

Older age, chronic medical conditions, and polypharmacy in Himalayan trekkers in Nepal: an epidemiologic survey and case series.*

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LK and BB conceived the idea and secured funding. LK, JS and SP designed the study. LK, LM, NR, BP, SP, JS, MM, DC, CD, TM, PP, DS, AS, DT and DY participated in data collection and data analyses. LM wrote the first draft. All authors were involved in revising and approving the final draft. LK takes responsibility for the work as a whole.

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Abstract

Background: The number of tourists in Nepal doubled between 2003 and 2013 to nearly 800,000. With the increased popularity of trekking, the number of those with pre-existing medical conditions requiring access to healthcare is likely to increase. We therefore sought to characterize the demographics and health status of trekkers on the Everest Base Camp route in the Solukhumbu Valley. Additionally, we report cases that illustrate the potential complications of an aging and medicated population of trekkers with underlying diseases.

Methods: Trekkers over 18 years were enrolled in a larger observational cohort study on blood pressure at high altitude at 2,860 m. They answered a questionnaire regarding demographics, medical history, and current medications. Acute medical problems relating to medication use that were brought to the attention of investigators were documented and are presented as case reports.

Results: We enrolled 670 trekkers, 394 (59%) male, with a mean age of 48 years (range 18-76). Pre-existing medical conditions were reported by 223 participants (33%). The most frequent conditions included hypertension, hypercholesterolemia, migraines and thyroid dysfunction. A total of 276 participants (41%) reported taking one or more medications. The most common medications were acetazolamide (79, 12%), antihypertensives (50, 8%), and NSAIDs (47, 7%), with 30 classes of drugs represented. Excluding acetazolamide, older trekkers (age greater than 50 years) were more likely than younger ones to take medications, (OR = 2.17; 95% CI 1.57-3.00; $p < 0.05$). Acetazolamide use was not related to age.

Conclusions: Our findings illustrate a wide variety of medical conditions present in trekkers in Nepal with wide-ranging potential complications that could pose difficulties in areas where medical care is scarce and evacuation difficult. Our cases illustrate the potential problems polypharmacy poses in trekkers, and the need for local and expedition healthcare workers to be aware of, and prepared for the common medical conditions present.

Introduction

Over the past decade Nepal has seen a dramatic increase in the number of visitors. Nearly 800,000 tourists traveled to Nepal in 2013, which is more than double the number of visitor from ten years prior[1]. Over 100,000 of those individuals in 2013 reported traveling to Nepal to trek or climb mountains [1]. Popular routes such as the Everest Base Camp trek in the Solukhumbu Valley have become more developed, and with increasing access to these areas, the number of trekkers has increased. Many of the individuals traveling to remote regions around the world for adventure travel are older and have preexisting medical conditions,[2] but it is unknown whether trekkers in Nepal reflect this evolving demographic.

Access to medical service and facilities on the Everest Base Camp trek remains limited. Although there are several health care facilities ranging from aid posts to hospitals, even the hospitals provide only basic or limited care for patients, and those with significant problems require air evacuation to Kathmandu for treatment. Leshem et al demonstrated that rates of helicopter evacuation for high altitude illness increased from 1999-2005 and they largely attributed this to increased access[3]. Even with more available helicopters, factors such as weather and the ability to pay in advance limit emergency evacuations. Additionally, emergency air evacuations carry inherent risks. It therefore is important that local healthcare providers, guides, expedition physicians, and pre-travel counselors are aware of the types of medical problems their clients have, and the potential risks these might pose.

Despite the large number of visitors, current epidemiologic data on the health status of Everest Base Camp trekkers is lacking. The goal of this survey is therefore to

describe the demographics and pre-existing medical conditions of a large sample of individuals trekking in the Solukhumbhu Valley, Nepal. In addition, we report three cases that illustrate the potential complications of an aging and medicated population of trekkers with underlying medical problems.

