Arterial oxygen saturation under hypoxic environment of high-altitude associates with routine physical activities of natives

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Per cent oxygen saturation of arterial haemoglobin levels (SaO_2), a measure of hypoxemia has been analysed in the permanent residents of Ladakh. The population recognized as high-altitude controls (HAC) and high-altitude monks (HAM), resided at the same altitude of 3600 m but differed in their routines. SaO_2 was measured with a Finger-Pulse Oximeter. The HAM had 3.08% higher SaO_2 ($P < 0.001$) compared to the HAC, with mean SaO_2 of 91.8 ± 6.1% and 89.0 ± 2.6%, respectively. Furthermore, the younger HAM also revealed an elevation of 4.55% SaO_2 than the HAC of identical age ($P < 0.001$). The HAM, who are less hypoxemic than their counterparts are physically more active, which may be a selective advantage in the extreme environment of higher altitudes.

HIGH-ALTITUDE (HA) environment is characterized by hypobaric hypoxia[1]. A low barometric pressure at high altitudes causes reduction in the partial pressure of oxygen in inspired air[2]. Accordingly, the oxygen saturation of haemoglobin is reduced in HA-living organisms. The resulting hypoxic condition stresses the metabolic processes of an individual for want of oxygen[3]. Nevertheless, the aerobic physiological processes must be maintained to avoid mountain disorders[4,5]. The native highlanders (HLs) have a long history of exposure and opportunity for natural selection[1]. Therefore, they show adaptive phenotypes with respect to physiological parameters[6] such as oxygen saturation, haemoglobin concentration[7], hypoxic ventilatory rate[8,9], and blood pressure[10]. Contrary to this, sojourners show variation in these parameters and experience various levels of physical discomfort at HA primarily due to significant fall in arterial blood-oxygen saturation[11,12]. This results in somewhat reduced level of performance in individuals when faced with tasks demanding high levels of physical abilities. The

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fact that the inhabitants from the two different highest altitudes perform the exhausting labour of mining (5950 m), and hard work of climbing (≥ 5400 m) under the extreme hypoxic condition[13] and rarely suffer from mountain disorders[14,15], provides ample evidence for their successful adaptive responses[1,6,13].

The literature is abundant with comparative studies on adaptation and physical activities of the Andeans[7], the Himalayans[8] and the migrant settlers[8,12,16]. These inhabitants, with almost identical per cent oxygen saturation of arterial haemoglobin (SaO_2) levels as that of the migrants, were shown to have superior physical performances suggesting better adaptation to the environment of their respective altitudes. It is, however, surprising that no concrete attempts were made to differentiate the phenotypic characteristics amongst the HLs on the basis of ethnicity, lifestyle or routine. One of the reasons could be that the environment at a specific altitude is generally uniform. This perhaps, makes one contemplate on uniform physiological effects in the resident population of various altitudes.

The study of such stressful environments can be performed only by a comparative analysis of population differences with respect to adaptation and the vulnerability to mountain disorders[7,8,11,12]. In the present study, we had an opportunity to investigate the Ladakhi population, which can be easily distinguished into two different groups of people by way of their routine. We, therefore, analysed the population as HA controls (HAC) and HA monks (HAM) for SaO_2. The outcome was rather unexpected. The present finding could perhaps be of immense utility, especially to the HLs who climb great heights frequently, as well as to sojourners, mountaineers, etc.

Subjects were unrelated, normal males of different ages were divided into three groups. One group comprised of 105 sea-level residents (LLs), and the remaining two groups, identified as HAC and HAM, comprised of 109 and 158 subjects respectively. The two highland groups were of the same ethnic background, but differed in their work patterns and routine. The HLs have lived most of their lives at an altitude of ~ 3600 m in Ladakh, which is situated in western Himalayas. The HAM (Buddhist priests) differed from the HAC in that they resided in the monasteries, which are situated a minimum of 100 ft above a township. Their religious rituals made them descend frequently to various towns and ascend back to the monastery. In addition, the HAM also ascended on an average about 35 times during their entire lifetime (> 60 years of age) to visit and stay at a monastery situated at a height of ~ 5400 m. The HAC, on the other hand, had a comparatively sedentary lifestyle and rarely climbed to 5400 m. The subjects were apprised of the study and a written consent was obtained from each of them. An approval for the study was obtained from the Institute's Human Ethics Committee.

