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ACUTE MOUNTAIN SICKNESS MANAGEMENT: CASE OF MOUNT KILIMANJARO AND REVIEW OF LITERATURE
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ACUTE MOUNTAIN SICKNESS MANAGEMENT: CASE OF MOUNT KILIMANJARO AND REVIEW OF LITERATURE

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ABSTRACT

Background: **High-altitude Illness is the collective term for all illnesses occurring at or during terrestrial elevations over 1500m, it encompasses acute mountain sickness (AMS), high-altitude cerebral oedema (HACE) and High-altitude Pulmonary Oedema (HAPE).High- altitude-related problems consist of the common syndrome of acute mountain sickness, which is relatively benign and usually self-limiting, and the rarer, more serious syndromes of high-altitude cerebral oedema and high-altitude pulmonary oedema. A common feature of acute altitude illness is rapid ascent by otherwise fit individuals to altitudes above 3000 m without sufficient time to acclimatize which is accompanies with many hypobaric hypoxia related complications which if not managed on time results into death, especially when ascending mountain with sharp ascent like Kilimanjaro Acute Mountain Sickness is the first manifestation of High-altitude illness, it can be easily prevented and managed but most of the time AMS symptoms are ignored or mismanaged hence resulting into death. The susceptibility of an individual to high-altitude syndromes is variable but generally reproducible. Prevention of altitude-related illness by slow ascent is the best approach, but this is not always practical, especially in Mountains like Kilimanjaro with very low medical resources. The immediate management of AMS requires oxygen and descent of more than 300 m as soon as possible, accompanied other pharmacological and non-pharmacological management from well-trained health care providers, tour guides, porters and mountain guards.**
Methods: **A Systematic review of case studies, research articles and guidelines for prevention and treatment of Acute Mountain Sickness (AMS) in Mt. Kilimanjaro. Searches from PubMed, MEDLINE and EMBASE from inception to October 2018, a total of 247 peer reviewed articles and case studies, 2 international guidelines, 17 books and 1 conference proceeding were used to prepare this article.**
Results: **Detailed review of Acute Mountain Sickness management and other High-altitude clinical complications in Kilimanjaro (HACE and HAPE). This review provides detailed information about each of these important clinical entities. After reviewing the clinical features, epidemiology and current understanding of the pathophysiology of each disorder, the article describe the current pharmacological**

and non-pharmacological approaches to the prevention and treatment of these diseases. A total of 247 articles and case studies, 2 international guidelines, 17 books and 1 conference proceeding were used for this review. All articles searches where from peer reviewed sources, majority were international though thorough searches and emphasis was for those written about AMS in Mt. Kilimanjaro. Majority authors were from were from the global north (Europeans and Americans)

Conclusion: **Currently there is an increase in number of cases of high-altitude illnesses and deaths reported in Mt. Kilimanjaro. Many of these travellers seek medical advice prior to expedition from inexperienced practitioners around world or under resourced and inexperienced health care providers in Tanzania. In this Review article, I describe the setting and clinical features of acute mountain sickness, an overview of the known pathophysiology, prevention, treatment and comprehensive evidence based recommendations for health care providers in Africa.**

INTRODUCTION

The year 2016 was the devastating for racing fans in South Africa, the death of Gugu Zulu shocked the core of knowledge of high-altitude illnesses amongst travel medicine experts and general practitioners around Southern Africa.[1, 2] Zulu died while taking part on the Trek4Mandela expedition on Mount Kilimanjaro in Tanzania in July 2016 after he complained of scratchy throat, blocked nose, nausea, vomiting and later was found unconscious a night before summiting.[2]

It is commonly reported that approximately 10 climbers die every year on the mountain, primarily due to acute mountain sickness, this rate is very debatable since most of the physicians in Tanzania believe there are number of cases that go unreported since the data relies on a number of deaths collected only at Kilimanjaro Christian Medical Center, the only tertiary hospital around the northern part of Tanzania.[3, 4]

There are a lot of trekkers who come for advice and medical checkups in the private and public health care facilities around South Africa prior to mountaineering expeditions all over the world. Kilimanjaro being the most favorable mountain amongst South African tourists visiting Tanzania[5]

At 5895m, Mount Kilimanjaro is the world's tallest free-standing mountain in the world. Mount Kilimanjaro attracts over 35,000 climbers a year, plus 5000 day visitors.[4, 6, 7] Most are North Americans and Europeans, South Africans leading in the African continent.[5]

Ascent to high altitudes requires adaptation to hypoxic and hypobaric environment, while failure to adapt results in Acute Mountain Sickness (AMS)[8-11]