Methods

Survey

We report here demographic details of patients enrolled in a larger observational cohort study on blood pressure and high altitude. The Nepal Health Research Council approved this study. Eligible subjects were trekkers and guides arriving in Lukla, Nepal (2860 m) who were over the age of 18 years old. Pregnant patients, those less than 18 years old, and those who declined to participate were excluded. We enrolled patients during the fall trekking season in the Solukhumbhu valley from October 7th, 2014 to November 2nd, 2014. We utilized posters, flyers, direct communication, and word of mouth to recruit subjects arriving in Lukla by air and foot. After trekkers voluntarily agreed to participate, they were enrolled in the study, assigned a number to preserve anonymity, and completed informed consent. Subjects responded to an English or Nepali language written questionnaire (available as an appendix at the editor's request) to assess demographics including age, weight, height, country and city of origin, fitness level, and other questions regarding their medical history and current medications.

BMI was calculated from self-reported height and weight and subjects were classified by the U.S. National Institute of Health guidelines as underweight, normal,

overweight or obese[4]. Altitude of residence was determined by searching for their hometown using Wolfram Alpha or Google search.

Statistical analyses

Survey data were entered into a spreadsheet and copied into Microsoft Excel. Descriptive statistics were calculated in Microsoft Excel and Google Sheets. Participants' baseline data were included in this report, even if the participant dropped out of the larger observational study on blood pressure for any reason. We used correlation statistics (Excel) and chi-squared analysis to determine the relationship of age to number of reported medications and calculated odds ratio and 95% confidence intervals (vassarstats.net.).

Case reports

Case reports were structured using the CARE guidelines[5] based on cases brought to the investigators attention by the study subjects. Additional verbal or written consent for case reporting was obtained from case report subjects.

Results

We enrolled 670 individuals. These participants comprised around 7% of the total individuals who passed into the Sagarmatha National Park during this time based on a total of 9463 trekkers registered between October 1, 2014 and October 31, 2014 at the Sagarmatha National Park entrance point (personal communication, 2014 [documented record from Park entrance point]). Subject characteristics are listed in Table 1. Trekkers were mostly middle aged men from sea level. Many did not consider themselves athletic and one third were overweight or obese.

Of the 670 respondents, nearly half, 41% (276), were taking one or more medications, both over the counter medications or prescription formulations (Table 2). The most common medications were acetazolamide (79, 12%), antihypertensives (50, 8%), and NSAIDs (47, 7%), with 30 classes of drugs represented. Thirty-eight (16%) of trekkers on any medication other than acetazolamide, were also taking acetazolamide.

Underlying chronic medical conditions of trekkers are listed in Table 3. One third (223) of all participants reported at least one underlying medical problem, though not all of these were treated with medications. Of the trekkers with a reported medical condition, 35 (16%) were taking acetazolamide.

Use of acetazolamide was similar across age groups ($p > 0.05$). In contrast, older trekkers (age greater than 50 years) were more likely to be taking medications other than acetazolamide compared to younger trekkers (OR = 2.17; 95% CI 1.57-3.00; $p < 0.05$).

Case vignettes

Case 1

A 76-year-old man with hypertension, hypercholesterolemia, coronary artery disease with six stents and bariatric surgery with a 36 kg weight loss four years prior presented for enrollment in the study in Lukla (2860 m). He intended to trek to Everest Base Camp with his daughter, an intensive care unit nurse. Prior to departure from Kathmandu (1400 m) he had a pre-syncopal episode in the airport, which resolved with a few minutes rest. When he arrived in Lukla and disembarked from the plane he again experienced lightheadedness and dizziness, which resolved with rest. After recovering, he walked without difficulty from the airport to the teahouse where our study was

headquartered and was asymptomatic at our interview. He had a similar episode one day before in Pokhara (800m).

His medications included clopidogrel, aspirin, amlodipine, carvedilol, hydralazine, losartan, olmesartan, finasteride, niacin, escitalopram, mirtazapine, pantoprazole, simvastatin, nitroglycerin as needed and tylenol with codeine as needed. The patient had all of his pills for morning, midday, and night in individual bags for each day of the trek pre-packed by his home pharmacy. He carried two medication lists with conflicting dosages and medications.

On exam the patient was alert with good color and non-ill appearing. His initial blood pressure was 90/50 mmHg with a heart rate in the 50s. The rest of his exam was unremarkable.

We used Epocrates pill identification software to identify the pills in his pre-packaged bags to determine exactly what medications he was taking. Some of the packets had amlodipine at 10 mg and some at 5 mg dose. Some of the bags also contained both olmesartan and losartan. The patient recalled that his physician had lowered his dose of amlodipine prior to his departure.