Data on health assessment characteristics such as age, blood pressure (BP), body weight, height, body mass index, per cent oxygen saturation of arterial haemoglobin (SaO_2), and heart rate (HR) are presented in Table 1. An Automatic Digital Blood Pressure Monitor (Omron MX2, Japan) was used to record BP and HR. Information was obtained from the HAM regarding their ascent to higher altitudes and the number of such trips made. A detailed questionnaire was administered about their demography, health, ethnicity, relationship and habits.

SaO_2 and HR were measured with a Finger-Pulse Oximeter 503 (Criticare Systems Inc, USA). The average of SaO_2 and ages of the three groups were recorded and compared. The SaO_2 of younger HLs in the age group range of 20–30 years was also compared. Mean SaO_2 was calculated for a block of 10 years, such as between 20 and 30 years and up to the age of 80 years, so as to check the correlation of SaO_2 with age. SaO_2, with the same motive, was also measured in two age groups of younger subjects. Average age of the HAM in this category was 18.2 ± 1.8 years and 28.7 ± 2.6 years and that of the HAC was 19.6 ± 1.6 years and 27.3 ± 2.1 years. Data are presented as mean ± SD and the differences between groups were analysed by one-way analysis of variance. A P value of less than 0.05 was considered statistically significant.

The characteristics of the three groups are presented in Table 1. The lowlanders seem to have normal characteristics. Between the two highland groups, the HAM are shorter in height and heavier in stature and have higher HR than the HAC. The remaining parameters, apart from SaO_2, were identical.

SaO_2 levels vary significantly between LLs and HLS, as is evident from the scatter plot in Figure 1. The SaO_2 levels for the LLs ranged between 96 and 99%, and for the two Himalayan groups, HAC and HAM, they ranged between 84 to 97%, and 88 and 98%, respectively. The LLs expectedly had the highest saturation level at the normal barometric pressure of 760 mm Hg, and between

Table 1. Characteristics of sea-level and high-altitude residents

	Subjects; altitude		
Characteristics	LLs; sea-level	HAC; 3600 m	HAM; 3600 m
Number, *n*	105	109	158
Age, years	23.9 ± 2.9	31.7 ± 12.9	49.5 ± 16.5
SBP, mmHg	120.5 ± 6.6	121.4 ± 12.3	125.7 ± 13.1
DBP, mmHg	73.2 ± 7.6	65.3 ± 8.1	78.3 ± 9.8
Weight, kg	60.3 ± 6.0	55.5 ± 4.7	61.7 ± 9.8
Height, cm	169.0 ± 3.9	166.2 ± 4.8	162.5 ± 6.3
BMI, kg/m^2	20.9 ± 1.7	20.2 ± 1.3	23.3 ± 3.5
SaO_2 (%)	97.7 ± 0.6	89.0 ± 2.6	91.8 ± 6.1
Heart rate, b/m	68.4 ± 8.1	65.7 ± 11.1	76.7 ± 12.2

SBP, Systolic blood pressure; DBP, Diastolic blood pressure; BMI, Body mass index; SaO_2, Per cent oxygen saturation of arterial haemoglobin. Values are mean ± SD.

