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## Endoscopic findings of acid peptic disease at low and high altitude: Kathmandu versus Rasuwa districts of Nepal

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### Abstract

**Introduction:** Features of Acid Peptic Disease (APD) have specific presentations from low to high altitudes. This study aims to compare the endoscopy findings of APD at low altitudes (Kathmandu Valley) and High Altitudes (Rasuwa District) of Nepal.

**Method:** Endoscopy findings of APD patients from Nov 2017 to Dec 2021 at Manmohan Medical College and Teaching Hospital (MMTH) were reviewed from the data kept in the endoscopy unit to compare the findings among patients from low altitudes (Kathmandu valley) and high altitudes (Rasuwa district). Variables included were age, sex, and endoscopy findings of APD. Microsoft Excel was used for data analysis. Chi-square analysis was used for the association between APD findings and altitude. A p-value  $\leq 0.05$  was considered statistically significant.

**Result:** Out of 2937 APD patients, 1560 (53.1%) were male and 1377(46.9%) female, age 48.5 years (range 16-81) with 2701(91.6%) having endoscopic findings of APD. Among 2701 APDs, 1448 (88.6%) were from the low altitude of Kathmandu valley, and 1253 (96.2%) were from high altitude (Rasuwa district), p-value  $< 0.0002$ . There were 736(50.8%) patients with gastritis from Kathmandu vs. 695 (55.46%) from Rasuwa, followed by gastro-duodenitis 219(15.1%) vs. 32 (2.5%), duodenitis 171 (11.8%) vs. 169(13.5%) respectively.

**Conclusion:** The incidence of endoscopic findings of overall APD was high among patients from the high altitude of Rasuwa district compared to the low altitude Kathmandu valley of Nepal.

**Keywords:** acid Peptic Disease (APD), endoscopy, high altitude, Kathmandu valley, Rasuwa district, Nepal

## Introduction

Peptic ulcer disease (PUD) has a lifetime prevalence of 5–10% globally.<sup>1,2</sup> Prolonged hypoxic exposure compromises the intestinal barrier and alters gut immunological function causing acid peptic disease (APD) including esophagitis, esophageal ulcer, gastritis, gastric ulcer (GU), duodenitis and duodenal ulcer (DU), and gastrointestinal bleeds (GIB).<sup>3,4</sup> The incidence of GIB increases with increasing altitude, a manifestation of “high altitude hemorrhage syndrome”.<sup>4,5</sup> High peptic activity is seen in sojourners but not in acclimatized lowlanders. Furthermore, a high incidence of an acute gastric mucosal lesion (AGML) of up to 16 to 49% has been reported in mountaineers.<sup>6</sup>

Compared to the Rasuwa district, Kathmandu valley is a low-altitude region of bowl-shaped surrounded by the mountain range and populated mostly in the central part at an elevation of 1,425 meters (4,675 ft) above sea level (MASL).<sup>9</sup> The Rasuwa district has 87.4% of its area at 2000 MASL (6,560 ft) ranging from 614 to 7,227 m (2,014 to 23,711 ft).<sup>10</sup> Nepal has a diverse terrain with a majority of the population living in the southern plain almost at sea level, whereas in the northern mountain regions the elevation reaches the world’s highest peak, Mount Everest.<sup>7</sup> We considered “high-altitude” for areas of  $\geq 2,400$  meters (8,000 feet).<sup>8</sup>

There is a lack of reports of endoscopic findings locally about APD from low and high altitudes. This study aims to provide information that may be helpful for the management and planning of APD patients at different altitudes. The findings may be useful for the climbers as well.

