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Original article

Objective criteria for diagnosing high altitude pulmonary edema in acclimatized patients at altitudes between 2700 m and 3500 m

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ABSTRACT

Background: The criteria used for diagnosing high altitude illnesses are largely based on Western literature. This study was undertaken to define objective, simple and reliable diagnostic criteria for high altitude pulmonary edema (HAPE) in Indian soldiers at altitudes between 2700 m and 3500 m.

Methods: Clinical data of 235 cases of HAPE that occurred between 2700 m and 3500 m were analysed. Receiver operator characteristic (ROC) curve analysis was used to select simple clinical parameters suitable for the diagnosis of HAPE at peripheral medical facilities. Cut-off values and their reliability for the diagnosis of HAPE were defined.

Results: HAPE occurred 2.8 ± 2.2 days after arrival at altitudes between 2700 m and 3500 m. Breathlessness, cough, chest discomfort and headache were the commonest symptoms. Low pulse oximetry (SPO_2) values than normal for this altitude were seen in 89% of patients. ROC analysis of clinical parameters identified a heart rate more than 95 beats per minute (bpm), respiratory rate more than 21 per minute and SPO_2 less than 86% while breathing ambient air at this altitude as diagnostic of HAPE. The sensitivity and specificity of these cut-offs was 0.66, 0.83 and 0.82 and 0.94, 0.95 and 0.93 respectively.

Conclusion: A heart rate of more than 95 bpm, respiratory rate more than 21 per minute and SPO_2 less than 86% breathing room air in individuals complaining of breathlessness, cough, chest discomfort or headache within the first 5 days of arrival at altitudes between 2700 m and 3500 m is highly suggestive of HAPE.

Introduction

High altitude (HA) medicine and physiology remains highly relevant to the Indian Armed Forces. A large number of troops, not native to HA, serve at altitudes greater than 9000 ft above mean sea level. The HA environment, with its low partial pressure of oxygen, low temperature, low atmospheric humidity and high levels of ultraviolet radiation challenges human physiological function. A better understanding of

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these physiological responses through both laboratory-based and field studies has resulted in a dramatic reduction in the incidence of high altitude illnesses (HAIs) over the last decade.

It is an accepted fact that some individuals are susceptible to HAI more than others, and hence, HAI would continue to occur, although with a lower incidence, as long as troops live and work in the HA environment.[1] The first point of contact between patients and medical facilities is usually the regimental medical officer (RMO), upon whose judgement and competence, the management of these patients depends. Since the diagnosis of HAI is often at remote locations without access to laboratory and imaging facilities, certain field-based diagnostic criteria, like the Lake Louise (LL) Consensus Criteria, have been described for the field diagnosis of acute mountain sickness (AMS), high altitude pulmonary edema (HAPE) and high altitude cerebral edema (HACE).[2]

Existing field-based diagnostic criteria for HAI have largely been arrived at from Western data gathered from mountaineers and tourists who develop HAI. This population may not be comparable with the Indian soldier population and hence the generalisability of these criteria requires study. Additionally, the LL criteria, such as tachycardia and tachypnoea, are non-specific and do not ascribe cut-off values for these parameters at a given altitude. The availability of more objective criteria for diagnosing HAPE at a given altitude would be beneficial, especially for paramedical staff at remote medical facilities. The present study was undertaken to examine the applicability of the LL Consensus Criteria for the diagnosis of HAPE in the Indian soldier and to suggest diagnostic criteria which could be more specific for a given altitude.

Material and methods

The HAI database of a HA Research Laboratory located at 3350 m above mean sea level was analysed. Clinical records of cases of HAPE available in the database were selected for analysis. The following cases of HAPE were included for analysis:

a. Altitude of occurrence between 2700 m and 3500 m.
b. Diagnosis of HAPE confirmed by a trained physician.
c. Records that were 'complete' (containing details of ascent profile, onset of symptoms and documented signs on clinical examination at the time of presenting to a medical facility).

