Acute Mountain Sickness in the Pyrenees: an observational cross-sectional study

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Research

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Abstract

Background

The prevalence of acute mountain sickness (AMS) ranges between 15% and 80% depending on the absolute altitude reached, speed of ascent, and individual susceptibility. However, there is a lack of information regarding AMS at moderate to high altitudes (2,500-3,500 m) and, even less, in the Pyrenees. Our aim is to determine the prevalence and risk factor of AMS in the Pyrenees.

Methods

A cross-sectional study including mountaineers who climbed a mountain with a height greater than 2,500 m in the Pyrenees region during July and August 2019. Sociodemographic data, medical history and activity information were collected using a questionnaire. The diagnosis of AMS was based on the 2018 modified Lake Louise Score. A logistic regression analysis was performed to examine the association of different variables (risk factors) and AMS.

Results

From 437 participants, 117 met diagnostic criteria of AMS, establishing a prevalence of 26.7% (95% confidence interval: 22.6%-30.9%). Individuals affected by AMS had mild (88%) or moderate (12%) affection. The most common symptoms (in addition to headache which is mandatory for AMS diagnosis) were fatigue or weakness, gastrointestinal symptoms and dizziness. In an adjusted multivariate analysis, heavy perceived exertion, bad physical condition, nonsteroidal anti-inflammatory drugs use and previous history of altitude illness were independent risk factors for developing AMS.

Conclusions

One fourth of climbers in the Pyrenees experienced mild or moderate AMS. Previous history of AMS, nonsteroidal anti-inflammatory drugs use and other modifiable risk factors such as physical exertion and physical condition were strong and independent predictors of AMS. These findings suggest that educational/informational programs for individuals planning to climb to moderate-high altitudes in the Pyrenees may contribute to prevent AMS.

Background

High-altitude illness (HAI) is an encompassing term for the range of pathology that the unacclimatised individual can develop at increased altitude. This includes acute mountain sickness (AMS), high-altitude cerebral edema and high-altitude pulmonary edema [1].
AMS is by far the most common HAI, arises after at least 4–6 hours spent at an altitude above 2,000–2,500 m and its reported prevalence ranges from 8–25% at 2,500–3,000 m and from 40–60% at 4,500 m [1]. The prevalence of AMS varies widely according to different ascent profiles. Studies conducted in Nepal, Colorado, Kilimanjaro, and the Alps show a prevalence of AMS ranging from 9–58%, with a higher prevalence at higher altitudes [2].

On the other hand, AMS has been associated with a number of potential risk factors including: age, gender, genetics, residence at an altitude below 800 m, pre-existing medical conditions, physical condition and intensity of exercise, rate of ascent and reached altitude, lack of acclimatization and previous history of HAI [3, 4].

There is a risk of AMS in the Pyrenees, but to our knowledge, no studies have determined the prevalence and risk factors of AMS in this area. For this reason, our aim is to determine the prevalence and risk factors for AMS in mountaineers exposed to moderate-high altitude in the Pyrenees region.

**Methods**

**Study design**

This is an observational cross-sectional study to determine prevalence.

**Study setting, study population and data collection**

The study population includes mountaineers who climbed a mountain with a height greater than 2,500 m in the Pyrenees (the maximum altitude in this area is 3,404 m at the Aneto summit) during July and August 2019.

Data were collected using a questionnaire at the Renclusa refuge (Benasque Valley, Huesca, Spain) at 2,138 m, where most of the mountaineers who climb mountains over 3,000 meters high pass through. During the study period all mountaineers passing through the refuge were asked to voluntarily participate in our study by answering the questionnaire. The questionnaire could be answered in two different ways, in person and online. The online form consisted of a link or QR code that was given to the mountaineers once the mountain activity was finished allowing to answer it in a quiet place and once the symptoms (if present) were resolved. The estimated time to answer the questionnaire was about 3 minutes and no personal data was collected to ensure data protection. The privacy and the safety of this online form has been always ensured. Once the questionnaire was completed all participants received a tryptic with more information about high-altitude diseases.