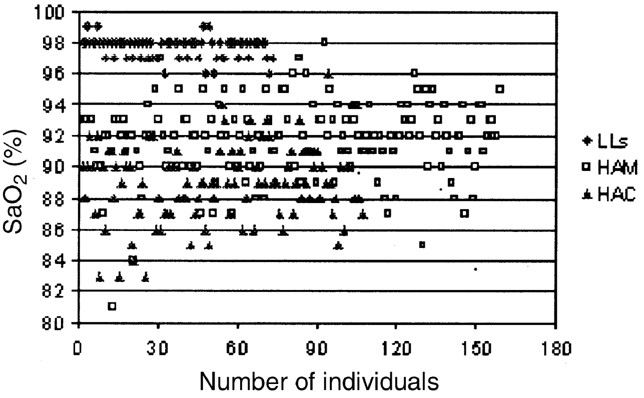

Figure 1. Scatter plot of SaO_2 levels of subjects in the three groups. SaO_2 was measured with a Finger-Pulse Oximeter. Each subject relaxed for at least 60 min prior to recording of SaO_2. The SaO_2 for LLs ($n = 105$) ranged between 96 and 99%, for HAM ($n = 158$) between 88 and 98% and for HAC ($n = 109$) between 84 and 97%. Subjects were unrelated, normal males of different ages and were divided into three groups.

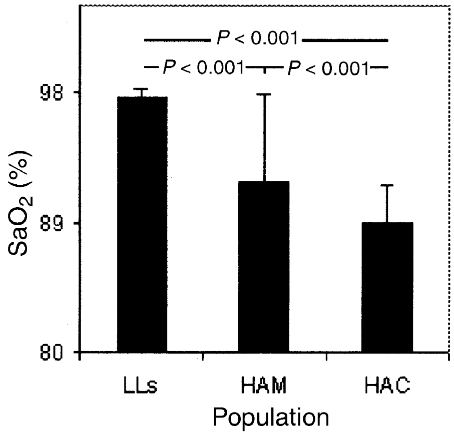

Figure 2. Comparative analysis of average of SaO_2 levels of subjects in the three groups. Bars represent the mean SaO_2 of each group. Both the HA groups, HAM and HAC, had significantly ($P < 0.001$) less SaO_2 compared to the LLs. Between the two HA groups, the HAM had higher SaO_2 level ($P < 0.001$) than the HAC.

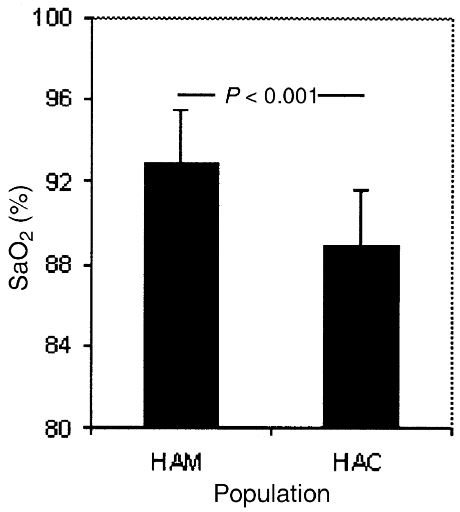

Figure 3. Comparison of SaO_2 levels between two young HA groups. Average SaO_2 of each group has been presented. The two groups markedly ($P < 0.001$) differed in maintaining the SaO_2 levels. The HAM comprised of 20 subjects and the HAC 25 subjects. Age of subjects ranged between 20 and 30 years.

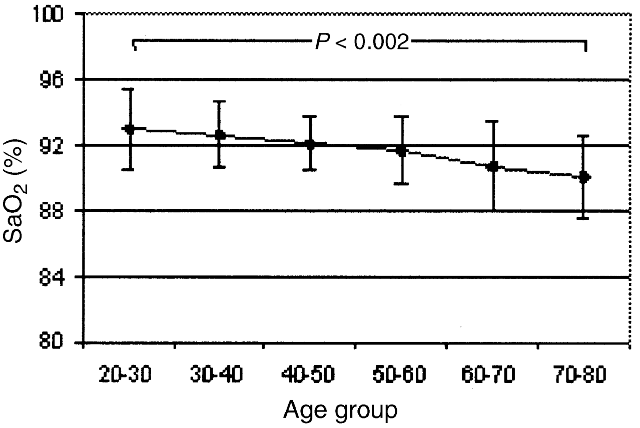

Figure 4. SaO_2 levels with respect to age. Subjects, starting from the age of 20 years till the age of 80 years, were grouped into 10-year blocks. Average SaO_2 level was plotted against the respective age group. Statistical analysis of SaO_2 between any two adjacent groups revealed no significance, except between the youngest and the eldest groups.