We attributed his symptoms and hypotension to medication overdose. We corrected the remaining pill packs by removing the double doses of angiotensin receptor blocker medication and all the amlodipine 10 mg pills. We discussed with both the study participant and his daughter the risks of continuing his trek, and advised against continuing until his blood pressure had improved and stabilized, but he insisted on continuing. A repeat blood pressure at that time was 110/52 mmHg.

The subject reported that he spent the next three days walking slowly from Lukla towards Namche Bazaar. He never reached the steep 500 m climb from Monjo to Namche Bazaar. Typically trekkers walk from Lukla to Namche Bazaar in 1-2 days. On the third day he “felt like he was having a heart attack” due to severe fatigue and weakness, but had no syncope. He was unable to check his blood pressure. After some difficulties finding an adequate landing zone, he was required to walk down past two villages where ultimately he could access a helicopter and was evacuated. He was admitted to a hospital in Kathmandu where a cardiologist wanted to perform angiography, but the patient refused. After several days he was able to arrange a flight back the United States where he was ultimately diagnosed with myasthenia gravis.

Case 2

A 67-year-old man with hypertension on amlodipine and lisinopril flew to Lukla (2860m) with the intention of trekking to Everest Base Camp and climbing Lobuche East (6119 m). On arrival to Lukla he began taking acetazolamide in addition to his usual medications. Two days later in Namche Bazaar he became very dizzy, as if he was going to faint, while on an acclimatization hike. His symptoms resolved when he lay down. He stopped taking acetazolamide and cut his blood pressure medication doses in half. On the way to Lobuche East Base Camp (4700 m) and again at Gorak Shep (5164 m) his dizziness recurred, but improved when he put his head between his knees and rested. He abandoned his climb of Lobuche East and did not ascend to Everest Base Camp from Gorak Shep due to his dizziness. He stopped taking all of his blood pressure medications with slight improvement.

He was unable to check his blood pressure during his trip, but his heart rate was in the 70s. On return home his blood pressure was elevated and he resumed his prior medications. A cardiac stress test was negative. The patient was not enrolled in the larger observational study but contacted the investigators after his trip wondering if his symptoms were blood pressure related.

Case 3

A 49 year old woman with hypothyroidism ran out of her levothyroxine three days into her trek. She attempted to get a refill at a local clinic in Namche Bazaar (3200m), but this medicine was not available. A provider at the clinic advised her to cancel her trip because of the risk of severe hypothyroidism. She consulted with study investigators for a second opinion. Patient denied any symptoms of hypothyroidism. She stated that she was diagnosed with low thyroid on a routine blood exam and that she has never been symptomatic. She was one week into a planned 3-week trip. Her exam was unremarkable. If she continued her trip, she would be without her thyroid medication for 18 days. She wondered if she should indeed cancel her trek.

Given that the half-life of levothyroxine is 6-7 days, the patient was not at risk for having reduced serum levels of T4 for another week. Signs and symptoms of severe hypothyroidism are extremely unlikely to occur in a time period as short as 1 or 2 weeks. The patient also had no history of any significant symptoms from her condition. We therefore reassured her that she could safely continue her trek without her levothyroxine. She reached Everest Base Camp (5,380 m) and returned home without adverse event where she resumed her usual dose of levothyroxine.

Discussion

An important proportion of trekkers on the Everest trail is older, has underlying chronic medical conditions, and is taking daily medications. Many of these medications, such as immunosuppressants or dual antiplatelet therapy, carry important risks in the wilderness. Our cases illustrate some of the complications that can arise when patients with underlying diseases on medications travel in a remote and rugged environment. Travelers may experience adverse effects of medications, medication interactions, or risk of abandoning or changing their plans due to medication related problems.

Our data suggest that individuals trekking on the main route to Everest Base Camp are older than the average adventure traveler in other areas around the world. A 2013 trade report looking at adventure travel in Europe, North and South America found that the average age for adventure travelers was 36 years[2]. Newcomb et al enrolled participants from the Solukhumbu valley during the spring of 2008 and found an average age of 44.1 years[6], which is slightly lower than the average age of the participants enrolled in our study. That study included only 131 trekkers, and they were recruited in Machermo, near a rugged high pass, off the main route to Base Camp[6].