Kilimanjaro is unusual in being a free-standing mountain that presents little opportunity to achieve early acclimatization, in comparison with other popular destinations of Himalayas and Andes.[4, 12] Typical high-altitude destinations include Cuzco, Peru (3,400 m), La Paz, Bolivia (3,780m), Lhasa, Tibet (3,660m), Everest Base Camp in Nepal (5,364m), and Kilimanjaro in Tanzania (5,895 m).[7, 9, 13] Kilimanjaro provides little opportunity for the climbers to acclimatize before arriving at the park entrance because, unlike other high altitude destinations, travel to the start of the climb usually involves no prior altitude exposure.[10, 14-21] Moshi town, which is the nearest town from the mountain is the 890m altitude above sea level.[22] This town is easily accessed from Kilimanjaro International Airport, which is less than 40 km from lowlands plateau of Mount Kilimanjaro. Being a mountain that is rising from lowlands plateau with no foothills, the mountain has been used by private tour operators and charity fundraisers to attract inexperience trekkers who later face poor acclimatization and high rates of AMS.[7, 12, 17]

Understanding the incidence of AMS on Mount Kilimanjaro is important because it is one of the world's most popular climbing destinations (regarded as "Everyman's Everest") and many climbers are exposed to risk of high-altitude illnesses.[10] mount Kilimanjaro combines easy access with financial imperative to ascend quickly as the significant national park fees induce climbers to ascend at rates of more than one thousand vertical meters per day.[10, 23]

Several routes exist to the summit of Kilimanjaro, Uhuru peak, ranging from 5 to over 10 Days.[12] There are seven major routes used to climb Kilimanjaro, Marangu(colloquially known as "Coca-Cola route"), Machame(colloquially known as "Whisky route") ,Umbwe, Rongai, Shira, Lemosho , Northern Circuit.[10, 17] It is estimated that tourists climb Kilimanjaro using the routes in the following percentages: Machame (45%), Marangu (40%), Lemosho (8%), Rongai (5%), Shira (1%), Northern Circuit (0%), Umbwe (0%).[4, 10, 17] The most popular amongst the unprofessional trekkers and charity organizers is the Marangu Route, colloquially known as the''Coca-Cola Route'' because of easy ascent and huts; most trekkers take 4 or 5 days to ascend from the Tanzanian lowlands (1500 m) to the summit.[10, 12] This contravenes established advice that a slow ascent is favorable, and once above 3000m an individual should not ascend more than 300 to 600 m in a 24-hour period, with occasional rest days in addition.[3, 4] Other routes take 6 to 8 days to ascend the mountain, but a combination of factors makes them less popular.[4] Table 1 summarizes all the reasons why trekkers choose short, less adaptive routes compared to unpopular routes that give them chances to adapt and hence less incidences of AMS and other related high-altitude related complications.[12] The most rapid and most popular ascent route (Marangu) is associated with appreciable high altitude morbidity. It is believed that the Machame route may enhance acclimatization because trekkers sleep in camps at a similar altitude on both the second and third nights, adhering to the ''climb high sleep low'' paradigm for that 24 hour period. It is documented by several researchers but all the studies were not very conclusive.

Several factors contribute to successful mountain summiting, physical characteristics and physiology, psychological preparedness, ascent route and time spent during the expedition, availability of medical personnel and equipment, expedition budget and the level of experience of the tour guide and his/her team. [24]

Mountain climbing requires a lot of adaptation and acclimatization to both lower air pressure and diminished partial pressure of oxygen.[9, 14, 15, 20, 25] Physiological adaptation to changes in altitudes is a must for the climbers to summit and return to the base camp uneventful. If the adaptation process fails due to rapid ascent rate or to the particular characteristics of the climber, one of three illnesses may result: acute mountain sickness (AMS), high altitude cerebral oedema (HACE), or high altitude pulmonary oedema (HAPE).[17] Acute Mountain Sickness AMS is the most common of these problems, affecting 25% of the people who ascend to altitudes of 1850 to 2750 m and 42% at altitudes of 3000 m.[9, 17, 20, 25, 26] In this paper, I describe the pathophysiology, prevention, and treatment of Acute Mountain Sickness (AMS).

Table 1
Reasons for choosing shorter route

Reasons for choosing a shorter route
1. Limited availability of huts and camp sites
2. Pro rata nature of Kilimanjaro National Park fee
3. Commercial pressures
4. Low budget
5. Competitiveness among groups
6. Disproportionate expectations and desire to succeed
7. Limited experience of expedition organizers
8. Poor access to travel medicine practitioners or lack of awareness of the importance of seeking an advice from travel medicine practitioner or General Practitioners.