## Method

Data of patients aged 16 y and above with a clinical diagnosis of APD who were referred for upper gastrointestinal (UGI) endoscopy at Manmohan Medical College and Teaching Hospital (MMTH), Kathmandu, Nepal, from December 2017 to November 2021 were

retrospectively analyzed. The MMTH is a tertiary care hospital of Nepal Health Care Cooperative Pvt Ltd. The hospital has outreach health camps in the Rasuwa district and arrangements for a referral for the patients. Patients with acute upper or lower GIB, endoscopy findings of mass, or requiring histopathology diagnosis were excluded from the analysis. The Ethics Committee of MMTH IRC (Ref. Num. MMIHS-IRC 693 On 27<sup>th</sup> May 2022) approved the study.

The age, sex, and endoscopy findings of APD, including esophagitis, gastritis, gastric ulcer, duodenitis, and duodenal ulcers were compared among the patients from Rasuwa district (high altitude) or Kathmandu valley (low altitude). Microsoft Excel was used for data analysis for the descriptive (mean and proportion) and Chi-square tests. Statistical significance was set at a p-value  $\leq 0.05$  level.

## Result

Out of a total of 2937 patients, 1634(55.7%) were from Kathmandu and 1303(44.3%) from Rasuwa. Males were 1560(53.1%) and females 1377(46.9%), with a mean age of 48.5 y (range 16-81). Overall 2701(91.9%) had endoscopy findings of APD. There were 88.6% (1448 of 1634) from Kathmandu valley who had APD compared to 96.2%(1253 of 1303) from Rasuwa district,  $p=0.0002$ , Table 1.

Among 2701 APDs gastritis was seen in 1431(53%), followed by duodenitis 340(12.6%), and gastro-duodenitis 251(9.3%), Table 2. Out of 1448 APDs from Kathmandu, 736(50.8%) were gastritis, 219(15.1%) gastro-duodenitis, and 171(11.8%) duodenitis. Among 1253 APDs from Rasuwa, 695(55.5%) were gastritis, 169(13.5%) duodenitis, and 106(8.5%) gastric ulcer, Table 2. Gastritis topped the list in both low and high altitudes. Ulcers were more among patients from Rasuwa compared to Kathmandu, Table 2.

The breakdown of APDs showed gastritis topped the list with 1431(53%), followed by duodenitis 340(12.6%), and gastro-duodenitis 251(9.3%), Figure 2.

**Table 1. Upper gastrointestinal (UGI) endoscopy findings in Acid Peptic Disease (APD), N=2937**

Region	UGI endoscopy, 2937					
	Normal 236(8.1%)	X <sup>2</sup>	P value	APD 2701(91.9%)	X <sup>2</sup>	p-value
Kathmandu 1634	186(11.4)	51.15	0.0000	1448(88.6)	14.08	0.0002
Rasuwa 1303	50(3.8)			1253(96.2)		

**Table 2. The endoscopy findings of APD among patients from a low altitude of Kathmandu valley compared to the high altitude of Rasuwa district**

Endoscopy APD findings	Total 2701		Kathmandu 1448		Rasuwa 1253	
	N	%	N	%	N	%
Gastritis	1431	53.0	736	50.8	695	55.5
Duodenitis	340	12.6	171	11.8	169	13.5
Gastro-duodenitis	251	9.3	219	15.1	32	2.6
D. Ulcer	198	7.3	101	7.0	97	7.7
Esophagitis	194	7.2	91	6.3	103	8.2
G. Ulcer	187	6.9	81	5.6	106	8.5
E. Ulcers	100	3.7	49	3.4	51	4.1

## Discussion

In the present study, 91.6% (2701 out of 2937) of patients with a history of APD had positive findings in upper GI endoscopy. The endoscopy findings of APD were high with 96.2%, i.e., 1253 out of 1303 patients from the high altitude area of Rasuwa district compared to 88.6%, i.e. 1448 out of 1634 from low altitude area of Kathmandu valley in Nepal. The finding of APDs was significantly high among patients from the high altitude of Rasuwa,  $p \leq 0.05$  ( $X^2$  14.08,  $p=0.0002$ ). The endoscopy findings of APD revealed gastritis was the most common finding in overall patients, and also among the patients from high and low altitude areas. The severity of acid peptic activities was more common in patients from the high altitude of Rasuwa with increased frequencies of ulcers, in all locations, i.e., duodenum, stomach, and esophagus compared to the low altitude of Kathmandu valley.