**Study variables**

The questionnaire included 28 questions with the following variables: sociodemographic (age, gender, height, weight, place of residence and sea level situation), smoking habits, medical conditions (including diabetes, cholesterol, hypertension, chronic obstructive pulmonary disease, obstructive sleep apnea...
syndrome (OSAS), cardiovascular diseases, asthma, migraine and anemia), drug consumption (including nonsteroidal anti-inflammatory drugs [NSAIDs] in the previous 48 hours), physical condition (bad / acceptable / good / very good), training habits (hours per week), recent (previous 3 days) activity at more than 2,500 m high, spending the previous night at the refuge (or at height) and previous history of HAI. We also collected the following variables related to the mountain activity: maximum altitude reached, time of ascension and altitude difference, physical exertion (normal / moderate / severe), sport or discipline (mountaineering, alpinism, trail-running) and liquid consumption during the activity. Finally, the questionnaire included five questions about four different AMS-related symptoms (experienced during the activity) to assess the diagnosis of AMS based on the Lake Louise Score (LLS) (see below).

**Diagnosis of acute mountain sickness**

For the diagnosis of AMS we used the 2018 modified LLS because is a well-accepted standard for AMS diagnosis. The LLS can be self-administrated and includes the following items: headache, nausea/vomiting, fatigue, and dizziness/light-headedness. For a positive AMS definition, it is mandatory to have a headache score of at least one point, and a total score of at least three points (Table 1) [5].
### Table 1
Lake Louise Score 2018*

| Symptom                     | Score |
|-----------------------------|-------|
| **Headache**                |       |
| 0. None at all              |       |
| 1. A mild headache          |       |
| 2. Moderate headache        |       |
| 3. Severe headache, incapacitating |   |
| **Gastrointestinal symptoms** |   |
| 0. Good appetite            |       |
| 1. Poor appetite or nausea  |       |
| 2. Moderate nausea or vomiting |     |
| 3. Severe nausea and vomiting, incapacitating | |
| **Fatigue and/or weakness** |       |
| 0. Not tired or weak        |       |
| 1. Mild fatigue/weakness    |       |
| 2. Moderate fatigue/weakness|       |
| 3. Severe fatigue/weakness, incapacitating | |
| **Dizziness/light-headedness** |   |
| 0. No dizziness/ light-headedness | |
| 1. Mild dizziness/weakness  |       |
| 2. Moderate dizziness/ light-headedness | |
| 3. Severe dizziness/ light-headedness, incapacitating | |
| **Acute mountain sickness Clinical Functional Score** | |
| 0. Not at all               |       |
| 1. Symptoms present, but did no force any change in activity or itinerary | |
| 2. My symptoms forced me to stop the ascent or to go down on my own power | |
| 3. Had to be evacuated to a lower altitude | |

*The Lake Louise Score for an individual is the sum of the score for the four symptoms (headache, nausea/vomiting, fatigue, and dizziness/light-headedness). For a positive AMS definition, it is mandatory to have a headache score of at least one point, and a total score of at least three points. The severity of AMS can be classified as follows: mild (3–5 points), moderate (6–9 points) and severe (10–12 points).
Altitude ranges definition

We defined altitude ranges according to the terminology recommended by an international expert panel: low altitude (500-2,000 m), moderate altitude (2,000–3,000 m), high altitude (3,000–5,500 m) and extreme altitude (> 5,500 m) [6].

Statistical analysis

Sample size: based on previous studies we estimated that a sample of 400–500 subjects would be enough to estimate with a 95% confidence and a precision of ± 4 per cent units, a population percentage considered to be around 25–30% [7, 8].

Descriptive analysis: Qualitative or categorical variables are expressed as number of patients and percentages and quantitative variables as median and interquartile range [IQR]. The Kolmogorov–Smirnov test was used to determine whether quantitative variables were normally distributed.

Bivariate analyses: The Chi-square test ($\chi^2$) has been used to compare qualitative variables (when the expected number of cases in any of the cells was lower than 5, the Fisher exact test was used) and the Student’s T test to compare normally distributed quantitative variables (the Mann-Whitney U test for the non-normally distributed ones). Multivariate analyses: A binary logistic regression analysis has been performed to assess the association between different predictor variables (independent variables) with AMS (dependent and dichotomous variable). This analysis has been adjusted for variables that are statistically significant ($p < 0.05$) in the bivariate analysis and those risk/protective factors previously described in the literature. We applied manual and automatic procedures (including backward and forward stepwise).