The finding that Everest Base Camp trekkers are older has implications for determining future needs of healthcare and medical evacuation resources in the region. In previous studies, older trekkers were more likely to be evacuated for altitude illness in Nepal[3]. Furthermore, in the Alps older age is a risk factor for traumatic[7] and sudden cardiac death in the mountains [8]. The vast majority of alpine casualties in a report from Japan were in people older than 40 years, and older trekkers were observed to have worse

balance than younger ones, potentially explaining the greater number of injuries in this group[9].

In addition to age, the fact that a third of trekkers are overweight or obese creates further potential complications. Patient size and weight can limit the feasibility of helicopter evacuation, especially at higher altitudes where helicopters are unable to produce as much lift and thus must have lighter loads to take off. Despite the rugged terrain and physical difficult nature of trekking in Nepal, almost half of our survey respondents considered their fitness level average or less than average, which may also increase their risk for injury.

Trekkers are taking a wide variety of medications. The effectiveness and possible side effects of different commonly used medications at high altitude are largely unknown. A consensus statement by The International Mountaineering and Climbing Federation (UIAA) warns of possible complications from common medications such as the increased effect from antihypertensive medications and thus the risk of orthostatic hypotension[10]. Two of our cases clearly illustrate this point. The UIAA guideline also highlights the need for trekkers to know how to safely carry and store their medications while traveling[10]. Other authors caution the risks of electrolyte imbalances, dysregulation of body temperature and impaired heart rate response to exercise with commonly used antihypertensive drugs[11] and our cases support these theoretical concerns.

Our cases illustrate several other important points about trekkers who are taking medications. Trekkers should be familiar with their medications and know the risks of both taking and not taking them while traveling. Health care providers should ensure patients are taking the correct doses in order to avoid overdose and adverse effects.

Prescribers also need to consider the potential for medication interactions when prescribing additional drugs for travel. For example, as seen in case 2, the diuretic effects of acetazolamide taken for acute mountain sickness prevention may interfere with blood pressure medications leading to symptomatic hypotension, or potentially worsen a dehydrated person's clinical status. Use of antibiotics for traveler's diarrhea or respiratory infections could increase or decrease metabolism of many drugs.

As illustrated in case 3, medication complications can lead to consequences that impact the quality of the trekking experience, including symptoms that affect travel, make enjoyment of travel difficult, or potentially lead to trip cancellations. We suggest that patients receive pre-trip counseling about their regular medicines and the consequences of taking them or not while traveling. All patients should carry a current medication list and avoid carrying inconsistent lists. We support the idea of having daily pills individually packaged, as was done for our patient in case 1, but would recommend that the patient have a way to identify the medications, and that the pharmacists ensure correct packaging to avoid accidental overdose and verify potential interactions for any new drugs prescribed for travel.

Limitations

We note several important limitations of this study. All of our data were self-reported. We could not verify medical conditions, medications and dosages with medical records. Self-reported information could be inaccurate. For example, many subjects listed psychiatric medications, but few listed psychiatric conditions as a medical problem.

Prior studies indicate that it is likely that individuals underestimated their weight and overestimated their height, thus their calculated BMI was likely under reported[12].

In addition this data was obtained from individuals who were recruited on a volunteer basis for a study requiring them to check-in and have repeat blood pressure and oxygen saturations taken at different locations throughout their trek. This may lead to important selection bias of participants. We cannot characterize those who declined to participate to determine if our population differed from them in any important ways. While the majority of subjects enrolled were healthy and not on any medications, there was a significant proportion with underlying medical conditions. Those with medical problems may have been more likely to enroll in the study in order to have monitoring during their trek. However, even if the proportion of individuals with underlying medical conditions is smaller than we report, there is clearly a significant group of individuals who are at risk for complications from their medical conditions who may need medical care while trekking. Our large number of subjects makes it more likely that this is a representative sample. Finally we had very few Nepali participants in the study and we also did not include persons below 18 years of age, which if possible could be rectified in future studies.