ACUTE MOUNTAIN SICKNESS (AMS)

High-altitude illness is the collective term for the syndromes that can affect unacclimatised travelers shortly after ascent to high altitude. The term encompasses the mainly cerebral syndromes of acute mountain sickness (AMS) and high-altitude cerebral oedema (HACE), and the pulmonary syndrome high-altitude pulmonary oedema (HAPE). HACE and HAPE occur much less frequently than AMS, but are potentially fatal. [11, 27, 28]

AMS has not only been reported from people with personal interest in mountain climbing and tourism, of recent the condition has been very common from people traveling enmass from low altitude to high. China lunar new year end holiday migration, where more than 2 million passengers traveling by train along the Qinghai-Tibet railway are exposed each year to high altitudes they not accustomed to.[29] AMS has also been reported by mountainous religious pilgrimages, for example thousands of Nepali pilgrims ascend every year to Gosainkund Lake (4380 m) during the Janai Purnima and AMS cases have been reported every year.[30]

Acute mountain sickness (AMS) is defined as headache in the setting of recent altitude gain and typical symptoms, which include anorexia, nausea, vomiting, insomnia, dizziness or fatigue. Though AMS symptoms are so common to many general patients, it can be easily diagnosed with the Lake Louise Scoring System (LLSS)[19] The Lake Louise Scoring System measures 5 clinical parameters, each with score of 0 to 3; these includes, headache, gastrointestinal symptoms, fatigue and weakness, dizziness and lightheadedness, difficulty sleeping.[19, 20, 31] LLSS come in form of a questionnaire which healthcare providers and mountain tour guides uses every day to evaluate high altitude travelers, pilgrims and expeditioners, from a score range of 0-15, a total score of 3 to 5 indicates mild AMS, a score of 6 or more signifies severe AMS; It can also be used as self-administered questionnaire to large groups and to individuals with basic learning capabilities.[19] According to LLSS, AMS can be diagnosed based on the following conditions: a rise in altitude within the last 4 days (a given on Kilimanjaro), presence of a headache, presence of at least one other symptom from the list of 5 clinical parameters mentioned above and a total score of 3 or more from the questionnaire.[19, 32] Headache is the cardinal symptom; it is bitemporal, throbbing, worse during the night and on awakening, and with Valsalva maneuvers as when an individual bends over to lift an object from the ground such as backpack. These initial symptoms are strikingly similar to an alcohol hangover and they can be easily be confused with viral-flu like illnesses, exhaustion, medication or drug effects. [9, 33, 34] The headache onset is usually 2-12 hours after arrival at a high altitude, often during and after first night and accompanied by fatigue, loss of appetite, nauseas occasionally vomiting. In children traveling in high altitudes majority present with headaches, irritability and paleness. AMS generally resolves within 24-72 hours after acclimatization but the symptoms might continue, indicating the severe form of AMS or other high-altitude conditions (High-Altitude Cerebral Oedema, and Pulmonary Oedema) or even death.[1, 9, 13, 16, 33, 34]. The diagnosis of AMS is purely clinical.[9]

Whether AMS and other high-altitude illnesses will develop in an individual depends on variables unique not only to the individual but to each ascent.[9] These variables include the ascent rate, the maximum altitude attained, the barometric pressure, the elevation at which one sleeps (sleeping altitude), the duration at high altitude, exertion, temperature, preacclimatization, the altitude of residence, a prior history of high-altitude illness, and certain pre-existing illnesses and medications.[3, 9, 35, 36] Variables that increase the likelihood of high-altitude illness can be divided into environmental, behavioral, and intrinsic risk factors.[37, 38] The risk of AMS can be put in three categories as highlighted in table 2 below.

Table 2

Risk categories for acute mountain sickness [from Peter H. Hackett, David R. Shlim, Chapter 2, Travel consultation[37]]

Risk category	Description
Low	• People with no prior history of altitude illness and ascending to less than 9,000 ft (2,750 m) • People taking ≥2 days to arrive at 8,200–9,800 ft (2,500–3,000 m), with subsequent increases in sleeping elevation less than 1,600 ft (500 m) per day, and an extra day for acclimatization every 3,300 ft (1,000 m)
Medium	• People with prior history of AMS and ascending to 8,200–9,200 ft (2,500–2,800 m) or higher in 1 day • No history of AMS and ascending to more than 9,100 ft (2,800 m) in 1 day • All people ascending more than 1,600 ft (500 m) per day (increase in sleeping elevation) at altitudes above 9,900 ft (3,000 m), but with an extra day for

	acclimatization every 3,300 ft (1,000 m)
High	• History of AMS and ascending to more than 9,200 ft (2,800 m) in 1 day • All people with a prior history of HAPE or HACE • All people ascending to more than 11,400 ft (3,500 m) in 1 day • All people ascending more than 1,600 ft (500 m) per day (increase in sleeping elevation) above 9,800 ft (3,000 m), without extra days for acclimatization • Very rapid ascents (such as less than 7-day ascents of Mount Kilimanjaro)

Although many pre-existing illnesses may be exacerbated by exposure to high altitude, a few illnesses increase susceptibility to high-altitude illness.[37, 38] The following table summarizes several condition and what should medical practitioner do while advising the traveler or expeditioner.

