

Changes in Plasma Electrolytes During Acclimatisation at High Altitude

Pages with reference to book, From 128 To 131

Dilshad Ahmad Khan (Department of Chemical Pathology, Armed Forces, Army Medical College, Rawalpindi.)
Muhammad Aslam, Zia Ullah Khan (Institute of Pathology and High Altitude Medical Research Council, Army Medical College, Rawalpindi.)

Abstract

The effects on plasma electrolytes and related hormones were determined in non-acclimatized lowlander males, exposed for 96 hours to an altitude of 4424 meters. Twenty healthy soldiers aged 18-34 years travelled by road from an altitude of 2303 meters to 4424 meters over a period of 10 hours. Plasma sodium levels (142.09 ± 1.14 mmol/l) and aldosterone (16.61 ± 5.70 ng/ml) decreased to 139.69 mmol/l and 11.6 ± 4.60 ug/ml respectively after 96 hours of acute exposure to high altitude ($p < 0.05$). The plasma potassium and chloride levels did not show significant change, while, plasma HCO_3^- decreased gradually from 21.06 ± 1.38 mmol/l to 18.55 ± 0.82 mmol/l after 96 hours exposure to this altitude ($p < 0.01$). The plasma ionized calcium and plasma phosphate concentration decreased from 1.32 ± 0.11 mmol/l and 1.58 ± 1.3 mmol/l to 1.20 ± 0.05 mmol/l and 1.47 ± 0.99 mmol/l respectively (p

Introduction

Acute mountain sickness (AMS), high altitude pulmonary edema (HAPE) and cerebral edema (HACE) are associated with fluid retention and weight gain in non-acclimatized men who rapidly ascend to high altitude¹⁻⁴. It has been suggested that increased capillary permeability and fluid retention are important factors in the causation of these high altitude disorders⁵⁻⁶. Acclimatization changes occurring in human body include changes in water, electrolytes and related hormones such as serum aldosterone, antidiuretic hormone (ADH) and parathyroid hormone (PTH). The urinary excretion of solutes such as sodium, potassium and bicarbonate may induce partial compensation of respiratory alkalosis in unacclimatized men at high altitude^{7,8}.

The experience shows that AMS, HAPE and HACE carry considerable importance for troops who ascend rapidly to high altitude^{9,10}. This study was planned to investigate the acute effects of exposure to high altitude on plasma sodium, potassium, HCO_3^- , calcium, phosphate and the related hormones (aldosterone and PTH) in unacclimatized lowlanders.

Subjects and Methods

The study was carried out in the Karakoram Range of Pakistan by the High Altitude Medical Research Cell (HAL-MARC) under auspices of Armed Forces Medical Research and Development Council (AFMRandDC), Pakistan Army in 1993.

Twenty non-acclimatized healthy male volunteers of 18-34 years of age were selected after proper medical examination for the study. They had never been exposed to high altitude before.

Study Protocol: At 2303 meter: The baseline arterial blood samples were collected from the volunteers in heparinized tubes and they travelled by road to a height of 4424 meters the same day.

At 4424 meter: The volunteers stayed at this altitude for 5 days, taking normal diet. The arterial blood samples were collected in basal conditions after 48 and 96 hours. Plasma was separated by centrifugation immediately after blood collection, samples were stored in liquid nitrogen for subsequent measurement of hormones.

Electrolyte analysis

Plasma sodium, potassium, ionized calcium and bicarbonate were determined from heparinized arterial blood samples immediately after their collection by Gem-stat blood gas analyzer (Mallinckmndt, USA) at mountainous area. Plasma chloride and phosphate were analysed at AFIP using commercially available kits. (Merck, Germany).

Hormonal analysis

Plasma aldosterone and PTH were assayed by standard radioimmunoassay technique^{11,12} at AFIP, Rawalpindi using commercially available kits (DPC; USA). The RIA hormonal controls were run at the same time and intra assay CV's for aldosterone and PTH were 5% and 6.2% respectively.