High altitude exposure is associated with a risk of APD and gastrointestinal (GI) bleeding and is thought to be related to hypoxia and cold exposure.<sup>3</sup> The bleeding generally appears within three weeks of altitude exposure and includes hematemesis, melena, or hematochezia.<sup>4</sup> Overall there is an increase in the incidence of peptic ulcer disease by almost three times in the last three decades.<sup>1</sup>

Expanding road, rail, and air networks, as well as mechanized mountain lifts, have seen an increase in travel and residence in high altitudes, resulting in an increased prevalence of APD.<sup>10</sup> This requires a re-look in the management of individuals who develop altitude sickness because historically ibuprofen is often used for the relief of headache and corticosteroid as prophylaxis in acute mountain sickness (AMS), all of which may not be appropriate, especially for individuals with underlying APD; and instead, acetazolamide may be more appropriate prophylaxis for AMS.<sup>11</sup>

Gastrointestinal symptoms of nausea and loss of appetite are further aggravated at altitudes >4000 m and 50-80% may suffer from mucosal gastrointestinal lesions and bleeding, as well as an acute exacerbation of GI disorders, like inflammatory bowel disorders (IBD).<sup>12</sup> Studies indicate that high altitude exposure and systemic hypoxia cause a decrease in blood flow to the gastric mucosa, leading to ischemia and destruction of the mucosal lining.<sup>13,14</sup> The high-altitude polycythemia (HAPC) induces gastric mucosal lesion (GML), and there is up-regulation of apolipoprotein genes APOA4 and APOC3, and down-regulation of gastric intrinsic factor (GIF) in gastric mucosa of GML patients compared to healthy controls (fold change  $\geq 2$ ,  $P < 0.01$  and FDR  $< 0.01$ ).<sup>14</sup>

Gastroscopy findings in two groups of randomly selected 22 native Tibetans with HAPC and 24 healthy controls living on the Tibet Plateau at 3650 m to 4800 m revealed that the HPAC group had significantly higher mucosal hyperemia and edema, and inflammatory lesions in the gastric mucosa compared with controls.

Observations from high altitudes in the Andes reveals there is a higher gastric acid production due to vagal stimulus caused by chronic hypoxia, resulting in a higher incidence of gastritis and duodenitis.<sup>15</sup> The dyspepsia, antral gastritis, mucosal atrophy, and *H. pylori* infection may lead to gastric ulcer perforations when exposed to hypobaric hypoxemia as observed in soldiers stationed at high altitudes (15,000ft). High altitude, hypoxia, and HAPC may cause GI mucosal damage and exacerbate APD.

The present study provides baseline data. Nepal has diverse terrain from near sea level to the world's highest peak of Mt. Everest. Mountain climbing and tourism activities will benefit from further epidemiological studies with the inclusion of wider areas from different altitudes to study the presentation and outcome of APDs. Studies have shown that acute high-altitude exposure is associated with delayed gastric emptying.<sup>16</sup> Neurologic and upper gastrointestinal symptoms like delayed gastric emptying are seen in AMS at high altitudes.<sup>17</sup> There is suppressed gastric motility and emptying due to changes in vagal activity which further results in gastric distension and sensation of satiety at high altitude; thus, an enthusiastic feeding may further aggravate nausea and vomiting which is commonly seen in AMS. In the present study, there were more cases of severe acid peptic activities in patients from the high altitude of Rasuwa compared to Kathmandu valley, with a comparatively higher percentage of ulcers, duodenal (7.7% vs. 7%), gastric (8.5% vs 5.6%) and esophageal (4.1% vs. 3.4%).