Statistical significance was set at 0.05. Analyses were performed with the software Statistical Package for Social Sciences version 20.0 (SPSS, Inc., Chicago, Illinois, USA).

Ethical Aspects

Before answering the questionnaire, all participants read and accepted a study information form and informed consent. To maintain the confidentiality and data security, no personal data were collected (including names, postcodes, addresses or birth dates). Data security was ensured with a locked network only accessible for the principal investigator of the study. According to the national and international laws regarding autonomy, the study is governed by the Organic Law (15-1999 December 13th ) for personal data protection. A local review board from Universitat de Girona approved the study.

Results

Four hundred and forty-seven individuals participated in the study (only 9 mountaineers refused to participate because they were not feeling well (two cases) or they did not have time (seven cases)). After reviewing the questionnaires, 10 participants were excluded for the following reason: 3 answered the
questionnaire inappropriately, 4 had climbed to heights greater than 3,404 m (it is not possible to climb these heights in the Pyrenees as the maximum altitude is 3,404 m at the Aneto summit) and 3 had climbed to heights less than 2,500 m. The final sample size included 437 individuals (124 filled out the questionnaire in person and 313 on-line).

Baseline characteristics are shown in Table 2 and variables related with the mountain activity in Table 3. Most participants were young males with normal body-mass index, with a good health status (low proportion of smokers and comorbidities) and good physical condition. Almost 90% lived below 800 meters from sea level and 24% had previous history of HAI. More than one fourth of participants had done a recent activity (previous 3 days) or slept above 2,500 meters. All the participants reached moderate-high altitudes in a median time of 5 hours, describing a moderate physical exertion in most cases.
| Variable          | Total          | No AMS         | AMS            | P value |
|-------------------|----------------|----------------|----------------|---------|
| Number            | 437            | 320            | 117            | -       |
| Male gender       | 314 (71.9%)    | 236 (73.8%)    | 76 (65.0%)     | 0.07    |
| Age (years)       | 34 [18]        | 34 [17]        | 33 [19]        | 0.70    |
| BMI (kg/m²)       | 22.8 [3.2]     | 22.8 [3.1]     | 22.9 [3.4]     | 0.92    |
| BMI category      | 13 (3%)        | -              | -              | -       |
| Low weight        | 348 (79.6%)    |                |                |         |
| Normal            | 69 (15.8%)     |                |                |         |
| Overweight        | 7 (1.6%)       |                |                |         |
| Smoking habits    | 307 (70.3)     | -              | -              | -       |
| No Smoker         | 85 (19.4)      | -              | -              | -       |
| Former smoker     | 45 (10.3)      | 32 (10.0%)     | 13 (11.1%)     | 0.94    |
| Smoker            |                |                |                |         |
| Comorbidities     | 1 (0.2%)       | 1 (0.3%)       | 0              | 0.55    |
| Diabetes          | 16 (3.7%)      | 12 (3.8%)      | 4 (3.4%)       | 0.87    |
| Cholesterol       | 11 (2.5%)      | 7 (2.2%)       | 4 (3.4%)       | 0.47    |
| Hypertension      | 3 (0.7%)       | 1 (0.3%)       | 2 (1.7%)       | 0.12    |
| Cardiovascular    | 12 (2.7%)      | 9 (2.8%)       | 3 (2.6%)       | 0.89    |
| Asthma            | 6 (1.4%)       | 2 (0.6%)       | 4 (3.4%)       | 0.03    |
| OSAS              | 0              | 0              | 0              | 0.91    |
| COPD              | 7 (1.6%)       | 5 (1.6%)       | 2 (1.7%)       | 0.49    |
| Migraine          | 8 (1.8%)       | 5 (1.6%)       | 3 (2.6%)       | 0.40    |
| Anemia            |                |                |                |         |