Table 3

Ascent risk associated with various underlying medical conditions [from Peter H. Hackett, David R. Shlim , Chapter 2, Travel consultation[37]]

Likely no extra risk	Caution required	Ascent contraindicated
Children and adolescents Elderly people Sedentary people Mild obesity Well-controlled asthma Diabetes mellitus Coronary artery disease following revascularization Mild chronic obstructive pulmonary disease Low-risk pregnancy Mild–moderate obstructive sleep apnea Controlled hypertension Controlled seizure disorder Psychiatric disorders Neoplastic diseases	Infants <6 weeks old Compensated heart failure Morbid obesity Cystic fibrosis (FEV1 30%–50% predicted) Poorly controlled arrhythmia Poorly controlled asthma Poorly controlled hypertension Moderate chronic obstructive pulmonary disease Severe obstructive sleep apnea Stable angina Nonrevascularized coronary artery disease Sickle cell trait Poorly controlled seizure disorder Cirrhosis Mild pulmonary hypertension Radial keratotomy surgery	Sickle cell anemia Severe–very severe chronic obstructive pulmonary disease Pulmonary hypertension with pulmonary artery systolic pressure >60 mm Hg Unstable angina Decompensated heart failure High-risk pregnancy Cystic fibrosis (FEV1 <30% predicted) Recent myocardial infarction or stroke (<90 days) Untreated cerebral vascular aneurysms or arteriovenous malformations Cerebral space-occupying lesions

PATHOPHYSIOLOGY

To understand properly the pathophysiology of AMS, a good knowledge of relationship between body physiology and change in altitude and atmospheric pressure is required, especially the relationship between barometric pressure changes and altitude and oxygen metabolism. Barometric pressure decreases in a non-linear fashion with altitude(vertical height gain above the Earth's surface).[39] The percentage of oxygen in the atmosphere remains constant (20.9%), but atmospheric partial pressure of oxygen (P_{O2}) reduces proportionally with barometric pressure. An individual acutely exposed to extreme altitude (>5500 m) may lose consciousness. Over 8000 m, this occurs reliably within <3 min. However, if the body is gradually exposed to increasing altitude, it can adapt and survive.[36, 38-40] This process is called acclimatization. The definition of high-latitude varies but high altitude generally refers to altitudes over 2500 m.[23, 36, 39]

Acute high-altitude illness describes the neurological or pulmonary syndromes experienced when unacclimatized individuals ascend too rapidly. [4, 9, 33, 39] AMS has been reported at altitudes as low as 2000 m, which is way below the proper definition of high-altitude.[39]AMS incidence increases with increasing altitude and has been reported in up to 40% of people at 3000m.[9, 39] Potentially fatal HAPE and high-altitude cerebral oedema (HACE) are less common; they are diagnosed in 2% of individuals ascending over 4000 m.[9, 26, 39] The faster the ascent and the higher the maximum altitude reached, the more likely individuals will suffer from high-altitude illness.[32, 35, 39]

Most of the high-attitude symptoms are contributed by hypoventilation which later exaggerates hypoxemia. Several factors plays a role in development of AMS and its sequelae. There are several physiological changes that can be observed in AMS, the changes are mostly seen to pulmonary, cardiac, renal and hematological systems.[41] The pulmonary response to high altitude follow the following sequence; arterial hypoxemia triggers increased peripheral chemoreceptor output leading to an increase in minute ventilation and a respiratory alkalosis, respiratory alkalosis blunts the initial ventilatory responses, with continued time at high altitude, minute ventilation rises further because of renal compensation for the respiratory alkalosis and increased sensitivity of the peripheral chemoreceptors, alveolar hypoxia triggers hypoxic pulmonary vasoconstriction, leading to an increase in pulmonary vascular resistance and pulmonary artery pressure. Pulmonary responses initially presents with the following symptoms, increased in respiratory rate and tidal volume, more frequent sighs and dyspnoea on exertion which resolves quickly on rest. In severe cases, the increase of hypoventilation exaggerates rise in pulmonary artery pressure in response to alveolar hypoxia and hence causing pulmonary oedema (high altitude pulmonary oedema-HAPE).[41] At this stage the patient experiences worsening tachycardia, tachypnea, lassitude, productive cough, cyanosis and eventually, altered mental status and coma develop, either from profound hypoxemia or concomitant HACE. Physical examination of the patient with AMS and HACE normally shows a prominent P2 and right ventricular heave on auscultation and palpation. Rales are often picked at the right mid-lung field, can be absent when a patient is at rest and present after brief exertion. Chest radiographs typically show patchy lung infiltrates with normal heart size, a typical feature of HACE.[16, 32, 41, 42] The ECG may show right heart strain which is a feature of acute pulmonary hypertension arterial blood gas analysis reveals respiratory alkalosis with severe hypoxemia (Partial pressure 30 and 40 mm Hg.)[41]