Dehydration at high altitudes is common due to decreased oral intake and excessive loss of water in dry cold air. In AMS, the use of

acetazolamide as prophylaxis or treatment may further inhibit bicarbonate excretion in the gastric mucosa, reducing the efficacy of the gastric mucosal barrier, and may cause acute gastritis.<sup>18</sup> Various environmental and pathophysiological factors affect gastrointestinal (GI) function at high altitudes. The physiological effects of hypobaric hypoxia, alterations in dietary habits due lack of varieties of food materials, a large amount intake of alcoholic beverages and Tibetan butter tea, which has large amounts of cooking soda and salt, poor water hygiene, low socioeconomic condition, and effects of malnutrition, and ethnic eating patterns among many groups may also influence GI symptoms and contribute to the development of APD. Dyspeptic symptoms are universal in people living in high-altitude areas.<sup>19</sup> The excessive use of NSAIDs for headaches, for example, in AMS may further aggravate upper GI symptoms. More work is needed to prove the association of sociocultural and food habits which may contribute to the APDs at high altitudes.

The GI symptoms of nausea and vomiting are seen in >80% of mountaineers, and anorexia is because of the effect of leptin and cholecystokinin. The *H. pylori* infection is also reportedly high (95%) in the high-altitude region of Ladakh, India.<sup>19</sup> Functional gastrointestinal disorders (FGIDs) are also reportedly high and reported in up to 39.22% (83 of 212) of Chinese pilots of civil airline companies.<sup>20</sup> At high altitudes, ghrelin concentration causes anorexia and oral intake.<sup>21</sup>

Nepal has a considerable percentage of people living in the mountain region with 15% of the country's total land area being mountainous and including 8 of the world's 14 highest peaks above 8000 meters.<sup>22-24</sup> Mountain tourism is an important activity with an increase in adventure tourism, trekking, and mountain climbing.<sup>24</sup> Mountain activities are an important source of income in Nepal, and the World Bank estimates US\$ 2.2, a significant contribution from the tourism industry contributing 3.6% to the GDP.<sup>25</sup> Thus, there is

a need for in-depth studies concerning differences in presentation and progression of APD and its complications compared to low altitude, especially with increased mountain travel and activities, as well as for the people living at high altitudes.

*Helicobacter Pylori* (H-pylori) infection is widely known to be the cause of APD, and PUD, especially in developing countries where the main route of entry is fecal-oral. The H-Pylori infection is acquired mainly in childhood and is closely associated with health and socio-economic conditions including sanitary conditions. It has been found that living at a higher altitude is associated with a higher H-Pylori infection rate, which is the leading risk factor for gastritis.<sup>26,27</sup>

In this study, we could not assess these parameters because of the lack of details in retrospective data and require further prospective study in a wider population involving different altitudes. Another limitation of this study is that we could not include not analyzing the presenting symptoms of APD, and the clinical outcome after the endoscopic diagnosis of APD, for example, the further evaluation of bleeding and/or mass lesions. Also, we could not analyze the food habits, hygiene, H-Pylori status, etc. among the high vs low altitude areas. A large-scale epidemiological study including a diverse population from different altitudes and regions of Nepal may be needed for an in-depth study of APD including the different presentation of GERD esophagitis, gastritis, and duodenitis.

## Conclusion

The overall endoscopy findings of APD were high with 96.2% among patients from high altitude area of Rasuwa district in comparison to 88.6% from low altitude area of Kathmandu valley. Among acid peptic disease (APD), gastritis topped the list (63.5%) followed by gastric ulcers (22.0%) and duodenitis (8.8%) in high altitude Rasuwa district.

## Conflict of Interest

None

## Funding

None

## Author Contribution

Concept, design, planning: All- DD, RNP, MS, BP, JS; Literature review: DD, JS, PR; Data collection: DD; Data analysis: DD, JS; Draft/revision of the manuscript: DD, JS; Final manuscript: All- DD, RNP, MS, BP, PR, JS; Accountability of the work: All- DD, RNP, MS, BP, PR, JS.

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