Quantitative variables are expressed as median [interquartile range]. Categorical variables are expressed as number and percentage. **Abbreviations**: AMS: acute mountain sickness; BMI: body mass index; NSAIDs: nonsteroidal anti-inflammatory drugs; OSAS: obstructive sleep apnea syndrome; COPD: chronic obstructive pulmonary disease; HAI: high altitude illness
| Variable                  | Total     | No AMS     | AMS        | P value |
|--------------------------|-----------|------------|------------|---------|
| Medication               | 47 (10.8%)| 32 (10.0%) | 15 (12.8%) | 0.40    |
| Drugs                    | 11 (2.5%) | 7 (2.2%)   | 4 (3.4%)   | 0.48    |
| Herbal medicine          | 60 (13.7%)| 36 (11.2%) | 24 (20.5%) | 0.01    |
| NSAIDs < 48 hours        |           |            |            |         |
| Residence below 800 m    | 393 (89.9%)| 283 (88.4%)| 110 (94.0%)| 0.09    |
| Previous HAI             | 105 (24%) | 65 (20.3%) | 40 (34.2%) | 0.003   |
| Physical activity (h/week)| 7 [5]     | 7.5 [5.0]  | 6.0 [4.0]  | < 0.001 |
| Physical condition       | 6 (1.4)   | 4 (1.2%)   | 2 (1.7%)   | 0.02    |
| Bad                      | 82 (18.8%)| 49 (15.3%) | 33 (28.2%) |         |
| Acceptable               | 268 (61.3%)| 203 (63.4%)| 65 (55.6%) |         |
| Good                     | 81 (18.5%)| 64 (20.0%) | 17 (14.5%) |         |
| Very good                |           |            |            |         |

Quantitative variables are expressed as median [interquartile range]. Categorical variables are expressed as number and percentage. **Abbreviations**: AMS: acute mountain sickness; BMI: body mass index; NSAIDs: nonsteroidal anti-inflammatory drugs; OSAS: obstructive sleep apnea syndrome; COPD: chronic obstructive pulmonary disease; HAI: high altitude illness.
Table 3
Mountain activity and univariate analysis risk for acute mountain sickness

| Variable                                         | Total  | No AMS | AMS   | P value |
|--------------------------------------------------|--------|--------|-------|---------|
| Number                                           | 437    | 320    | 117   | -       |
| Recent (previous 3 days) activity > 2,500 m       | 148 (33.9%) | 116 (36.2) | 32 (27.4) | 0.08    |
| Slept > 2,500 m                                   | 116 (26.5%) | 83 (25.9) | 33 (28.2) | 0.64    |
| Maximum reached altitude (meters)                 | 3,404 [263] | 3,404 [294] | 3,404 [260] | 0.10    |
| Mean                                             | 3,275  | 3,264  | 3,294 |         |
| Was altitude > 3000 meters reached? (yes answer)  | 387 (88.6%) | 281 (87.8%) | 106 (90.6%) | 0.42    |
| Ascension time (hours)                            | 5 [9]  | 5.0 [1.0] | 5.0 [2.0] | **0.03** |
| Mean                                             | 4.7    | 4.64   | 4.87  |         |
| Altitude difference (meters)³                   | 1,500 [300] | 1,500 [313] | 1,500 [290] | 0.08    |
| Mean                                             | 1,516  | 1,503  | 1,553 |         |
| Ascension rate (meters/hour)                      | 300 [110] | 320 [95] | 316 [108] | 0.54    |
| Mean                                             | 335    | 337    | 329   |         |
| Physical exertion                                 | 99 (22.7%) | 84 (26.2%) | 15 (12.8%) | < **0.001** |
| Normal                                           | 237 (54.2%) | 183 (57.2%) | 54 (46.2%) |         |
| Moderate                                         | 101 (23.1%) | 53 (16.6%) | 48 (41.0%) |         |
| Intense                                          |        |        |       |         |
| Discipline b                                     | 284 (65%) | 206 (64.4%) | 78 (66.7%) | 0.74    |
| Mountaineering                                   | 48 (11%) | 36 (11.2%) | 12 (10.3%) |         |
| Running                                          | 102 (23.3%) | 75 (23.4%) | 27 (23.1%) |         |
| Alpinism                                         |        |        |       |         |
| Fluid intake (liters)                             | 2 [1]  | 2 [1]  | 2 [1] | 0.57    |

Quantitative variables are expressed as median [interquartile range] and mean when specified. Categorical variables are expressed as number and percentage. ³Altitude difference means difference in altitude from the starting point to the highest altitude. ⁴Runners had a significantly lower ascension time and higher ascension rate in comparison with other disciplines, but no significant differences regarding maximum altitude were found.
The prevalence of AMS and the severity of symptoms are detailed in Table 4. According to the 2018 LLS, 117 participants met diagnostic criteria of AMS, establishing a prevalence of 26.7% (95% confidence interval: 22.7–30.9%). The prevalence of AMS in online and in person responders was 26.6% and 29.9%, respectively (this difference did not reach statistical significance). All cases were mild (88%) or moderate (12%) and the most frequent (and severe) symptom (apart from headache, which is mandatory for diagnosis) was fatigue (98.3%) followed by gastrointestinal symptoms (59%) and dizziness (47%).