The following records were not included in the analysis:

a. Where the diagnosis of HAPE was suspected but not confirmed.
b. Incomplete records.
c. Patients with documented history of having being administered drugs/oxygen prior to being examined by a medical professional.

Based on the above criteria, a total of 235 cases of HAPE were included for the analysis.

The acclimatisation medical data of 235 healthy soldiers at 3350 m, available with the HA Research Laboratory, was also analysed to determine values of heart rate, respiratory rate and pulse oximetry values during the first 6 days at an altitude of approximately 3000 m. A daily record of these parameters over the first 6 days of arrival at HA is maintained by the centre. This database contains data of more than 1000 healthy soldiers. Based on the mean day of occurrence of HAPE in the study group, acclimatisation medical data of the healthy soldiers for the corresponding day were chosen for analysis. The sampling was done using the 'Random' function in Microsoft Excel. These data served as healthy controls. Since the study and control group comprised a mixed soldier population, it was assumed that the groups were comparable in ethnic composition. A detailed matching for the same was not carried out.

The heart rate, respiratory rate and SPO_2 values of HAPE cases and controls were compared for statistically significant differences using an unpaired *t*-test and then subjected to a receiver operator characteristic (ROC) curve analysis.[3] This was done to identify which of these easily measurable clinical parameters would serve as good diagnostic criteria for HAPE occurring between 2700 m and 3500 m. This identification was done using the area under the curve (AUC) value for each of the parameter recorded.[3,4] The best operating point on the ROC curve was then identified to suggest cut-off values for diagnosing HAPE occurring between 2700 m and 3500 m. The best operating point in an ROC analysis is that point where the highest possible sensitivity and specificity are obtained for the given data. The value of a clinical parameter corresponding to this point is the logical choice for a cut-off value proposed as criteria for diagnosis of the clinical condition being studied.

The existing LL criteria for diagnosis of HAPE were applied to the HAPE cases and the sensitivity, specificity, positive and negative predicted values of the LL criteria calculated for this cohort. Since the LL criteria mention tachycardia and tachypnoea as two signs in patients with HAPE but do not specify values for the same, a heart rate of greater than 100 beats per minute (bpm) and a respiratory rate greater than 20 breaths/min were used to define tachycardia and tachypnoea respectively, as is the norm in clinical practice. A similar calculation was done using the cut-off values of HR, RR and SPO_2 obtained from the ROC analysis. The two sets of data obtained were analysed to compare the performance of the existing and proposed cut-off values for the diagnosis of HAPE in the Indian soldier.

Results

The mean time of onset of symptoms of HAPE was 2.8 ± 2.2 days after arrival at altitudes between 2700 m and 3500 m. The frequency of various clinical symptoms reported by HAPE patients at the time of diagnosis is shown in Table 1. Breathlessness, headache and cough were the commonest symptoms. The least common symptom was fatigue. The findings on clinical examination in patients of HAPE at the time of reporting to a medical facility and in the healthy acclimatising controls on day three at HA are shown in Table 2. Patients of HAPE had significantly higher heart rates and respiratory rates and lower SPO_2 values compared to healthy acclimatising soldiers at a comparable altitude. A frequency distribution of heart rate, respiratory rate and SPO_2 values in

Table 1 – Clinical symptoms in patients of HAPE in order of frequency.

Clinical symptom	Number of patients (% of patients)
Breathlessness	202 (79.5%)
Headache	183 (72%)
Cough	155 (61%)
Chest discomfort	99 (39%)
Expectoration	31 (12.2%)
Insomnia	20 (7.9%)
Fatigue	11 (4.3%)

Table 2 – Findings on clinical examination in patients of HAPE at the time of initial diagnosis. Corresponding values of the same parameters in healthy controls, recorded on the third day in HA, are shown for comparison.