the two Himalayan groups, the SaO_2 was higher in HAM (Figure 1). An analysis of the average SaO_2 levels among the three groups has been presented in Figure 2. The LLs had a mean SaO_2 of 97.7 ± 0.6%, whereas the HAM and HAC had a mean of 91.8 ± 6.1% and 89.0 ± 2.6%, respectively. The data revealed a decrease of 6–8.8% ($P < 0.001$) in SaO_2 at HA.

Although the HA groups inhabited the altitude for generations, they showed distinct variations in SaO_2, which was 3.08% higher ($P < 0.001$) in the HAM compared to the HAC (Figure 2). The increase in SaO_2 was irrespective of age (20–80 years). Furthermore, when a younger age group (20–30 years) in the two HA populations was compared (Figure 3) for SaO_2 levels, there was a remarkable demarcation. The averages were 92.9 ± 2.5% in the HAM and 88.9 ± 2.7% in the HAC. The young HAM showed an elevation of 4.55% ($P < 0.001$).

It was observed that SaO_2 levels decreased steadily with increasing age at altitude, as can be seen from Figure 4. A comparison of the SaO_2 levels of younger (20–30 years) and older (70–80 years) HAM revealed a difference of 2.99% ($P = 0.002$), with the mean value of 92.9 ± 2.5% and 90.2 ± 2.5% respectively. A comparison between the maximum and minimum SaO_2 levels within each of the two younger age groups of subjects such as 18.2 ± 1.8 years versus 28.7 ± 2.6 years in the HAM and 19.6 ± 1.6 years versus 27.3 ± 2.1 years in the HAC revealed no significant differences.

The variation in SaO_2 of normal people at HA is an evidence of differences in adaptive response to hypobaric hypoxia[7,17,18]. It is invariably a health parameter under the extreme environment of an altitude. In the present study, the SaO_2 levels in the three Indian population groups were investigated with identical objectives. The normal atmospheric pressure at sea level maintained near 100% arterial oxygen saturation, as has been observed in the LLs, whereas the lower barometric pressure at HA decreased the SaO_2 levels significantly ($P < 0.001$) in the natives such as the HAC and the HAM. However, the overall higher (91.8%) SaO_2 levels in the HAM compared to the HAC (89.0%) were not anticipated because the two populations lived at the same altitude (~ 3600 m) since birth, and as a result were exposed to virtually the same reduced barometric pressure and partial pressure of inspired oxygen. In fact, the HAM faced lower barometric pressure, when they travelled to heights greater than 3600 m, at times up to 5400 m. Expectedly, their SaO_2 levels should have been lower in comparison to the HAC, but surprisingly, they were higher ($P < 0.001$). This strongly favours that the genetic locus for SaO_2 was influenced differently in the two populations under the given environmental conditions, resulting in altered gene expression[5,19,20]. More significantly, several such exposures over a period of time apparently resulted into developmental adaptation (fixed traits acquired during the period of growth and development[12,18]). Hence, it may be possible that the post-transcriptional changes occurred when the routine and the environment changed, thus, differentiating few of the phenotypic characteristics[5,21,22].

We envisage that the higher SaO_2 levels may prove advantageous during constant ascent to higher altitudes as in the case of the HAM, who often ascend to higher altitudes to visit and stay in a monastery as part of their religious assignments. Senior HAM (> 60 years of age) had frequented a monastery at a height of 5400 m on an average about 35 times; their residence otherwise were the monasteries situated at an altitude of approximately 3600 m. The SaO_2 remained higher by 2.99% in the HAM, although they were elder (49.5 ± 16.5 years) than the HAC (31.7 ± 12.9 years). When a comparison was made within the various inhabitants of different geographical background, the SaO_2 levels of the HAM matched that of the Aymara, whereas the SaO_2 levels of the HAC were similar to that of the Sherpas and the Tibetans (Table 2).