Conclusions

Our data demonstrate that an important fraction of trekkers in the Everest region are older, have underlying medical problems and are taking many medications. We have illustrated some of the potential problems these medications can pose. While it is impossible for local clinics or the guides to prepare for every medical complication that

could arise in the mountains, having a better understanding of the overall health of the visitors to the region can help them prepare for likely scenarios. This information should aid in directing future research into how an older population with multiple medical conditions responds to altitude and highlights the need for more research on the effectiveness of medications at high altitude.

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TABLE 1: Demographic Characteristics of Trekkers in the Solokhumbu region of Nepal

Characteristics	N (%)†	Range	Mean (95% CI)	Median (IQR)
Total enrolled	670 (100)			
Sex				
Men	394 (59)			
Women	275 (41)			
Age (years)				
Total		18-76	48 (46-47)	50 (36-57)
Under 30	73 (11)			
Under 40	191 (29)			
Over 50	314 (47)			
Over 60	97 (15)			
Body Mass Index*				
Total			24 (23.5-24.1)	24 (23-24)
Underweight/Normal (<25)	437 (65)			
Overweight (25-30)	198 (30)			
Obese (>30)	26 (4)			
Activity Level				
Sedentary	8 (1)			
Average	276 (41)			
Athletic	303 (45)			
Very Athletic	62 (9)			

Unreported 23 (3)

**Home Country
Elevation (meters)**

Total -2-3810 241 67 (30-103)
(204-278)

Below 1000 631 (94)

Over 1000 32 (5)

Over 2500 6 (1)

*BMI= Mass(kg)/(Height(m))²

†Not all numbers add up to total due to missing data from some participants. Percentages are calculated based on total number of responses to that questionnaire item.

TABLE 2: Medications taken by participants, both prescribed and over the counter

Medications	N (%)	Percent of those taking any medication
Total	276 (41)	
Acetazolamide	79 (12)	29%
Antihypertensive	50 (8)	18%
NSAIDs	47 (7)	17%
Cardiac	44 (7)	16%
Aspirin	40 (6)	15%
Thyroid	37 (6)	13%
Asthma	24 (4)	9%
Hormones	20 (3)	7%
Tylenol/Paracetamol	14 (2)	5%
Migraine	13 (2)	5%
Psychiatric	13 (2)	5%
Immunosuppressives	9 (1)	3%
Alpha-Blockers	9 (1)	3%
Diabetes	7 (1)	3%
Proton Pump Inhibitors	5 (1)	2%
Opiates	4 (1)	2%
Other*	24 (4)	9%

*Allopurinol, balsalazide, mesalamine, famotidine, ferrous sulfate, ginkgo, modafinil, omega-3, oxybutynin, probiotics, amoxicillin/clavulanic acid, ciprofloxacin, carbamazepine, levetiracetam, valproic acid, dexamethasone, ophthalmic beta-blocker, cinnarizine, dimenhydrinate.

TABLE 3- Medical conditions reported by participants

Medical Condition	N (%)
Any Condition (excluding trauma/orthopedic)	223 (33)
Hypertension	60 (9)
High Cholesterol	56 (8)
Migraines	40 (6)
Thyroid	37 (6)
Smoker	36 (5)
Asthma	31 (5)
Heart Disease	15 (2)
Diabetes Mellitus	12 (2)
Appendicitis/appendectomy	6 (1)
Borderline Hypertension	6 (1)
Hysterectomy	5 (0.7)
Cardiac Arrhythmia	4 (0.6)
Cancer*	4 (0.6)
Heart Murmur	2 (0.3)
Glaucoma	2 (0.3)
Seizure disorder	2 (0.3)
Other†	26 (4)

*1 unspecified cancer, 1 colon cancer, 1 prostate cancer, 1 CLL.

†Other conditions with incidence of 1: anemia, ankylosing spondylitis, bronchitis, colon resection, depression, Crohn disease, gallbladder disease, gastroesophageal reflux disease, intervertebral disc disease, meningitis, narcolepsy, nephrectomy (Reported as

“one kidney” nephrectomy vs developmental anomaly), nephrolithiasis, ovarian torsion, pancreatitis, parotid angioma, polycystic ovary disease with oophorectomy, pericarditis, renal transplant, rheumatoid arthritis, scoliosis with spinal fusion, stroke, SLE, thalassemia minor, ulcerative colitis, and von Willebrand deficiency.