

Risk Determinants of Acute Mountain Sickness in Trekkers in the Nepali Himalaya: A 36-Year Follow-Up

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Abstract

Introduction: Non-acclimatized trekkers risk developing acute mountain sickness (AMS) at high altitudes. We surveyed trekkers on the Annapurna Circuit in Nepal (peak 5,416 m) to assess AMS incidence and risk factors. Results were compared to 1986, 1998, and 2010 surveys.

Methods: Paper and electronic surveys were distributed to English-speaking trekkers who stopped at the Manang Aid Post (3,500 m). AMS was assessed with the Lake Louise Score (LLS; cutoffs ≥ 3 and ≥ 5) and the Environmental Symptom Questionnaire AMS-C score (cutoff ≥ 0.7).

Results: One hundred and forty-three surveys were returned. Incidence of AMS was 45%, 29%, and 19% (LLS ≥ 3 , LLS ≥ 5 , and AMS-C). AMS incidence was similar to that in 2010 and lower than in 1986 and 1998. In this study, body mass index (BMI) was a significant risk factor for AMS. Seventy-five percent of trekkers had elementary awareness of AMS, compared to 42% in 2010. Trekkers had slower ascent rates and 49% used prophylactic acetazolamide, compared to 44% (2010), 12% (1998), and 1% (1986).

Conclusions: BMI was a predictor of AMS. Awareness of AMS was greater when compared to past studies; however, AMS rates stayed relatively stable between 2010 and the present. Whether awareness reduces the incidence of other potentially lethal altitude illnesses requires further investigation.

Keywords: altitude; Himalaya; mountain sickness; travel medicine

Background

As high-altitude trekking continues to gain popularity around the world, more trekkers face the threat of developing acute mountain sickness (AMS). AMS is a symptom complex found in otherwise healthy non-acclimatized individuals at altitudes above 2,500 m (Luks et al., 2017; Luks et al., 2024). The 1993 Lake Louise consensus originally defined AMS as the onset of a headache with a recent ascent to altitude and presence of one or more of the following symptoms: gastrointestinal symptoms, fatigue and/or weakness, dizziness/lightheadedness, and difficulty sleeping (Roach et al., 1993). More rapid ascent and higher final altitude reached are associated with more severe AMS (Luks et al., 2017). AMS is considered a self-limiting and benign illness; uncomfortable, but not lethal. However, the circumstances that lead to AMS may precede more malignant and life-threatening illnesses such as high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE) (Luks et al., 2017). Because the symptoms of AMS mimic many other conditions, including

exhaustion, dehydration, intoxication, infection, metabolic abnormalities, hypothermia, and more, it may not be recognized in time to prevent more serious illness. Therefore, awareness of the signs and symptoms of AMS is important in preventing other, more serious, altitude illnesses.

One of the most popular trekking routes in Nepal is the Annapurna Circuit, hiked by thousands of tourists every year. The highest point on the circuit is Thorong La, a mountain pass which stands at 5,416 m (17,759 ft) above sea level. At this altitude, AMS is common; early studies in the Himalaya have shown that >50% of trekkers who hiked to altitudes greater than 4,000 m over 5 or more days developed AMS (Hackett and Rennie, 1976), while 84% of those who flew directly to altitudes greater than 3,700 m were affected (Murdoch, 1995). A recent meta-analysis of South American studies reported that 50% of people acutely exposed to high-altitude experienced AMS (Zila-Velasque et al., 2024).

The Himalayan Rescue Association is a volunteer-run nonprofit organization that has operated aid posts in Nepal

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since the 1970s, with the primary goal to reduce casualties in the Himalaya through educational outreach, including free daily lectures about altitude illness, and access to remote medical care. One such post is located in Manang (3,500 m) along the Annapurna Circuit, on the way to the Thorong La. In 2023, the Manang Aid Post saw 376 patients over a 2-month period during the fall trekking season, with 38% being non-Nepali (Timilsina et al., 2024). Since the post's opening in 1981, rates of AMS along the circuit have decreased, as reported by three previous studies along the circuit (Kayser, 1991; Gaillard et al., 2004; McDevitt et al., 2014).