Cardiac responses to high altitude is as follows, increase in cardiac output, this is due to increase in heart rate, decrease in stroke volume, which also come as a result of decrease in plasma volume (a sequela of pulmonary and cerebral oedema) and increase in systemic blood pressure.[41] This initially will present as dyspnoe on exertion, transient lightheadnesess on rising to a standing position. Cardiac responses most of the time results in severe cerebral features in the form of cerebral oedema (HACE).[10, 13, 41] HACE most of the time presents with altered mental status and ataxia, often occurring 24 to 24 hours after AMS and HAPE. These symptoms come after early onset drowsiness, subtle psychological and behavioral changes e.g. apathy and social withdrawal. [36, 41]

Renal responses includes, variable increase in diuresis and natriuresis following ascent leads to a decrease in circulating plasma volume, arterial hypoxemia triggers increased secretion of erythropoietin (EPO) within 24–48 hours of ascent increased bicarbonate excretion as compensation for the acute respiratory alkalosis. Renal features of AMS will present as increased frequency in urination.[36, 41]

Hematologic responses includes, initial increase in hemoglobin concentration and hematocrit caused by reduction in plasma volume, over days to weeks, further increases in red blood cell mass, haemoglobin concentration, and hematocrit owing to increased EPO concentrations. Patients with HAPE sometimes presents with mild leukocytosis.[41]

The differential diagnosis of AMS is bit tricky for unexperienced physician. Two conditions deserve special attention when evaluating a patients suspected to have AMS, carbon monoxide poisoning and migraine.[1, 27, 41] Carbon monoxide poisoning is a risk at high altitude owing to use of heaters or stoves within confined spaces (camping tents or huts e.g. Marangu huts-Marangu route). Carbon monoxide poisoning is easily misdiagnosed as AMS, given the similar symptoms.[41] Migraine can also be confused with AMS, and hypoxia is a known trigger for migrainous headache in those with and without a previous history of migraine. Headache being the commonest symptoms in AMS, it can be easily distinguished from other forms of headaches by supplemental oxygen.[32, 41] In AMS the headache disappears after 15-20 minutes of giving supplemental oxygen and other condition the headache persist. Supplemental oxygen can be very useful in the diagnosis of AMS in a setting where it is available throughout the elevation route.[41] Other differentials of acute mountain sickness includes, dehydration, viral syndrome, alcohol hangover, physical exhaustion and heat exhaustion.[3, 10, 36, 38, 41, 43]

PREVENTION

The main goal of early prevention and management of AMS is to optimize acclimatization and to manage the AMS and its compilations correctly and timely.[9, 37, 41] There are four guiding principles in management of high-altitude illness;[37]

- Know the early symptoms of altitude illness, and be willing to acknowledge when they are present.
- Never proceed to a higher sleeping altitude with symptoms of high-altitude illness.
- Descend if symptoms do not improve despite expectant management or temporizing pharmacologic treatment.
- Descend and/or treat immediately in the presence of confusion, ataxia, or dyspnea at rest with relative hypoxemia.

Practicing physician or travel medicine specialist most often receives 3 types of clients requesting more information regarding high- altitude travel, the altitude naïve travelers, the returning traveler and potentially risk traveler. The altitude naïve travelers are those who have never ascended to high altitude and always seek advice to ensure a safe trip. The returning traveler who had problems on a prior trip, and seeks information about what happened and how to prevent such problems in the future[42]The potentially risky traveler who has underlying medical problems that may worsen at high altitude or predispose to acute altitude illness. The altitude naïve travelers and potentially risk travelers contribute a lot to high-altitude illness and mortality hence proper risk assessment and counseling is needed prior to their expeditions. For altitude naïve travelers, counselling about the normal changes to expect at altitude and the recognition, prevention, and management of altitude illness is very important.[42] The decision on which preventive management plan should be taken should be based on assessment of risk associated with planned ascent, especially the moderate risk to high risk groups (Table 2). Potentially risky travellers need thoroughly assessment to determine whether underlying condition(s) will worsen at high altitude or affect the risk of acute altitude illness.[4, 42] Underlying conditions that affects the respiratory and cardiovascular systems are to be assessed extensively in a multidisciplinary approach. The risk assessment to these two groups can wither be in a form of questionnaire that assess the risk of severe hypoxemia or tissue oxygen delivery, impaired ventilatory responses to hypoxia, presence of underlying medical conditions considered to be high ascending risk, physical examination and respiratory, cardiovascular and haematological investigations.[4, 42]

There are two approaches in preventing AMS and other high-altitude illness, nonpharmacologic and pharmacologic. Nonpharmacologic prevention measures to AMS includes, graded ascent, preacclimatization and oxygen. [4, 42, 44]