Results

The plasma sodium, potassium, chloride and bicarbonate showed individual variation in base line and at high altitude (Table).

Table. Changes in plasma electrolytes in non-acclimatized adults at high altitudes (2303 m and 4424 m).

Parameters (mmol/l)	2303 m		4424 m (48 h)		4424 m (96 h)	
	Mean	SD	Mean	SD	Mean	SD
Sodium	142.09±1.14		141.8±1.29		**139.69±0.96	
Potassium	4.06±0.33		3.88±0.37		3.99±0.32	
Bicarbonate	21.06±1.38		*19.50±1.24		**18.55±0.82	
Chloride	98.26±3.1		95.47±2.8		97.68±2.3	

* = p<0.05 vs values at 2303 m

** = p<0.01 vs values at 2303 m

The results are presented as mean±SD. Plasma sodium decreased from 142.09±1.14 to 139.69±0.96 mmol/L after 96 hours of acute exposure to high altitude (p<0.01).

Plasma bicarbonate also decreased from 21.06±1.38 to 19.50±1.24 and 18.55±0.82 mmol/L after 48 and 96 hours exposure (P

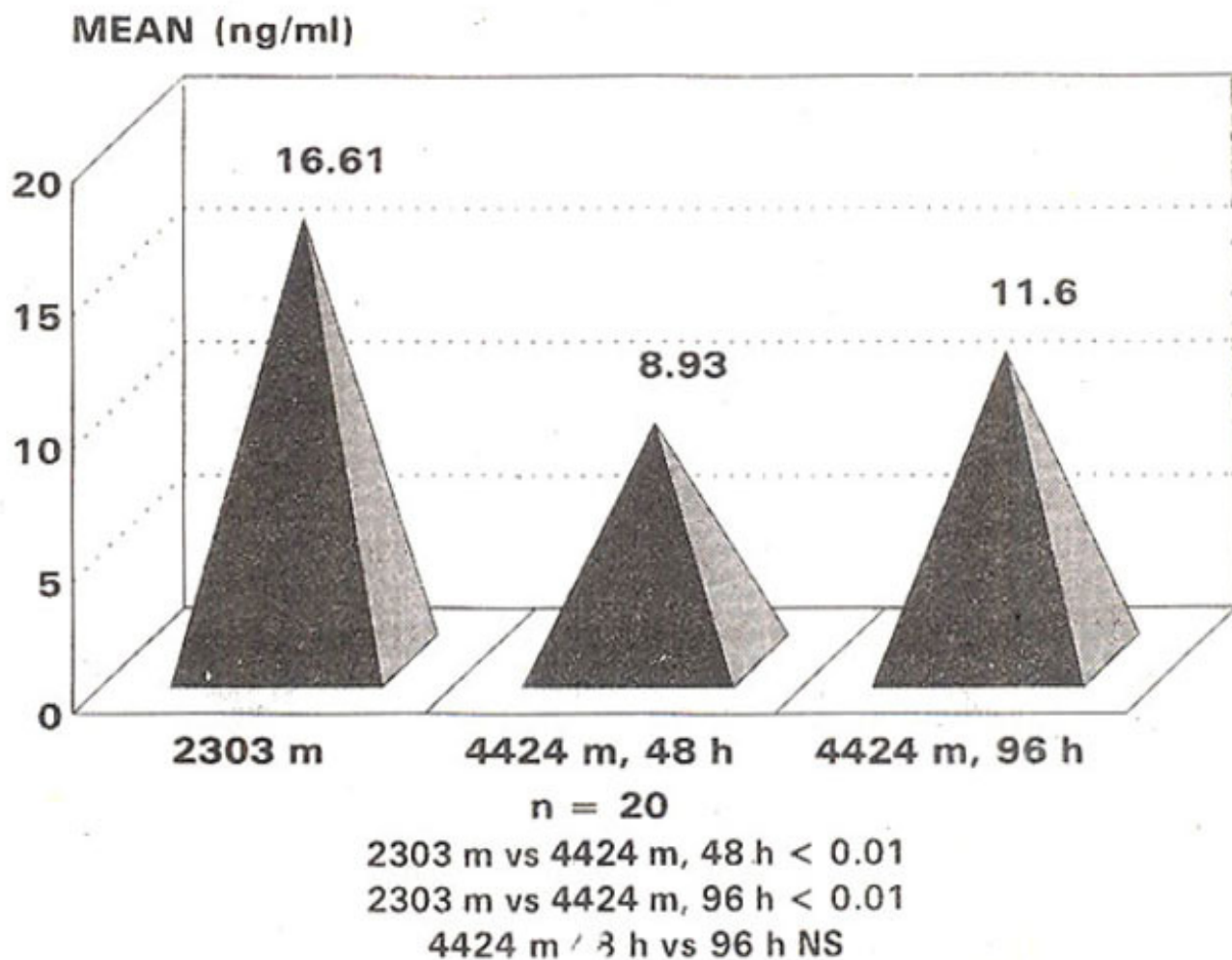


Figure 1. Changes in plasma aldosterone in non-acclimatized adults at high altitudes (2303m and 4424m)

Plasma ionized calcium and plasma phosphate concentration decreased from 1.32 ± 0.11 and 1.58 ± 1.3 to 1.20 ± 0.05 and 1.47 ± 0.94 mmol/l ($p < 0.01$) respectively at high altitude after 96 hours exposure (Figure 2).