The best evidence-based method for preventing AMS is slow ascent. It is recommended that those traveling to altitudes above 3,000 m should not increase their sleeping elevation by more than 500 m per day and should include an extra rest day for every 1,000 m in altitude gain (Luks et al., 2024). Many pharmacologic and "natural" options for AMS prophylaxis have been studied including oral and inhaled steroids, nonsteroidal anti-inflammatory drugs, calcium channel blockers such as nifedipine, carbonic anhydrase inhibitors, coca leaves, and ginkgo (Nieto Estrada et al., 2017; Luks et al., 2024). For acetazolamide, a carbonic anhydrase inhibitor, there is strong evidence for AMS prophylaxis (Nieto Estrada et al., 2017).

Along with slower ascent, past studies have suggested that greater understanding of AMS and other altitude illnesses may have contributed to a decrease in rates of AMS. In 1986, Kayser found that 80% of trekkers who crossed Thorong La had elementary awareness of AMS, and trekkers spent an average of 10.5 days between 2,500 m and the highest point on the trek, 5,416 m. In that year, 43% met criteria for having AMS using the Environmental Symptoms Questionnaire III (ESQ-III) (Kayser, 1991). Twelve years later, in 1998, Gaillard et al. repeated the study and found that 95% of trekkers had elementary awareness of AMS. Trekkers in 1998 spent 10.8 days between 2,500 m and 5,416 m, and 29% met criteria for having AMS using the ESQ-III (Gaillard et al., 2004). A third study, conducted in 2010, found that the incidence of AMS had further decreased to 22% using the ESQ-III, and the average time taken to ascend to Thorong La from Manang (3,500 m) had increased from 2 to 3 days, despite lower rates of elementary awareness of AMS (42%) (McDevitt et al., 2014). We conducted another study testing the hypothesis that AMS incidence would have further decreased from the 1986, 1998, and 2010 studies of the same circuit (Kayser, 1991; Gaillard et al., 2004; McDevitt et al., 2014).

Methods

This was a prospective cohort observational study. Data collection was conducted in Manang (3,500 m) between October 2022 and May 2023. During the 2022 fall and 2023 spring trekking seasons, volunteer physicians gave free daily lectures at the Manang Aid Post on how to prevent, identify, and treat altitude illnesses. Travelers, guides, and porters attending the lecture were given access to a survey (either paper or electronic) and instructed to fill it out on the evening after crossing Thorong La. Exclusion criteria included age <18 years, no English literacy, and pregnancy. This study was approved by the University of British Columbia Behavioural Research Ethics Board (H20-01426-A003) and the

Nepal Health Research Council (Registration No. 374/2022). All participants were free to leave the study at any time.

The first part of the survey was designed to gather demographic and health information; assess preparedness for the trek, including prophylactic medication use; and assess basic knowledge of AMS. As in the three previous surveys, participants had attended a lecture by the time they filled out the form; they were asked to fill out the form without the knowledge they had gained from the lecture. Trekkers were given either a paper survey or a business card with a quick response (QR) code that linked to a Google Form electronic survey, depending on individual preference. Based on previous studies from this region (Kayser, 1991; Gaillard et al., 2004; McDevitt et al., 2014), if trekkers identified two AMS symptoms and listed descent as a treatment, we classified them as having elementary awareness of AMS. Trekkers were asked to fill out this section of the form without the knowledge they might have gained from the lectures at the Manang Aid Post.

The second part consisted of two different scores that are used to indicate the presence or absence of AMS. The first, the 1993 Lake Louise Score (LLS), consisted of five symptoms (headache, gastrointestinal upset, fatigue and/or weakness, dizziness or light-headedness, and difficulty sleeping), self-rated from 0 (absent) to 3 (severe, incapacitating) (Roach et al., 1993). The maximum possible score was 15. In the presence of a headache, a total score ≥ 3 indicates AMS (Roach et al., 1993). In 2018, the original authors of the LLS convened to update the score. The symptom of "difficulty sleeping" was removed from the score, suggesting that difficulty sleeping at altitude is more likely a function of hypoxia and less related to AMS (Roach et al., 2018). Due to the widespread use of the 1993 LLS, including in the three previous iterations of the present study, we have elected to calculate both the old and new LLS scores for our participants. We also used the cutoffs of ≥ 5 for reasons of comparison to the AMS-C and previous studies, which used the AMS-C as well as LLS with ≥ 3 and ≥ 5 cutoffs.