Parameter	HAPE patients (n = 235) [Mean ± std dev]	Healthy controls (n = 235) [Mean ± std dev]
Heart rate (beats/min)	100.6 ± 17.8	88.5.1 ± 8.3*
Respiratory rate (breaths/min)	26.1 ± 5.5	16.1 ± 3.0*
Systolic blood pressure (mmHg)	124.8 ± 15.6	126.7 ± 11.5
Diastolic blood pressure (mmHg)	81.2 ± 10.7	79.2 ± 11.8
SPO_2 – breathing room air (%)	72.2 ± 12.9	88.5 ± 2.2*

* $p < 0.001$ (unpaired t-test).

patients of HAPE is shown in Figs. 1–3 respectively. Majority of HAPE patients had SPO_2 values lower than expected at that altitude and 48.9% of them had tachycardia (HR > 100 bpm) at the time of being diagnosed (Table 3).

ROC curves and the AUCs for HR, RR and SPO_2 are shown in Figs. 4 and 5. All the three parameters were found to have a high AUC ranging from 0.86 for HR to 0.88 for SPO_2. The best operating point on each curve corresponded to HR of >95 bpm, RR of >21 per minute and SPO_2 of <86%. The sensitivity, specificity, positive and negative predictive values of these cut-off values are as shown in Tables 4–6. A comparison of the sensitivity and specificity of these proposed cut-off values and the existing criteria of tachycardia (HR > 100 bpm) and tachypnoea (RR > 20 per min) for diagnosing HAPE at altitudes between 2700 m and 3350 m is as shown in Table 7.

Discussion

The symptoms of HAPE are known to develop within the first few days at altitude.[5] The mean time of occurrence of HAPE at 2700–3500 m in the study population was 2.8 ± 2.2 days. This fact is emphasised since symptoms suggestive of HAPE, in the absence of a history of recent gain in altitude or a possible precipitating factor such as severe unaccustomed exercise or respiratory infection, must be viewed with caution.

The symptoms reported by patients in the present study merit attention. While symptoms of breathlessness, chest discomfort and cough are well-known features of HAPE, a large percentage of patients (72%) were also found to complain of headache. Headache is a non-specific symptom and its occurrence at HA could be the result of a number of factors ranging from dehydration, lack of sleep and tiredness of travel to co-existence of acute mountain sickness. Interestingly, patients of HAPE have been reported to complain of headache in other reports as well.[6,7] Though the pathophysiology of HAPE, as per current understanding, cannot explain the occurrence of headache, the frequent association of this symptom with HAPE might merit consideration of the symptom in the criteria for diagnosis of HAPE.

The absence of fatigue as a major symptom in our patients is interesting since fatigue/weakness/decreased exercise performance is an important diagnostic symptom of HAPE as per the Lake Louise criteria.[2,8] Only 4.3% of our patients reported this symptom. A possible reason could be that soldiers do not undertake significant physical activity during the initial days at altitude as compared to mountaineers, trekkers and tourists indulging in adventure sport at altitude. The average sedentary soldier may not, therefore, notice fatigue as an early and prominent symptom of HAPE.

Not all patients of HAPE in our study showed tachycardia as defined by a heart rate of more than 100 bpm. Only 48.9% of patients had a heart rate of more than 100 bpm, suggesting that more than half of the patients (51.1%) developing HAPE at altitudes of 2700–3500 m may not manifest tachycardia.

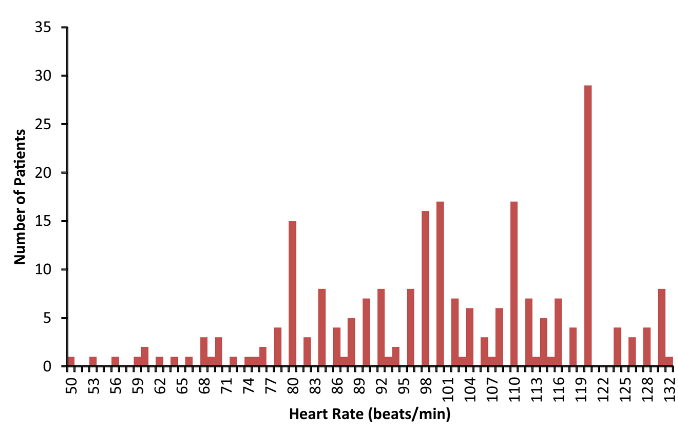

Fig. 1 – Frequency distribution of heart rate values in 235 patients of HAPE showing that only 48.9% of patients had heart rates more than 100 bpm.