Graded ascent: Prevention of all altitude illnesses requires ascent at a gradual rate allowing time for acclimatization. It is recommended that at altitudes greater than 3000 m, one should not spend subsequent nights 300 m higher than the previous night.[4, 9, 13, 36, 42, 44] A rest day is recommended every 2 to 3 days.[4, 32] Travelers with symptoms of AMS should not ascend until the symptoms are improved. Travelers should be taught the mountaineers rule, "climb high, sleep low".[34] During ascent travelers should advised to do moderate exercise, and avoiding strenuous exercise, doing strenuous exercises has been highly associated with development of AMS, HAPE and HACE.[34, 41, 42] Travelers need to maintain adequate hydration, eating a high carbohydrate diet and avoiding the use of sedative/hypnotic drugs, including alcohol. Over hydration is not effective in preventing AMS, this practice has the potential to cause hyponatremia.[30, 45] Aerobic exercise training offers no advantage for acclimation though it is helpful for trekking and climbing at low and high altitudes.[30] Individuals traveling in organized groups are at increased risk for developing high altitude illness, primarily due to the need to follow an itinerary that may be too rapid for slow acclimatizers.[13, 24, 30, 42]

Preacclimatization: it involves intermittent exposure either to hypobaric hypoxia or normobaric hypoxia through a commercial hypoxia tent, chamber, or mask. These devices vary considerably in hypoxic "dose" (simulated altitude) and exposure time. [30, 41, 42]. Preacclimatization methods are commonly used by commercial guarding companies, the method is not very popular in Kilimanjaro.

Oxygen: To prevent AMS, low-flow oxygen (less than 2 L/min) delivered via nasal cannula, especially during sleep. Oxygen relieves the physiologic stress of hypobaric hypoxia and if used effectively below 3000 m.[32, 41, 42] The method is not commonly used in Kilimanjaro but some commercial guarding companies offer oxygen concentrators to climbers. The use of pulse oximeter in predicting AMS susceptibility has been proven not effective by many researchers.[30]

Pharmacologic: moderate- high risk individuals listed on table 2 above should be advised to use prophylactic medication to prevent AMS.[13, 30, 32, 41] Travelers need to warn also, the use of prophylactic medication is not a guarantee against AMS development.[30, 42] It can only limit symptoms severity. The commonly used prophylactic medication is acetazolamide and to some occasion dexamethasone. [20, 30, 32, 41, 42, 45]

Acetazolamide is a carbonic anhydrase inhibitor, causes metabolic acidosis by increasing renal excretion of bicarbonate.[46] This promotes hyperventilation by increasing hypoxic ventilatory drive and allowing increased respiratory alkalosis. Its actions mimic the natural process of acclimatization.[30, 46] The recommended prophylactic dose of acetazolamide is 125 mg twice daily, increase of dosage to above 500mg should not be recommended as it has been proven to be ineffective in preventing AMS.[4, 30, 32, 42] The pediatric dose is 2.5 mg/kg twice daily up to 125 mg/dose. Acetazolamide doses above 125mg twice daily is associated with parasthesias, commonly affecting fingers and can be confused as early stages of frost bites.[4, 30, 32, 42] The initial dose of acetazolamide should be taken one day before ascent and continued for two days after ascent. If ascent continues, as in trekking or mountaineering, acetazolamide can be stopped after two days at the highest sleeping altitude or at the beginning of descent.[4, 30, 42] Being a diuretic it causes increased urination, it is recommended that the second daily dose should usually be taken at dinnertime rather than at bedtime.[4, 30, 32, 42] Apart from being potent diuretic acetazolamide is a derivative of sulfonamide, it has cross reactivity with sulfa antibiotics e.g. Sulfadoxine, Sulfadiazine and others.[30, 46] Just like other sulfa containing drugs, acetazolamide can cause minor allergic reactions, for travelers with sulfa allergies, they are advised to take a test dose prior to journey. The most common allergic reaction associated the drug is a body rash. [30, 32, 41] Periodic breathing and poor sleep is very common at high altitude and can cause fatigue which later can contribute to AMS, acetazolamide taken in small doses of 62.5 -125 mg orally at dinner time eliminates periodic breathing and improves quality of sleep at high altitude. It is the most preferred drug in managing sleep disturbances at high altitude.[13, 30, 32, 38, 41, 45] The risk categorization and recommendation is summarized on table 4 below.

Table 4

(From Peter H. Hackett, David R. Shlim, Chapter 2, Travel consultation)

Risk category according to table 2 above	Prophylaxis recommendations
Low	Acetazolamide prophylaxis generally not indicated.
Medium	Acetazolamide prophylaxis would be beneficial and should be considered.
High	Acetazolamide prophylaxis strongly recommended.