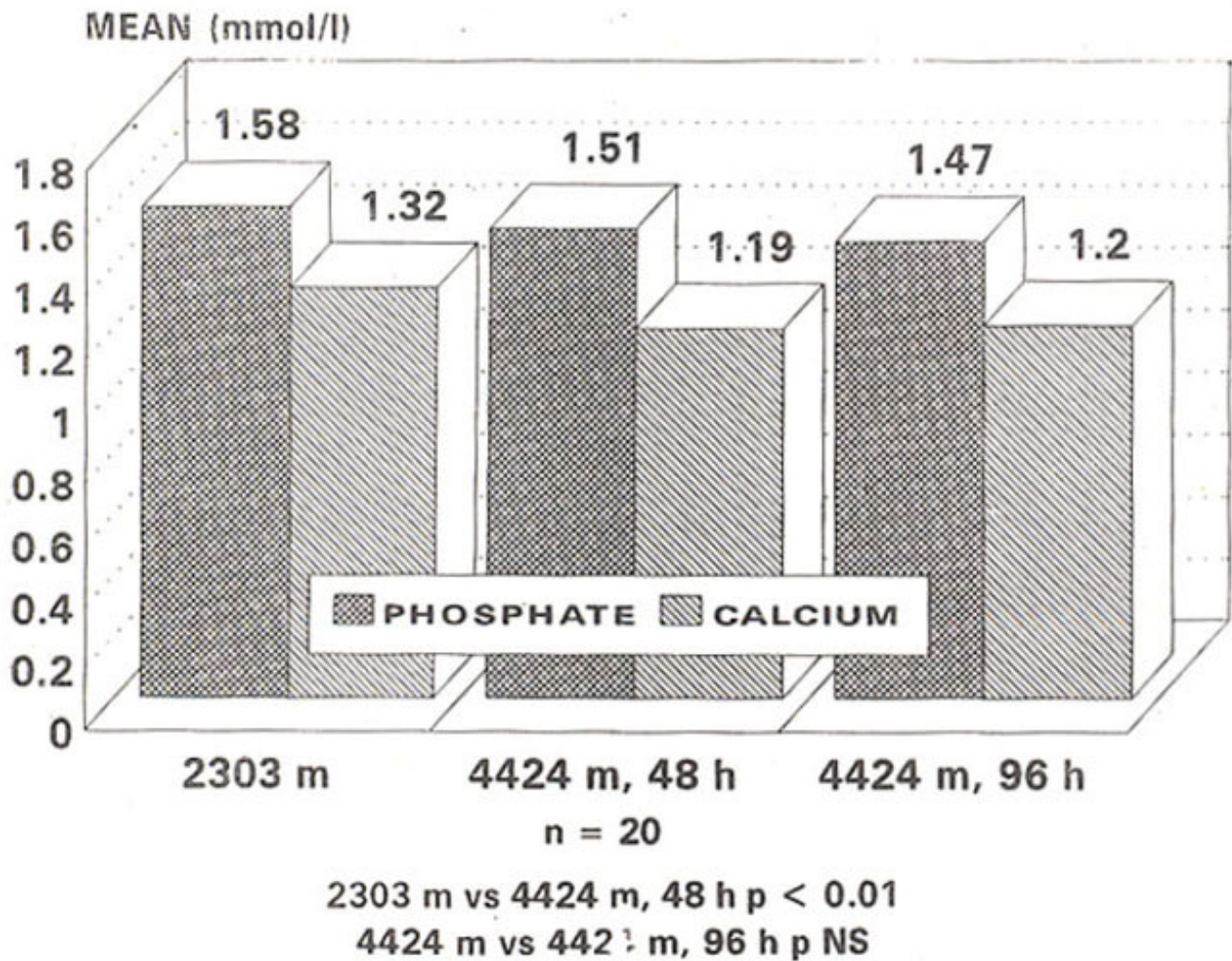


Figure 2. Changes in plasma calcium and phosphate in non-acclimatized adults at high altitudes (2303m and 4424m).

Discussion

Homeostatic mechanism for sodium and water are interlinked and distribution of fluid between intra and extracellular fluid compartments depends on changes in extracellular sodium concentration. Plasma sodium level significantly decreased after acute exposure to high altitude in this study. This could be due to decreased serum aldosterone. Decreased level of serum aldosterone and arterial chemoreceptor stimulation by hypoxic hypoxia is counteracted by excretion of sodium, water and bicarbonate from the body¹³ - Many studies have demonstrated the excretion of sodium from the body for initial several days at high altitude^{14,15}.

Potassium and hydrogen compete for exchange with sodium in renal tubules and other body cells membranes. 96 hours exposure (Figure 3).