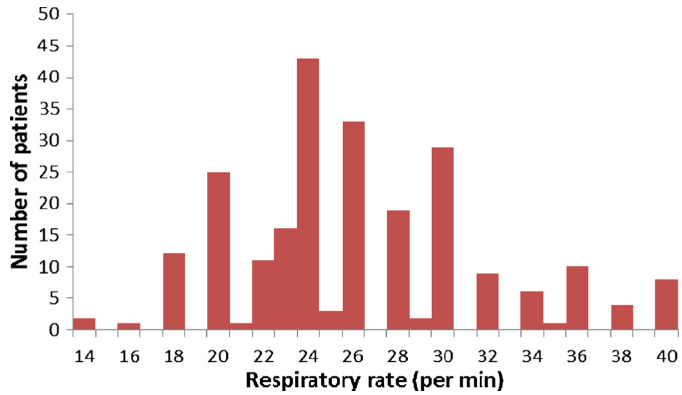

Fig. 2 – Frequency distribution of respiratory rate values in 235 patients of HAPE.

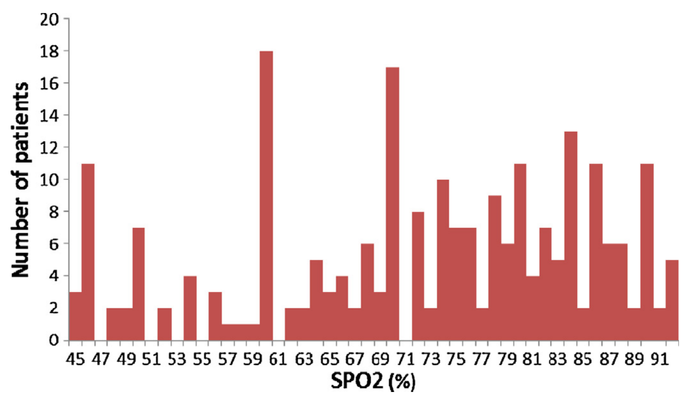

Fig. 3 – Frequency distribution of SPO_2 values in 235 patients of HAPE.

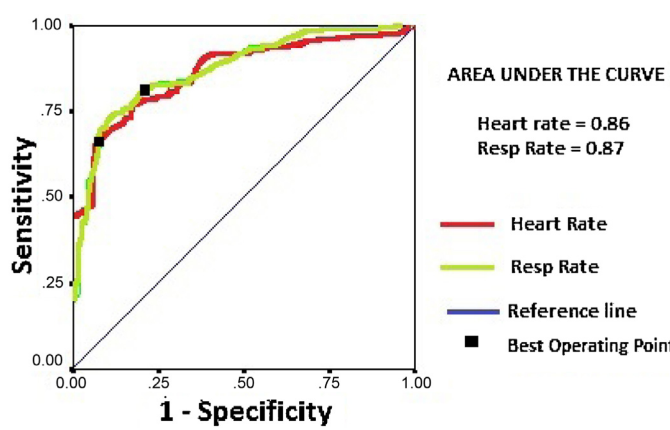

Fig. 4 – ROC curve for heart rate (HR) and respiratory rate (RR) showing areas under the curve of 0.86 and 0.87 for HR and RR respectively.

The magnitude of increase in heart rate is known to be proportional to the altitude of ascent and the severity of illness.[9,10] The lower heart rates in the study population could be due to a number of reasons. Possible among these are the altitude in question (2700–3500 m), which is lower compared to some of the other reports of HAPE, a less severe illness in these patients, possibly the result of the condition being diagnosed early, the relatively sedentary nature of activities performed at HA by acclimatising soldiers and a possible lower resting heart rates in soldiers due to their physical conditioning. The proposed criterion of a heart rate greater than 95 bpm appears to have better sensitivity for diagnosis of HAPE compared to a value of >100 bpm (0.66 vs 0.49), while retaining a high specificity (0.94).