The second score was the ESQ-III, which has 67 symptoms that are self-rated from 0 (absent) to 5 (severe) (Sampson et al., 1983). A shortened version with only 11 questions was validated for the assessment of AMS (Beidleman et al., 2007). As in the prior studies, we had our participants answer all 67 questions. We then used the 11 questions from the short version and multiplied the scores by established factorial weights to produce a final score called the cerebral AMS (AMS-C). The threshold for AMS-C is ≥ 0.7 (Sampson et al., 1983).

Using SPSS (IBM SPSS Statistics for Mac OS, Version 29.0.2.0; IBM Corp., Armonk, NY, USA), we analyzed demographic features, data about preparedness for the trek, and responses to the LLS and ESQ-III questionnaires. We calculated descriptive statistics including means and standard deviations for demographic features. We then applied logistic regression. Absence or presence of AMS, according to score used, was the binary dependent variable (0 = absence, 1 = presence). Independent variables were dichotomized, and the effect of risk factors was measured using stepwise multivariate logistic regression. Given that we measured five independent variables (age, sex, body mass index [BMI], smoking status, and AMS awareness), our sample size of 143 was not sufficiently powered to be reproducible.

Results

The Annapurna Conservation Area Project sold 10,936 and 13,739 permits to trekkers in the 2022 fall and 2023 spring seasons, respectively. Of those trekkers, 472 (fall 2022) and 413 (spring 2023) attended AMS lectures at the Manang Aid Post. Five hundred paper surveys were distributed, and 143 total surveys (paper and electronic) were returned and analyzed.

The age range of participants was 20–80 years of age, with a mean of 36.9 ± 12.7 years. Forty-four percent were men. Most trekkers were from the United Kingdom ($n = 33$), United States ($n = 22$), and Germany ($n = 14$) (Fig. 1). Overall, 51% were from primarily English-speaking countries. Smokers made up 7.7% of trekkers. BMI ranged from 16 to 34 kg/m^2 , with a mean of $23 \pm 2 \text{ kg/m}^2$. According to the World Health Organization classification of nutritional status (Purnell, 2023), 2% of trekkers were underweight (BMI <18.5), 74% were of normal weight (18.5–24.9), 21% were pre-obese (25.0–29.9), and 2% were obese class I (30.0–34.9). None were categorized as either obese class II or III (>35.0).

Just under half of participants (49%) reported using acetazolamide during the trek. Of those who used acetazolamide, 70% used a dose of 125 mg twice daily (BID). Those who did not use the 125 mg BID dose used a range of other doses including 250 mg once daily, 125 mg once daily, and 62.5 mg one or two times daily. Two participants used acetazolamide for only 1 day while crossing Thorong La.

Based on the definition outlined for elementary awareness of AMS, 75% of our population qualified. The number of days between Manang and Thorong La ranged from 3 to 6 days, with an average of 3.5 days.

The incidence of AMS was 45%, 29%, and 19% (LLS 1993 ≥ 3 , LLS 1993 ≥ 5 , and AMS-C, respectively). As expected, the different thresholds produced very different results. A previous study (Wagner et al., 2012) showed that the ≥ 5 threshold produces results that are more congruent with the ESQ-III, despite ≥ 3 being the accepted definition of AMS. When using the 2018 LLS, AMS incidence was 39% and 20% for ≥ 3 and ≥ 5 , respectively. AMS scores were similar to those in 2010 using the ESQ-III and still lower than in 1986 and 1998 (Fig. 2). Using the 1993 LLS ≥ 3 , only BMI

(odds ratio [OR] = 1.217; 95% confidence interval [CI]: 1.06–1.397) was a significant predictor for AMS. Using the 1993 LLS ≥ 5 , female sex (OR = 2.959; 95% CI: 1.334–6.563) and BMI (OR = 1.212, 95% CI: 1.053–1.395) were significant predictors for AMS (Table 1). Using the ESQ-III, none of age, sex, smoking status, BMI, or elementary AMS awareness were significant predictors (Table 1). Use of acetazolamide was not a significant predictor by any score.

