alkalosis which is compensated by the alkaline urinary pH. This increase in urinary pH in response to acute ascent has already been demonstrated by Heath and Williams.¹⁷ On the other hand, Waterlow and Bunje¹⁸ found alkaline urine only in three specimens out of a total of 500 specimens. This paradoxical observation as explained by Ward¹⁹ is that during acute ascent many visitors suffer from acute mountain sickness, anorexia and loss of weight which may lead to acetonuria and thus abolishing the alkaline response of urinary pH to acute ascent.

Twenty four hours excretion of potassium decreased in response to acute ascent, remained stable at high altitude and increased beyond pre ascent levels after coming back to the starting point but there was no statistically significant difference between values at different altitudes. The tendency of the body to conserve potassium in response to acute ascent has been observed already.²⁰ It has been demonstrated that there is increase in serum potassium in response to acute ascent.²¹ This is another indirect evidence of potassium conservation by the body. On the other hand, Sutton²² has demonstrated normal serum potassium with decreased urinary excretion of potassium. This can be explained by intracellular shift of potassium in response to acute ascent.²³ Waterlow and Bunje believe that potassium depletion as an important factor in inducing signs and symptoms of acute mountain sickness. They demonstrated that symptoms of acute mountain sickness were more prolonged and

severe in subjects with potassium intake. Therefore by conserving potassium depletion from the body, the nature probably tries to save the mountaineers from the signs and symptoms of acute mountain sickness. Increased potassium excretion on return in our study can be explained on the basis that potassium conservation by body was no longer required and the excess potassium collected in the body poured out through the urine.

Twenty four hours urinary sodium excretion decreased in response to acute ascent and then normalized on reaching back to the base and there was no statistically significant difference between the values. Mountaineers usually love to climb and walk around over the mountains. Williams²³ et al have shown that in mountaineers who are up and about, there is conservation of urinary sodium and this was due to activation of renin aldosterone system. Conservation of sodium due to activation of renin aldosterone system has also been confirmed by Milledge²⁴ et al.

Deterioration in calcium homeostasis in response to hypoxia is well known.²⁵ Khan¹³ has demonstrated that there was no significant change in urinary calcium excretion in response to rapid ascent to 3780 meters. In our study, there was statistically significant drop in urinary calcium excretion. This may be explained on the basis that in our study the ascent was upto 4450 meters instead of 3780 meters and probably the excess altitude resulting in more severe hypoxia and drop in urinary calcium excretion. Calcium conservation by body is protective in nature because severe hypoxia leads to diminish uptake at neuronal synapses²⁶ resulting deterioration in electrical activity in the neurons.

Urinary inorganic phosphate levels decreased with rapid ascent and then normalized after returning to the base. There was no statistically significant difference between the values at different altitudes. Similar were the findings in expedition

conducted by Khan.¹³ Probably phosphate excretion is immune to the hypoxic effects.

There was fall and rise in urinary oxalate excretion but the difference was statistically not significant. Available literature at hand does not reveal any study in which the oxalate levels are calculated in response to rapid ascent. Anyway, acute ascent does not lead to aberration in urinary oxalate excretion.

Statistically significant increase in proteinuria was a predominant finding in our study and the proteinuria attained pre ascent level after reaching back to the starting point. Proteinuria in response to rapid ascent has also been reported by others.^{27,28} They have shown that there is a time lag of 1-3 days before the appearance of significant difference in proteinuria. But in our study even on the next day of acute ascent the difference in proteinuria was statistically significant. Rennie et al²⁹ have shown that the increase in proteinuria barely exceeded physiological levels while in our study it was about one gram/day. The proteinuria started decreasing with stay at high altitude and reached baseline after return. Similarly it has been demonstrated by Pines³⁰ that repeat ascent to the same altitude induces less degree of proteinuria. Findings by Rennie et al³¹ are still interesting that high altitude residents excrete more protein in urine than subjects of the same race at sea level. Hypoxia leading to renal trauma has been thought to be the possible aetiological factor. It has also been found by Rennie³² that the patients with cyanotic heart disease who are chronically hypoxic from birth also have increase proteinuria, the degree being directly related to the degree of polycythemia and hence hypoxia. It has also been demonstrated that the proteinuria is predominantly albuminuria as the albumin/globulin ratio decreases with acute ascent.¹³ The mechanism for high altitude proteinuria may be either reduction in tubular reabsorption of protein or increased glom-

erular permeability to protein or both in response to injury due to hypoxia.

Urinary uric acid excretion did not show statistically significant rise or fall in response to acute ascent. Similar were the findings in study conducted by Khan¹³ that there was initial rise and then fall in urinary uric acid.

Urinary creatinine excretion did not show any statistically significant response with rapid ascent. Previously Khan¹³ has shown that the urinary creatinine excretion initially decreased at an altitude of 3180 meters and then increased with further rise upto 3780 meters. He also demonstrated a concomitant fall in serum creatinine with rise in urinary excretion of uric acid.

Thus we conclude that rapid ascent to high altitude produces a series of biochemical changes in the body and the body tries to compensate. The changes in the excretory and secretory system of the kidney are the compensatory response of the body towards high altitude ascent. The slogan presented by Himalayan Rescue Association "Don't go too fast too high" is valid because slow ascent lead to the activation of the compensatory mechanisms of the body and the body is saved from the injury due to acute ascent.

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