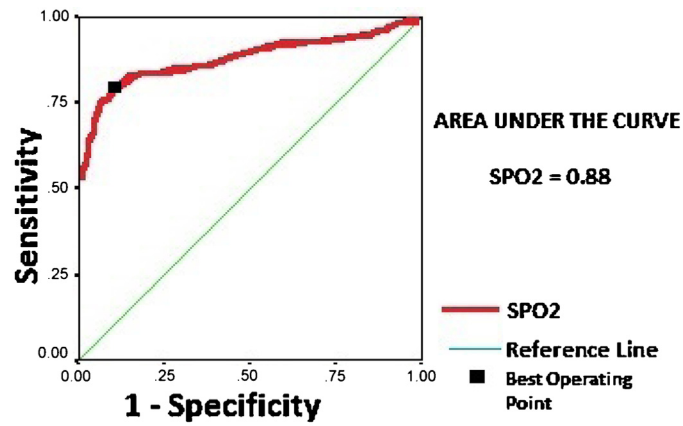

Fig. 5 – ROC curve for pulse oximetry values (SPO_2) showing an area under the curve of 0.88.

Patients of HAPE are known to have high respiratory rates. How high should these rates be to suggest a diagnosis of HAPE? Using the conventional definition of tachyapnea, i.e. a respiratory rate greater than 20 per minute, the sensitivity and specificity of this parameter for diagnosing HAPE are found to be 0.83. However, selecting a value of 21 breaths/min improved the specificity to 0.95 while maintaining a sensitivity of 0.83.

Table 3 – Analysis of heart rate, respiratory rate, and pulse oximetry findings in 235 HAPE patients.

Clinical parameter	Percentage of patients
Heart rate > 100/min	48.9%
$SPO_2 < 88\%$ breathing ambient air	89%
Respiratory rate > 20 breaths/min	83%

Table 4 – Specificity, sensitivity, positive, and negative predictive value calculation for selected cut-off value of heart rate.

	HAPE patients	Controls
Heart rate > 95/min	156	13
Heart rate < 95/min	79	222

Sensitivity = 156/(156 + 79) = 0.66; specificity = 222/(13 + 222) = 0.94; positive predictive value = 156/(156 + 13) = 0.92; negative predictive value = 222/(79 + 222) = 0.74.

Table 5 – Specificity, sensitivity, positive, and negative predictive value calculation for selected cut-off value of respiratory rate.

	HAPE patients	Controls
Respiratory rate > 21/min	194	12
Respiratory rate < 21/min	41	223

Sensitivity = 194/(194 + 41) = 0.83; specificity = 223/(12 + 223) = 0.95; positive predictive value = 194/(194 + 12) = 0.94; negative predictive value = 223/(41 + 223) = 0.84.

Though pulse oximetry at HA has its limitations and may not by itself serve as a diagnostic parameter, the information obtained via pulse oximetry, if carried out with due caution, may supplement the overall clinical picture. In the present series of patients, 85% of the patients had SPO_2 values below 88%, which is the expected SPO_2 value in healthy individuals breathing room air at 3000 m. Pulse oximetry may have utility in monitoring the progress of the condition and efficacy of treatment in HAPE patients.

The ROC analysis of HR, RR and SPO_2 revealed that each of the three parameters is very good as diagnostic parameters for HAPE since their areas under the curve range from 0.86 to 0.88. Areas between 0.8 and 0.9 indicate good tests and between 0.9 and 1.0, excellent.[4] Of the three parameters, SPO_2 appears the best parameter since it had the highest AUC (0.88). The cut-off values suggested from the ROC analysis for these three parameters show very encouraging levels of specificity and sensitivity for their use as parameters for diagnosing HAPE occurring between 2700 m and 3500 m.

Positive and negative predictive values of a diagnostic test are influenced by the prevalence of the disease. As disease prevalence increases in a population, application of the test criteria to that population yields higher positive predictive values and lower negative predictive values. Since the true prevalence of HAPE has been variably reported in literature and may differ among population groups, the values presented in this study should be interpreted keeping this fact in mind and would change, should the disease prevalence be different from that of the present study.