Table 4
Prevalence and severity of symptoms of acute mountain sickness

| AMS    | Number | Percentage |
|--------|--------|------------|
| Total  | 117    | 26.7%      |
| Mild   | 103    | 88%        |
| Moderate | 14    | 12%        |
| Severe | 0      | 0%         |

| Symptoms | Not at all | Mild   | Moderate | Severe | Total |
|----------|------------|--------|----------|--------|-------|
| Headache | 0          | 88 (75.2%) | 25 (21.4%) | 4 (3.4%) | 117 (100%) |
| Gastrointestinal | 48 (41%) | 65 (94.2%) | 3 (4.3%) | 1 (1.4%) | 69 (59%) |
| Fatigue  | 2 (1.7%)   | 57 (49.6%) | 48 (41.7%) | 10 (8.7%) | 115 (98.3%) |
| Dizziness| 62 (53%)   | 45 (81.8%) | 9 (16.4%) | 1 (1.8%) | 55 (47%) |

*According to the 2018 Lake Louis score. Results are expressed as number and percentage.

Abbreviations: AMS: acute mountain sickness.

In the univariate analysis the following variables were associated with an increased risk of AMS (Tables 2 and 3): history of OSAS, the use of NSAIDs in the previous 48 hours, previous history of HAI, less physical activity per week, worse physical condition, slower ascension time and intense physical exertion during the activity. We also observed a greater risk of AMS in women, residents below 800 meters from sea level and not performing a recent activity above 2,500 meters, but these differences didn’t reach statistical significance.

We found no differences in AMS with respect to the maximum altitude reached, but those who climbed above 3000 meters suffered more intense symptoms (mild AMS in 90.6%) compared to those who climbed below 3000 meters (mild AMS in 63.6%), being these differences statistically significant (p = 0.009)

The individuals with AMS who took NSAIDs in the previous 48 hours had higher scores in the LLS compared to those who did not take them (median [IQR]: 4.5 [2.5] and 4.0 [1.0], respectively [p value
In addition, the intensity of AMS was different according to NSAIDs consumption; AMS was moderate in 25% of those who took NSAIDs and in 8.6% of those who did not take them (p value 0.02). There were no differences in the proportion of patients who took NSAIDs based on whether they had previous history of AMS (14% vs 14%, p value 0.85). Thus, NSAIDs use was not associated with the history of AMS.

Table 5 summarizes the univariate and multivariate analysis risk factors for AMS. In the multivariate adjusted analysis the following variables remained as risk factors for developing AMS: physical exertion during ascent (OR 2.24; 95% CI 1.22–4.12), use of NSAIDs in the previous 48 hours (OR 1.95; 95% CI 1.09–3.50) and previous history of HAI (OR 1.98; 95% CI 1.22–3.21). On the other hand, having a good physical condition was a protective factor against suffering AMS (OR 0.48; 95% CI 0.29–0.79).