Discussion

We assessed the incidence of AMS among trekkers who crossed Thorong La in the spring of 2022 and fall of 2023, and compared the findings with prior studies from 1986, 1998, and 2010. Additionally, we sought to evaluate risk factors for developing AMS, awareness of AMS, and trekkers' efforts to prevent AMS. Our main findings in comparison to those of the earlier studies are a further reduction in ascent rate, increased prophylaxis with acetazolamide, but no further decrease in AMS incidence as compared to the most recent study.

Incidence of AMS

The incidence of AMS in our study, measured using different scores and cutoffs, ranged from 19% to 45%. When using the 1993 LLS with a cutoff of ≥ 3 , which is the validated threshold for diagnosis of AMS, the AMS incidence was 45%. The incidence was 29% when using a stricter but not validated cutoff of ≥ 5 . Using the 2018 updated LLS (without the sleep item), incidence at a cutoff of ≥ 5 (20%) matched the ESQ-III incidence of 19%. This corroborates past findings that ESQ-III ≥ 0.7 and LLS ≥ 5 cutoffs yield more similar incidence rates, although past studies compared the ESQ-III with the 1993 LLS (Dellasanta et al., 2007; Wagner et al., 2012).

The observed rates using the ESQ-III were similar to those from the 2010 study but remained lower than the AMS rates reported in 1986 and 1998. These findings support the hypothesis that AMS incidence has continued to decline over time but does not support prior findings that increased awareness and acetazolamide use have contributed to this decline, as neither was associated with decreased risk of AMS. This

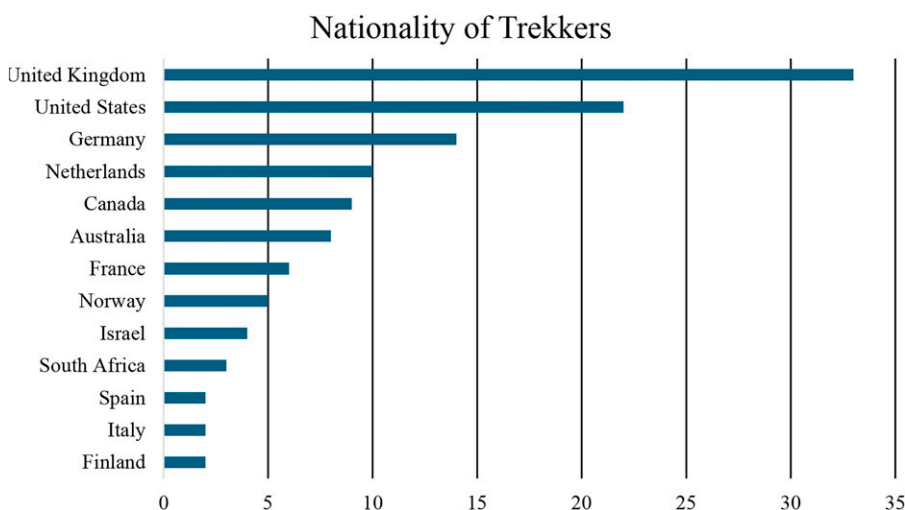
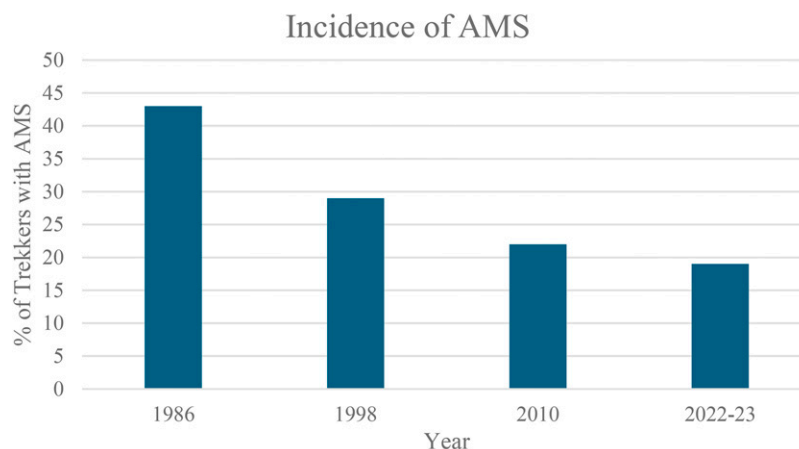


FIG. 1. Nationality of trekkers. Note: There was one trekker each from the following countries: Austria, Belgium, Czechia, Estonia, the Philippines, Hungary, India, Lithuania, Mexico, Poland, Switzerland, Ukraine/Romania (self-reported), and Venezuela.