Table 6 – Specificity, sensitivity, positive, and negative predictive value calculation for selected cut-off value of pulse oximetry values (SPO_2).

	HAPE patients	Controls
$SPO_2 < 86\%$	193	16
$SPO_2 > 86\%$	42	219

Sensitivity = 193/(193 + 42) = 0.82; specificity = 219/(16 + 219) = 0.93; positive predictive value = 193/(193 + 16) = 0.92; negative predictive value = 219/(42 + 219) = 0.83.

Table 7 – A comparison of the sensitivity and specificity of existing LL criteria and proposed cut-off values and of heart rate, respiratory rate, and SPO_2 for diagnosing HAPE occurring at 2700–3500 m.

	Heart rate (bpm)		Respiratory rate (breaths/min)		SPO_2 (%)	
	Proposed >95	Existing >100	Proposed >21	Existing >20	Proposed <86%	Existing nil
Sensitivity	0.66 (59.9–72.0)	0.49	0.83 (78.1–87.8)	0.83	0.82 (77.0–86.9)	
Specificity	0.94 (90.9–97.0)	1.0	0.95 (92.2–97.7)	0.83	0.93 (89.7–96.2)	
Positive predictive value[a]	0.92 (88.5–95.4)	1.0	0.94 (90.9–97.0)	0.83	0.92 (88.5–95.4)	
Negative predictive value[a]	0.74 (68.3–79.6)	0.66	0.84 (79.3–88.6)	0.83	0.83 (78.1–87.8)	

A heart rate of greater than 100 bpm and a respiratory rate of greater than 20 breaths/min have been used to define 'tachycardia' and 'tachypnoea' for the existing LL criteria. Values in brackets indicate 95% confidence limits.

[a] Valid for a disease prevalence as evident in the given study population.

Despite best attempts to prevent its occurrence, HAPE does occur in a number of individuals at HA. A prompt diagnosis of the condition is thus essential, to prevent worsening of the condition and possible fatality. The criteria for diagnosing HAPE need to be reliable, objective, yet simple to use in remote locations by non-medical and para-medical personnel at peripheral medical facilities. While the LL criteria are accepted globally for the clinical diagnosis of HAPE, they are fairly general and not altitude specific. It is therefore suggested that in the setting of recent arrival at 2700–3500 m, an individual with symptoms of breathlessness, cough, chest discomfort and headache, with values of HR, RR and SPO_2 as discussed above, is likely to be a patient with HAPE and should be managed accordingly (Table 8). The criteria suggested by this study show better specificity, without compromising the sensitivity, as compared to the existing LL criteria for diagnosing HAPE.

Table 8 – A comparison of the existing Lake Louise criteria for diagnosis of HAPE and the proposed criteria of the present study.

Existing criteria (Lake Louise)	Proposed criteria
History of recent ascent to high altitude	**History of arrival at high altitude (2700–3500 m) within last 5 days**
Any two of the following symptoms	**Symptoms**
• Dyspnoea at rest	• Breathlessness
• Cough	• Cough
• Weakness or decreased exercise performance	• Chest discomfort
• Chest tightness or congestion	• Headache
Any two of the following signs	**Signs**
• Crackles or wheeze in at least one lung field	• Heart rate > 95 beats/min
• Central cyanosis	• Respiratory rate > 21/min
• Tachycardia	• SPO_2 < 86%
• Tachypnoea	

Limitations

This study is based on the retrospective analysis of clinical records and limited by the information contained therein. It is assumed that the documentation of the clinical history and findings in the records are accurate. The clinical criteria suggested for the diagnosis of HAPE by this study need to be validated by applying them prospectively to cases of HAPE being diagnosed and managed at HA and documenting the applicability of these criteria. Once validated, these criteria can be suggested for the field diagnosis of HAPE at altitude between 2700 m and 3500 m.

Conflicts of interest

The authors have none to declare.

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