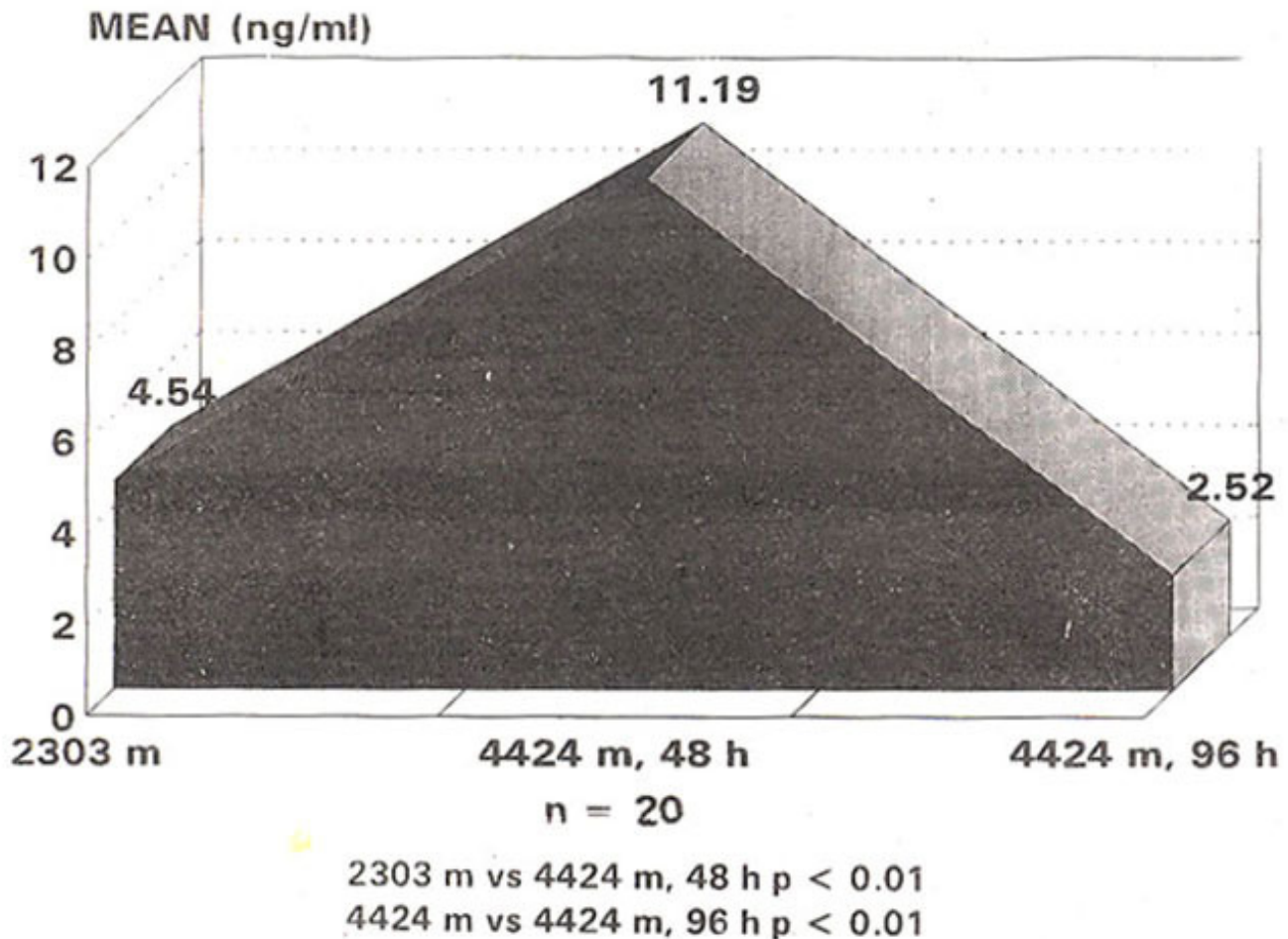


Figure 3. Changes in plasma PTH in non-acclimatized adults at high altitudes (2303m and 4424m).

Hypoxia causes impairment of the pump in all cells, with a net gain of potassium within the extracellular fluid. Such impairment in the distal tubules causes potassium retention and hyperkalaemia¹⁶. But, in this study no significant change was observed in plasma potassium level after acute exposure to high altitude. The possible explanation could be that respiratory alkalosis at high altitude leads to decreased plasma potassium in extracellular fluid. Sutton and his colleagues¹⁷ found no change in plasma potassium concentration in men exposed to simulated altitude of 4700 m for 2 days but like other observers, they found a decrease in urinary potassium excretion. There is a tendency of the body to consume potassium on acute exposure to high altitude especially during the first three days¹⁸. Hypoxia at high altitude stimulates respiratory centres and causes hyperventilation in normal subjects. This hyperventilation lowers plasma Pco₂ and bicarbonate concentrations primarily by inhibiting the excretion of net acid¹⁹. Aldosterone appears to regulate sodium and water balance by its action exerted mainly on the distal renal tubule stimulating sodium reabsorption and potassium excretion. The aldosterone levels decreased after 48 and 96 hours exposure to high altitude as compared with the baseline level (p<0.01) in this study. The fall in aldosterone is related to the increased blood volume that occurs in acclimatization process to altitude. This leads to stimulation of the stretch receptors in the right atrium which is known to depress aldosterone secretion²⁰. Jung and his colleagues²¹ found that the fall in blood aldosterone at high altitude occurs in older subjects rather than in the young. The reduction in aldosterone secretion has been confirmed in climbers. The exact mechanisms of this