Dexamethasone, it is not commonly used as prophylaxis, it is recommended to individuals who can take acetazolamide e.g. individuals with history of severe sulfa reactions etc.[9, 13, 16, 30, 32, 38, 41, 45] The mechanism of action unknown but is believed to related to euphoric and antiemetic effects. The drug effectively masks AMS symptoms but compared to acetazolamide, it does not aid acclimatization.[30, 32, 41] Since acetazolamide speed acclimatization and dexamethasone abort illness, the combination of two has been used by some but there are no studies that proves their effectiveness when used in combination (the combination is used in emergency situations only).[13, 30, 41] Dexamethasone should be taken continuously, discontinuation unmasks AMS symptoms causing a "rebound effect." It is recommended mostly to be taken by individuals who do not have time for gradual ascent and who cannot take acetazolamide.[30, 32, 33, 35] The effective dose is 4 mg every 12 hours (or 2 mg every 6 h). This should be taken on the day of ascent since high altitude illness takes several hours to develop. It should be discontinued after 2-3 days at the highest sleeping altitude or when starting descent and should not be used for more than 10 days in order to prevent steroid toxicity and adrenal suppression. The use of dexamethasone is not recommended to children, this is due to safety concerns[30, 32, 33]

Apart from the above, other medication used in AMS preventions includes, Ibuprofen, Ginkgo biloba, Coca tea/leaves and Sorojchi pills. Though used in different part of the world, there are few studies that show their effectiveness. Nifedipine and Salmeterol, Sildenafil and tadalfil are only used in prevention of HAPE and HACE.[30, 32, 41]

Therapeutic approaches after making a definitive AMS diagnosis: Factors influencing therapy for AMS include the severity of symptoms, a prior history of severe high-altitude illness (HAPE or HACE), the altitude at which symptoms present and whether further ascent is planned, treatment options that are readily available, and the proximity to definitive medical care.[36] Higher elevations, greater severity of illness, continued ascent, and a history of prior severe high-altitude illness carry an increased risk of AMS progressing to HACE or the development of concomitant HAPE[32, 36] Many trekking mountains around the world are located in remote areas, with limited medical supplies, the ability to provide definitive medical care becomes more difficult.[29, 43] Lack of continuous oxygen supply and evacuation units in most of these areas make AMS management almost impossible. Kilimanjaro being located in a low income country the evacuation services are only done with walking tour guides and game reserve police. All the evacuation process is done on the stretcher regardless of the altitude. Airlifting operations are rarely done, few commercial guarding companies offer the service and the cost is exorbitant.

Treatment decisions for AMS are relatively straightforward in the hospital setting but not in the wilderness area.[36] It is even more difficult when symptoms are only mild or moderate in severity, the inconvenience of stopping, resting, or descending may not appear worthwhile to the patient or the inexperienced practitioner. [30, 36, 41, 42] Trekking and mountaineering expeditions are best served by employing medical practitioners who have experience in field treatment of high-altitude illness. If these individuals are not available, like in the case of Kilimanjaro trekking, the available inexperienced practitioner is advised to treat any sign of altitude illness conservatively.[30, 32, 36, 41]

Prior to therapeutic treatment, care should be taken to exclude disorders whose symptoms and signs may resemble those seen in AMS and HACE, such as dehydration, exhaustion, hypoglycemia, hypothermia, or hyponatremia.[36] Individuals with altitude illness of any severity should stop ascending and may need to consider descent depending on the clinical circumstances and severity of illness. Treatment decisions should be done after making thorough assessment on the risks and expected complications. In some circumstances patients with AMS can remain at their current altitude and use nonopiate analgesics for headache and antiemetics for gastrointestinal symptom relief; that may be all that is required.[30, 32] The decision making in this circumstances must be very precise and quick to avoid HAPE, HACE and even death [30, 32, 33, 35]

Potential therapeutic options for AMS include the following:

Decent: It is the best treatment of AMS but is not necessary in all circumstances (as discussed above).In case of established AMS diagnosis, the patient should descend until symptoms resolve, unless impossible because of terrain. Symptoms typically resolve after descent of 300 to 1000 m, but the required descent will vary between persons. Individuals should not descend alone, particularly in cases of HACE.[32, 36]

Supplemental oxygen: this is to be done in severe circumstances where descent is not feasible and when patients condition deteriorates very fast (suspecting HAPE or HACE).[30, 41, 42] Unlike at hospitals or large clinics, the supply of oxygen may be limited at remote high altitude clinics or on expeditions, necessitating careful use of this therapy. Oxygen delivered by nasal cannula at flow rates sufficient to raise SpO_2 to 90% provides a suitable alternative to descent (2-15 L/ min to maintain SaO2 of more or equal 90%, until symptoms improve.[32, 41] The problem with this method is, Oxygen tanks are bulky, heavy and often unavailable or in limited quantity. It is advice to use this method in HAPE, HACE and moderate-severe AMS.[32]