FIG. 2. Change in incidence of AMS as compared to prior studies (AMS-C ≥ 0.7). AMS, acute mountain sickness; AMS-C, cerebral AMS.



is potentially due to a ceiling effect, whereby the incidence of AMS has plateaued.

Factors associated with AMS

BMI was a significant predictor of AMS as measured using the 1993 LLS (≥ 3 and ≥ 5 cutoffs). This is in accordance with prior research suggesting that individuals with higher BMI may have increased risk of altitude illnesses; potential mechanisms include relative hypoventilation and increased absolute and relative levels of exertion during trekking, especially on climbs (Kayser, 1991; McDevitt et al., 2014; Kayser and Verges, 2021). Female sex was also a significant predictor when using the LLS ≥ 5 cutoff. Whether this implies that females may be more susceptible to AMS or score their symptoms differently from males is unknown. The association between sex and AMS was not observed when using the ESQ-III, calling further into question the impact of sex on AMS risk. Our results corroborate those of studies in other regions, which have found either weak or indistinct associations between female sex and AMS risk (Berger et al., 2023).

Age, smoking status, and basic AMS awareness were not found to be significant predictors of AMS. The lack of association with age is congruent with prior but not all studies (Kayser, 1991). The lack of association with smoking differs from previous studies. However, our study had such a small sample of smokers (7.7%, only 11 trekkers) that this may not be a generalizable finding.

Ascent rate between Manang and Thorong La was slower as compared to earlier studies. We suspect that the main reason is that lodging options along the route have increased in number and in comfort over the past 30 years. Having access to more lodges likely caused trekkers to plan more overnights between Manang and the Thorong La. The Manang Aid Post lectures also strongly recommend a slow ascent, taking at least 2 days. As our participants were lecture attendees, they were possibly influenced by this advice.

It was notable that in participants traveling in groups, symptoms tended to appear in clusters. Participants were presumed to be traveling in a group if either (a) they traveled during the same dates using the same tour company or (b) they traveled during the same dates, had the same party size, and followed the same route. The authors noted that certain entire groups rated themselves as having no symptoms at all during the trek, while other entire groups reported low-level (1 or 2 on the ESQ-III) severity of a wide variety of symptoms. There may be an effect of differences in individual groups' attitude toward trekking: while some groups may consider fatigue unremarkable and not worth reporting during a multiday high-altitude hike, other groups may have discussed their fatigue more and therefore considered it a more notable part of their experience. Another effect of group travel is the low likelihood that all group members have the same level of fitness; if some group members are fitter and would prefer to trek faster, other members may be pushed along and develop more symptoms as a result.

TABLE 1. PREDICTORS OF ACUTE MOUNTAIN SICKNESS

Variable	LLS ≥ 3			LLS ≥ 5			ESQ-III		
	OR	Lower 95% CI	Upper 95% CI	OR	Lower 95% CI	Upper 95% CI	OR	Lower 95% CI	Upper 95% CI
Age	0.971	0.941	1.003	0.994	0.961	1.028	0.964	0.922	1.008
Female	1.833	0.927	3.626	2.959	1.334	6.563	1.346	0.564	3.214
Smoking	0.802	0.216	2.978	1.038	0.255	4.226	0.428	0.052	3.499
BMI	1.217	1.060	1.397	1.212	1.053	1.395	1.098	0.979	1.232
AMS awareness	0.962	0.446	2.075	0.873	0.381	2.001	0.567	0.227	1.415

Bolded numbers are those in which the 95% CI does not include the null value (1).

AMS, acute mountain sickness; BMI, body mass index; CI, confidence interval; ESQ-III, Environmental Symptoms Questionnaire III; LLS, Lake Louise Score (1993 version); OR, odds ratio.