decrease in aldosterone have not been elucidated. Aldosterone concentrations at high altitude appear to depend on the duration of exposure. Okazaki et al²¹ reported significant increase in aldosterone on arrival at a simulated altitude of 6000 m. This increased level appeared to be due to increased adrenocorticotrophic hormone (ACTH) because the concentrations of serum cortisol were also elevated significantly²². After longer periods of exposure to hypobaric hypoxia, there occurs significant decrease in both blood and urinary aldosterone^{23,24}. Plasma ionized calcium and phosphate depression at high altitude after 48 hours of exposure, could be due to respiratory alkalosis. Krapt et al²⁵ reported sustained decrease in ionized calcium in four normal male subjects at 3450 m altitude but the plasma phosphate level increased. Hypoxic pulmonary vasoconstriction and respiratory alkalosis at high altitude also enhances penetration of ionized calcium across sarcolemma of smooth muscle cells. This causes increased cytosol free ionized calcium concentration due to alteration in sodium handling and in the sodium-ionized calcium exchange system²⁶. Hypophosphataemia is associated with disturbances of ionized calcium metabolism and phosphate is lost from the body in urine. Phosphate may be reduced because like potassium, it enters the cells from extracellular fluid because of increased rate of glucose metabolism at high altitude²⁷. Low plasma free ionized calcium concentration with normal total calcium due to respiratory alkalosis leads to increased plasma PTH after 48 hours of exposure but subsequent decrease in PTH level after 96 hours cannot be explained at the moment. It may be concluded that the human body tends to acclimatize to high altitude by decreasing plasma aldosterone, with associated fall in sodium and bicarbonate levels. There occurs a significant decrease in plasma ionized calcium and phosphate levels while PTH concentration fluctuates according to the duration of exposure to high altitude.

References

1. Bartsch, P.S., Shaw, M. and Francioli, M. Atrial natriuretic peptide in acute mountain sickness. *J. Appl. Physiol*, 1988;65:1929-37.
2. Bartsch, P.P. Vock, M, Maggiorini, M. Respiratory symptoms, X-ray and physiological correlations at high altitude. In: Hypoxia. The adaptations, Sutton, J.R. Castes, O., and Remmers, L.E. (eds). Toronto, Decker 1990, pp. 241-5.
3. Hackett, P.H., Rennie, D., Rales, J.E. Peripheral edema, retinal haemorrhage and acute mountain sickness. *Am. J. Med.*, 1979;67:214-8.
4. Hackett, P.H., Rennie, D., Hoflucister, S.E. et al. Fluid retention and relative hypoventilation in acute mountain sickness, *Respiration*, 1982;43:321-9.
5. Hackett, P.H., Rennie, D., Grove, R.F. et al. Acute mountain sickness and the edema of high altitude: A common pathogenesis. *Respir Physiol.*, 1981,46:383-90.
6. Sutton, J.R. and Lassan, N. Pathophysiology of acute mountain sickness and high altitude pulmonary oedema: An hypothesis. *Bull. Eur Physiopathol. Respir*, 1979;15:1045-52.
7. Ullmann, E. Acute anoxia and the excretion of water and electrolyte. *J. Physiol.*, 1961;155:417-37.
8. Van-Liere, E.J and Stickney, J.C. Hypoxia, Chicago, University of Chicago Press, 1963, pp. 236-55.
9. Chaudhry, M.A., Khan, Z.U. and Malik, I.A. Incidence of medical problems at high terrestrial altitudes: A retrospective study. *Pak. Armed Forces Med. J.*, 1994;44:128-33,
10. Oelz, O., Maggiorini, M., Ritter, M. et al. Pathophysiology, prevention and therapy of altitude pulmonary edema. *Schweiz Med Wochenschr.*, 1992;122: 1151-8.
11. Chard, T. An introduction to radioimmunoassay and related techniques, ed 3, New York, 1987, Elsevier Science Publishing Co., Inc. Theorell, J.I. Editor: Radioimmunoassay design and quality control. World Federation of Nuclear Medicine and Biology, Oxford, Pergamon Press, Inc., 1983.
12. Ekins, R.P. The physiological significance and measurement of free hormones in blood. In