| Risk Factor                          | Unadjusted OR (CI 95%) | Unadjusted p value | Adjusted OR (CI 95%) | Adjusted p value |
|--------------------------------------|------------------------|--------------------|----------------------|------------------|
| Age                                  | 0.99 (0.98–1.01)       | 0.62               | 0.98 (0.96–1.0)      | 0.091            |
| Male gender                          | 0.65 (0.42–1.04)       | 0.072              | 0.62 (0.36–1.06)     | 0.081            |
| Residence < 800 meters               | 2.06 (0.89–4.75)       | 0.086              | 1.75 (0.72–4.26)     | 0.220            |
| BMI                                  | 1.01 (0.95–1.09)       | 0.74               | 1.04 (0.93–1.16)     | 0.477            |
| OSAS                                 | 5.63 (1.02–31.4)       | **0.026**          | 3.54 (0.52–24.2)     | 0.197            |
| NSAIDs < 48 hours                    | 2.04 (1.16–3.56)       | **0.013**          | 1.95 (1.09–3.50)     | **0.026**        |
| Smoke                                | 1.07 (0.67–1.69)       | 0.78               | 1.03 (0.62–1.73)     | 0.889            |
| History of HAI                       | 2.04 (1.23–3.26)       | **0.003**          | 1.98 (1.22–3.21)     | **0.006**        |
| Physical activity (hours/week)       | 0.92 (0.82–0.98)       | **0.004**          | 0.94 (0.89–1.00)     | 0.062            |
| Good physical condition              | 0.47 (0.28–0.76)       | **0.002**          | 0.48 (0.29–0.79)     | **0.004**        |
| Maximum altitude (meters)            | 1.0 (1.0–1.0)          | 0.25               | 1.0 (0.99–1.0)       | 0.327            |
| Ascension time (hours)               | 1.19 (0.99–1.44)       | 0.063              | 1.06 (0.82–1.36)     | 0.672            |
| Altitude difference (meters)<sup>a</sup> | 1.0 (1.0–1.0)     | 0.15               | 1.0 (0.99–1.0)       | 0.603            |
| Physical exertion                    | 2.42 (1.33–4.40)       | **0.003**          | 2.24 (1.22–4.12)     | **0.009**        |
| Recent (3 days) activity > 2,500 m   | 0.66 (0.42–1.06)       | 0.082              | 0.69 (0.42–1.14)     | 0.150            |

Results are expressed as OR (odds ratio) and 95% CI (confidence interval).<sup>a</sup>Altitude difference means difference in altitude from the starting point to the highest altitude. Abbreviations: BMI: body mass index; NSAIDs: nonsteroidal anti-inflammatory drugs; OSAS: obstructive sleep apnea syndrome; HAI: high altitude illness.
Discussion

Using the modified LLS criteria, we found a prevalence of AMS of 26.7% in mountaineers ascending to moderate-high altitudes in the Pyrenees region. To our knowledge, this is the first study that analyses the prevalence and risk factors of AMS in this region.

There is less information regarding the prevalence of AMS at moderate to high altitudes (around 3,000 m) in comparison with high to extreme altitudes. Our impression is that the prevalence found in our study is higher than the expected but it is difficult to compare our results with previous studies performed at similar heights because of differences in geographic locations and studied populations. AMS occurred in 25% of visitors to moderate altitudes (1,920-2,956 meters) in the Rocky Mountains of Colorado [7]. The prevalence of AMS in other studies performed at Mount Fuji [9] and Western and Eastern Alps [10] was 29.5% (3,776 meters), 34.9% (3,817 meters) and 38.0% (3,454 meters), respectively. It is also important to highlight that these studies were conducted before the LLS was modified in 2018 and, to our knowledge, no studies regarding AMS prevalence have been published using this modified score. Other factors could explain the differences in AMS prevalence at similar altitudes (different hut locations, different weather conditions, different levels of mountaineer experience, etc.) but the explanation to them is beyond the scope of this study.

We have also found different risk factors for AMS, many of them already described in the literature that deserve discussion.

Men and women appear to be equally at risk for AMS although some observational studies suggest a slightly higher risk for women [7]. We also found a higher risk for AMS in women but the statistical significance of this difference was borderline (p value = 0.07).

Regarding pre-existing medical conditions we only found that OSAS was associated with a greater risk for AMS in the univariate analysis. Several studies have shown that obesity and nocturnal hypoxemia are risk factors for the development of AMS. Patients with OSAS and significant arterial desaturation at sea level would be expected to have more profound arterial desaturation during apneic periods at high altitude, but there are no data on this issue [11].

The most relevant risk factor (with a higher odds ratio) for developing AMS in our study was the intensity of exertion perceived by mountaineers. Those individuals who reported heavy exertion had more than 2 fold risk of developing AMS. This finding has also been found in other studies and could be explained due to the stress caused in the autonomic nervous system by additional hypoxia that generates an intense exercise [3, 10]. The role of exercise in this study must be discussed. We found a high proportion of subjects being fatigued (half of them moderately to severe) and it is difficult to assess whether these symptoms are secondary to AMS or indicate the effect of exercise. Furthermore, Moore et al have recently drawn attention to the inclusion of fatigue in the LLS. These authors suggest that fatigue may contribute to increase false positive AMS diagnoses and propose to remove this symptom from the score [12]. For
this reason, we believe the reported AMS scores would have been lower without the inclusion of fatigue and the prevalence of AMS would have been lower.