Table 2. Comparison of characteristics of the HA residents of different geographical backgrounds

	Ladakhis			
	HAC	HAM	Tibetans[7]	Aymaras[7]
Altitude, m	3600	3600	3800–4065	3900–4000
Age, years	31.7 ± 12.9	49.5 ± 16.5	38.0 ± 14.0	41.0 ± 16.0
SaO_2 (%)	89.0 ± 2.6	91.8 ± 6.1	88.3 ± 3.3	92.2 ± 2.8
Heart rate, b/m	65.7 ± 11.1	76.7 ± 12.2	73.0 ± 13.0	67.0 ± 11.0

SaO_2, Per cent of oxygen saturation of arterial haemoglobin (after Beall[7]).

It has been demonstrated that SaO_2 decreases in all the groups with increasing work output[8,17,23]. Nevertheless, native populations of the Andes and Himalayas maintain higher SaO_2 during maximal exercise at HA compared to acclimatized LLs[24], by virtue of superior lung diffusion capacity and larger DLO_2[8,12,16,25]. A decrease from 92.7 to 88.1% (mean) at rest and working level respectively, was reported by Brutsaert *et al.*[12]. Taking a lead from these reports, we presume that the higher SaO_2 level of 91.8 ± 6.1% in the HAM as against 89.0 ± 2.6% in the HAC could be beneficial during their mobility towards higher altitudes (> 3600 m), where atmospheric pressure drops further and physical movements (exercise) would demand more oxygen[1,2]. The glycolysis pathway[20,22], vasodilation and other related metabolisms where oxygen has a definitive role, could be the immediate beneficiaries[3,26–28]. The higher SaO_2 levels may thus, be advantageous during acclimatization (physiological mode of adaptation, which is short-term and reversible) to the new environment of the altitude[22,28]. However, this would need confirmation by performing the exercise experiments in both the groups.

A comparison between the young (20–30 years) HAM and HAC revealed the SaO_2 levels to be higher by 4.55% in the former. This is again a significant ($P < 0.001$) difference, suggestive of superior lung pulmonary diffusion capacity in HAM[16,25]. It also favours that the genetic locus for SaO_2 might be influenced differently in the two populations. At present, there are no data available on the two groups of inhabitants of HA of same geographic and demographic background. It is imperative to note that both the groups were physically active due to the work demands imposed by their subsistence lifestyle. However, the HAM, because of their frequent movements to different heights were comparatively more physically labour-oriented, and consequently taxed more in terms of oxygen consumption. This study, thus, imparts imperative knowledge about the SaO_2 phenotype in relation to HA adaptation and may prove fruitful in defining physical activity, even high endurance and altitude-related pulmonary and cerebral disorders. Higher SaO_2 levels may be achieved at any of the links in the chain of oxygen transport. Possibilities include the oxygen affinity of haemoglobin, the pulmonary arterial pressure and the pulmonary diffusion capacity[3,29].

Age plays a role in regulating SaO_2 levels at HA. It is evident from our data that SaO_2 levels decrease with age (20–80 years), which was in confirmation with earlier reports[7,12]. A difference of 2.99% was found between SaO_2 level of the younger (20–30 years) and the older (70–80 years) age groups of HAM (Figure 4). Similar variance was not evident across a narrow age range, such as between ~ 20 and ~ 30 years of both the HA groups.

Our data show that repeated exposure to extreme environment of HA such as in the case of HAM, increases and stabilizes the SaO_2. It strongly suggests that the

HAM, who are less hypoxic than their counterparts, the HAC, at the same altitude, may have a selective advantage in a new extreme environment in maintaining routine physical activities. Higher level of SaO_2, if present in an individual, could be of immense utility, especially to mountaineers, trekkers, etc.

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