- radioimmunoassays and related procedures in medicine. ed: Sonski ER: 1st edition: Vienna, International Atomic Energy Agency, 1982, pp. 191-218.
13. Koller, E.A., Buhner, A. Felder, L. et al. Altitude diuresis: Endocrine and renal responses to acute hypoxia of acclimatized and non-acclimatized subjects. *Eur. J. Appl. Physiol*, 1991 ;62:228-34.
 14. Janoski, A.H., Whitten, B.K., Shields, J.L. et al. Electrolyte patterns and regulation in man during acute exposure to high altitude. *Federation Proc.*, 1969;28:1183-9.
 15. Slater, J.D.H., Williams, E.S., Edwards, R.H.T. et al. Potassium retention during the respiratory alkalosis of mild hypoxia in man: Its relationship to aldosterone secretion and other metabolic changes. *Chin. Sci.*, 1969,37:311-26.
 16. Philip, D. Mayne. Sodium and Water balance. In: *Clinical Chemistry in Diagnosis and Treatment* (6th ed) London, ELBS, 1994, pp.25-57.
 17. Sutton, J.R., Viol, G.W., Gray, O.W. et al. Renin, aldosterone, electrolyte and cortisol respiratory in hypoxic decompression. *J. Appl. Physiol.*, 1977;43:421-4.
 18. Hannson, J.R Chinn, K.S.K. and Shields, J.L. Alterations in serum and extracellular electrolytes during high altitude exposure. *J. Appl. Physiol.*, 1972;31:266-70.
 19. Krapf, R., Becler I., Healner, D. et al. Chronic respiratory alkalosis. The effect of sustained hyperventilation on renal regulation of acid base equilibrium. *N. Engl. J. Med.*, 1991;324:1394-401.
 20. Halhuber, M.J. and Gabl, F. 17-OHCS excretion and blood eosinophils at an altitude of 2000 m. In: *The physiological effects of high altitude* (W.H. Weihe, Ed) Oxford, Pergamon Press, 1964, p. 131.
 21. Okazaki, S., Tamura, Y., Hatano, T. et al. Hormonal disturbance of fluid electrolyte metabolism under altitude exposure in man. *Aviat. Space Environ. Med.*, 1984;55:200-5.
 22. Khan, D.A., Khan, Z.S. and Aslam, M. Hormonal changes in non-acclimatized men at high altitude. *Pak. Armed Forces Med. J.*, 1994;44:51-56.
 23. Milledge, J.S., Catley, D.M., Blume, F.D. et al. Renin angiotensin-converting enzyme and aldosterone in humans on Mount Everest. *J. Appl. Physiol.*, 1983;55:1599-1604.
 24. Maresh, C.M., Noble, B.J., Robertson, K.L. et al. Adrenocortical responses to maximal exercise in moderate altitude natives at 447 Torr. *J. Appl. Physiol.*, 1984;56:482-6.
 25. Krapf, R., Jaeger, P. and Hulter, H.N. Chronic respiratory alkalosis induces renal PTH-resistance, hyperphosphatemia and hypocalcemia in human. *Kidney Int.*, 1992;42:727-34.
 26. Guazzi, M.D., Alimarto, M., Barti, M. et al. Enhanced hypoxic pulmonary vasoconstriction in hypertension. *Circulation*, 1989;79:337-43.
 27. Philip, D. Mayne. Calcium, phosphate and magnesium metabolism. In: *Clinical Chemistry in Diagnosis and treatment* (6th ed) London, ELBS, 1994, pp. 171-91.