AMS awareness and preparedness

A key finding of previous studies was that understanding of AMS was associated with lower risk of developing the illness; our study did not find such an association. We found that 75% of trekkers in the fall 2022 and spring 2023 seasons demonstrated elementary awareness of AMS by identifying at least two symptoms and listing descent as a treatment. This was less than the 95% reported in 1998, but more than the 43% reported in 2010. Our participants filled in their survey after attending lectures at the Manang Aid Post, unlike the 2010 participants, which may explain the difference over only 12 years. In our study, the internet was the most-used resource for learning about AMS, with 45% of participants listing it as a source of their knowledge of AMS. The next most common sources of information were “other” (29%) and personal experience (24%). Notably, trekking guidebooks were barely used by our population, despite being the most common source of information about AMS in the 1998 study (Gaillard et al., 2004). Of the participants who checked “other” as a source of information, the majority listed either family members’ experiences or formal education (e.g., medical school) as their primary sources.

Self-medication

Nearly half (49%) of trekkers reported using acetazolamide for AMS prevention, with 70% of acetazolamide users taking 125 mg twice a day. Although this dosing regimen is the current standard of care for AMS prophylaxis (Luks et al., 2024), a 2019 study showed that taking a reduced dose of 62.5 mg twice a day was noninferior for preventing AMS (McIntosh et al., 2019). Not using acetazolamide was not predictive of AMS, regardless of the score used. We would propose that the ease of use of acetazolamide in preventing AMS contributes to its popularity, while other prevention methods (e.g., not climbing too quickly, taking rest days) involve a degree of restraint. This may appeal to trekkers who are keen to take an active role in maintaining good health or who choose a faster-than-recommended ascent rate.

Limitations and future directions

Our study included only 143 participants, lending it less statistical power than the previous three studies, which each had around 350 participants. Because we reached <1% of visitors to the region, results may not be generalizable to all trekkers of the Annapurna Circuit. Selection bias may have also played a role in the responses; trekkers who experienced AMS may have been more likely to complete the survey; alternatively, the study may have been more popular among trekkers who took the threat of AMS seriously and wanted to test their prevention efforts. Certainly, all participants who were recruited into the study demonstrated a desire to learn about AMS, as they were recruited from lectures at the Manang Aid Post. Although the LLS and ESQ offer objective scores, diagnosing AMS is inherently subjective, which contributes to the high variability in responses. The sole language of the study being English may have also excluded useful data and limited our ability to extrapolate the results.

In contrast to the previous studies, Manang and several points on the Annapurna Circuit now have reliable internet access. Future studies should focus on electronic submission

of surveys, which was popular in our cohort. QR codes provide an easy, portable method for directing participants to surveys. Future studies could also measure the number of QR codes scanned compared with the number of surveys filled; this could give an estimate of attrition.

Future research should include a larger sample. Researchers could consider offering a small reward to those who complete the survey. Future researchers could also consider incorporating objective measurements; although none have been validated for measuring AMS, an approach combining qualitative and quantitative measures could have considerable value. These could help corroborate self-reported symptom data. The recently published STrengthening Altitude Knowledge statements of minimal knowledge for lay persons traveling to high altitude can be used in future studies to provide direction and objectivity when examining preparedness for high-altitude activities (Berendsen et al., 2022).

Conclusion

Our study contributes to the evidence surrounding AMS on the Annapurna Circuit. AMS remains a common issue, with nearly half of trekkers in our study affected when using the more sensitive score. Increased awareness of AMS compared to previous studies was not accompanied by lower rates of AMS. Future studies should examine whether awareness of altitude illnesses reduces the risk of potentially life-threatening HACE and HAPE.

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Authors’ Contributions

H.C.: Formal analysis, writing—original draft, and writing—review and editing. M.M. and S.D.: Methodology, visualization, writing—original draft, and writing—review and editing. B.K.: Study design, data curation, formal analysis, methodology, resources, supervision, visualization, writing—original draft, and writing—review and editing. C.K.: Investigation, resources, visualization, writing—original draft, and writing—review and editing. A.H.: Data curation, formal analysis, investigation, methodology, project administration, resources, supervision, visualization, writing—original draft, and writing—review and editing.

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Supplementary Material

Supplementary Data

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