Moreover, self-assessed bad physical condition was found to be another significant risk factor for AMS. This can be explained, in part, by the fact that physical condition is related to the level of exertion during the ascent, suggesting that low fitness climbers do not tolerate the unusual exertion of mountaineering, or they appear to workout excessively. The results regarding this issue in the literature are inconclusive, with some studies finding that physical condition is a risk factor for AMS [7, 10] while others not [4, 13]. This variability between studies may be explained because self-reported physical condition is difficult to objectively evaluate with considerable variability between individuals.

We also found that history of HAI on previous exposures was also a risk factor for suffering AMS (almost more than two fold risk). Based on our findings and previous studies, a strong relationship seems to exist between a self-report of previous HAI and the risk of subsequent development of AMS. There are different theories regarding individual susceptibility to HAI, but it is likely to be derived from both genetic and environmental variables. The genetic influence of AMS remains an active area of investigation with no identified specific genetic predisposition [2, 4, 7, 13–15].

Finally, we also found that NSAIDs consumption in the previous 48 hours was associated with an increased risk for AMS. However, caution should be applied when interpreting this apparently confusing result. We do not believe that taking an analgesic places one at a greater risk for subsequent AMS. It is likely that many of our participants who used NSAIDs did so after they started experiencing symptoms associated with AMS in an effort to alleviate those symptoms. The findings that LLS was higher and AMS was more severe in those taking NSAIDs supports this hypothesis. The same finding and interpretation has also been reported in previous studies [13]. On the other hand, the use of NSAIDs was not associated with a previous history of AMS, so it seems unlikely that their use was preventive to avoid symptoms.

It is commonly accepted that residing at an altitude above 800 meters from sea level offers protection against AMS [7, 16]. In our study, we found a higher proportion of participants living below 800 meters from sea level in the ones who suffered AMS compared with those who not, but these differences did not reach statistical significance (p = 0.09). This may be explained, in part, because only 10% of participants were living above 800 meters from the sea level.

This study has some limitations that must be taken into account. First, data were collected in person and on-line and this could to contribute to a participant selection bias. Despite this, we did not found differences in the prevalence of AMS between the two types of data collection. Second, the individuals who participated in the study did so voluntarily (non-probabilistic method), allowing perhaps to select individuals with “different” characteristics to those who decide not to participate (more motivation, less severity of symptoms, etc.). Third, the results presented here have performed in a specific area of the Pyrenees and probably cannot be generalized.
Conclusions

The prevalence of AMS (using the modified 2018 LLS) in mountaineers at moderate-high altitudes (lower than 3,404 meters) at the Pyrenees region is not negligible (26.7%) but probably slightly overestimated. Most cases of AMS were mild (88%) or moderate (12%) and we did not find any severe case. The independent risk factors for developing AMS were previous history of HAI, NSAIDs use, and other modifiable risk factors such as physical exertion and bad physical condition. In light of these results, we believe that more educational/informational programs for individuals planning to climb to moderate-high altitudes in the Pyrenees would contribute to prevent AMS. We also encourage researchers to conduct new studies to confirm these results.

Abbreviations

AMS
Acute mountain sickness
HAI
High-altitude illness
IQR
Interquartile range
LLD
Lake Louise Score
NSAIDs
nonsteroidal anti-inflammatory drugs
OSAS
Obstructive sleep apnea syndrome

Declarations

Ethics approval and consent to participate:
A local review board from Universitat de Girona approved the study and all individuals read and accepted a study information form and informed consent before participation.

Availability of data and materials:
All data generated or analysed during this study are included in this published article. In addition, the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:
The authors declare that they have no competing interests.

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None

**Authors' contributions:**

study concept and design (all authors); acquisition of the data (CW); analysis of the data (JCT and CW); drafting of the manuscript (JCT and CW); critical revision of the manuscript; and approval of the final manuscript (all authors)

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**Authors' information:**

The results of this study were presented on February 2020 by the first author (CW) as her Final Degree Project at the School of Medicine, University of Girona, Girona, Spain. The final qualification was excellent (9.7/10).

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