Portable hyperbaric chambers: These devices are effective for treating severe altitude Illness but require constant tending by care providers and are difficult to use with claustrophobic or vomiting patients. Symptoms may recur when individuals are removed from the chamber.[36] It is advice that the use of a portable hyperbaric chamber should not delay descent in situations in which descent is feasible. In case Gamow bag and Chambelite are used, 2-15psi should be maintained until symptoms improve or possible descent. The problem with Gamow bag is, it requires continuous pumping to pressurize and ventilate, its effects is short lived and symptoms rebound is common. The method has no proven advantage over oxygen.[36]

Acetazolamide: should also be considered for acute therapy of AMS with moderate or severe persistent symptoms, providing the subject has not been taking the drug prophylactically.[4, 32, 42, 45] For the treatment of AMS, an oral dosage of 125- 250 mg every 12 hours is recommended.[32] The medication can be discontinued once symptoms resolve. Children may take 2.5 mg/kg body weight every 12 hours. Acetazolamide causes paresthesias, poryuria and alters taste of carbonated beverages. It is contraindicated to travelers with history of sulfonamide allergy and in pregnancy.[32, 36] Because up to 90% of acetazolamide elimination occurs via the kidney 50% of clearance depends on tubular secretion, dose adjustments are necessary in renal insufficiency and failure.[36] Patients with a GFR of 10 to 50 mL/min should not take the medication more frequently than every 12 h, while patients with GFR less than 10 mL/min should not use the drug. Patients with preexisting metabolic acidosis should totally avoid the medication.[32] Patients with liver disease should not receive acetazolamide. Because acetazolamide alkalinizes the urine, ammonium ion is diverted from urine to the bloodstream. In the setting of impaired synthetic liver function, the extra ammonium ions cannot be converted to urea and accumulates to levels that can cause encephalopathy. [32, 46]

Acetazolamide should be avoided in patients receiving long-term high doses of aspirin. By decreasing protein binding and renal tubular secretion of acetazolamide, concurrent aspirin use can impair acetazolamide elimination. This leads to a greater degree of metabolic acidosis, which, in turn, increases CNS penetration of aspirin, thereby increasing the risk of aspirin toxicity.[32, 44, 46] It should be avoided or taken with care in patients taking ophthalmic carbonic anhydrase inhibitors (dorzolamide), topiramate and carbamezapine. [44]

Dexamethasone: The corticosteroid dexamethasone is an alternative to acetazolamide for the prevention and treatment of AMS and is the primary drug in the management of HACE (Can be life saving for AMS or HACE).[44] Dexamethasone 4 mg every 6 hours is effective for treatment of AMS. Dexamethasone can be administrated PO, intramuscularly, or intravenously depending on available resources and the presence of vomiting.[41, 44] It's an ideal drug for management of AMS with patients with underlying renal insufficient and hepatic insufficiency. It should be avoided by patients with amebiasis, strongyloidiasis and active peptic ulcers disease or upper GI tract bleeding. Proper dose adjustment should be considered when taken by diabetic patient on medication.[44]

DISCUSSION

Acute mountain sickness, high-altitude pulmonary oedema, and high-altitude cerebral oedema are potentially fatal diseases that are avoidable with appropriate preparation. Many travelers around the world plan their trekking and mountaineering trips without considering the risk of high –altitude illnesses. It's a duty as healthcare practitioners to educate travelers on the risk involved and prepare them whenever they come to public or private health care facilities. Tanzania, Kenya and South Africa being the largest contributors to Kilimanjaro mountaineering expeditions, most of these individuals approach private and public clinics for medical checkup prior to expedition or for routine clinical visits. Providing appropriate education on the risks and prevention of different forms of high- altitude illnesses will be lifesaving to inexperienced travelers.

This Review article is written to assist practitioners caring for people planning to travel or already at high altitude and the general public with Mt Kilimanjaro expedition interest. Itprovides evidence-based guideline for prevention and treatment of acute altitude illnesses, including the main prophylactic and therapeutic modalities for AMS that's fits the Kilimanjaro context. This Review article has highlighted the need of understanding AMS occurring most commonly in Kilimanjaro Mountain.

RECOMMENDATIONS

Since most of AMS, HAPE, HACE cases and deaths goes unreported at Kilimanjaro Christian Medical Centre (the nearest hospital to the mountain), the information in this Review article will be very crucial to practitioners in Tanzania to think about improving high-altitude illnesses reporting and management. Since tourism contributes to large proportional of gross domestic product (GDP) in Tanzania and Kilimanjaro being the number one attraction to tourist visiting the country there is a need of creating a guideline for management of high-altitude Illnesses. .

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