ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Seasonal variation in acute variceal upper gastrointestinal tract bleeding: Experience of one decade from Northern India

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Submission: 30-04-2021 Revision: 07-07-2021 Publication: 01-08-2021

ABSTRACT

Background: There have been several reports of seasonal variations in the incidence of esophageal variceal bleeding but the data available from this part of the world is scanty. **Aims and Objective:** We aimed to study whether monthly and seasonal climatic changes during the year have an influence on the incidence of variceal bleeding in our setting and whether a particular time in the year can be defined as a high-risk period for variceal bleed. **Materials and Methods:** Data of all the patients with diagnosis of acute variceal upper gastrointestinal bleed who presented to our endoscopy centre from January 2010 to December 2019 was retrieved and analysed. The demographic data, clinical presentations and seasonal and monthly variation was analysed. **Results:** Out of a total of 10200 patients presenting with upper gastrointestinal bleed during the study time period, 530 patients had a diagnosis of variceal bleed after esophagogastroduodenoscopy (EGD). The majority of variceal bleed patients (48.5%) were seen between May to August months of the year. **Conclusions:** Contrary to the most of the literature which shows increased frequency of variceal bleed during winters, our patients bleed more during the months of May and August. This could be explained on the basis of unique socio-cultural and demographic pattern of this part of the world.

Key words: Acute variceal upper gastrointestinal bleed (AVUGIB); Varices; Seasonal variation; Upper gastrointestinal bleed (UGI Bleed)

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v12i8.36803

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Variceal bleeding (VB) constitutes an important decompensating event in the natural history of cirrhosis and its impact differs whether it presents as an isolated complication of cirrhosis (20% 5-year mortality) or in association with other complications (over 80% 5-year mortality).[1] VB occurs at a rate of around 10%-15% per year and depends on the severity of liver disease, size of varices and presence of red wale marks (areas of thinning of the variceal wall).[2,3] Six-week mortality, which is now recognized as the primary endpoint to assess the impact of therapies for acute VB, ranges between15% and 25%.[4,5] Other factors associated with poor outcomes in patients with VB are the presence of bacterial infections and an HVPG >20mm Hg, which is mostly observed in patients belonging to the CTP-Cclass.[6,7]

There have been several reports of seasonal variations on the incidence of esophageal variceal bleeding. Although seasonal differences are still controversial, many reports suggest that esophageal variceal bleeding occurs more often in winter.

To our knowledge not much experience is available from our country to address this issue. The aim of this study is to assess whether climatic factors throughout the 12 months

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and 4 seasons of the year have an influence on the incidence of variceal bleeding. Anticipation of such variations in the incidence of (AVUGIB) during a particular time or season of the year might allow primary medical care centres and hospitals to adopt related interventions so as to have a favourable impact on management of patients.

MATERIALS AND METHODS

This was a retrospective observational study carried out in the Department of Gastroenterology at Government Medical College Srinagar over a period of ten years between January 2010 to December 2019. This is a tertiary care hospital and runs a 24 x 7 emergency endoscopy services with round the clock availability of an experienced endoscopy staff.

Inclusion criteria

Adult patients (>18 years) of either gender with diagnosis of AVUGIB after UGI endoscopy were included in the study. Patients were included irrespective of cause of portal hypertension i.e. both cirrhotic and non-cirrhotic patients were included. In all UGI endoscopy was performed within 24 hours of admission.

Informed consent for endoscopy was obtained by the endoscopy staff before the procedure. EGD was performed in a standard manner with the patient in the left lateral position after topical xylocaine spray/jelly using *GIF LV1 and GIF Q150 Video endoscope from Olympus optical Co., Ltd., Tokyo, Japan.* Majority of the procedures were done using intravenous midazolam. Intravenous propofol was used in few cases.

Data extracted from their records included gender, age, patient's demographic and clinical characteristic, the date of admission, the background aetiology of portal hypertension and blood tests including liver and renal function tests and parameters of complete blood count.

Patients were categorized into twelve *1-month intervals* and into four *3-month intervals (seasons)*: winter was defined as January-March, spring as April-June, summer as July-September, and autumn as October-December. The data were analysed according to month and season.

This study protocol was undertaken after being approved by the Institutional Ethical Review Board.

Statistical analysis

Collected data was compiled and entered in spread sheet Microsoft excel and exported to Data editor of SPSS computer software, version 20 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables were summarized as frequency and percentage.

RESULTS

Patients' demographic characteristics

A total of 10200 patients presented with diagnosis of UGI Bleed to our endoscopy centre between January 2010 to December 2019.Out of them 530 patients were diagnosed as AVUGI Bleed (Table 1).

Two hundred twenty-two (42%) patients had first episode of variceal bleeding and 58% of patients had recurrent variceal bleeding episode. There were 54% males and 46% females in our study. The mean age was 46.5 ± 12.7 years.

Majority of the patients presented in spring (32 %) season followed by summer (30 %) (Table 2). May (16.6 %) had the highest percentage of cases followed by July (13.2 %) (Table 3).

DISCUSSION

Variceal bleeding is an important landmark in the natural history of cirrhosis with significant morbidity and mortality. Despite improvement in the management strategies, the mortality can still be as high as 15-30 %.[4,8] Various factors predict higher mortality and re-bleed in variceal bleed like severity of liver disease, Hepatic venous pressure gradient (HVPG) > 20 mmHg,[9] diabetes mellitus and serum bilirubin more than 3mg/dl.[10]

Besides these factors, seasonal variation in variceal bleeding has been reported in number of studies with majority of them showing higher frequency of gastrointestinal bleed in winter season.[11-14]Although some literature has refuted any seasonal variation in gastrointestinal bleed.[15,16]

Siddiqui MT et al.,[11] reported a higher frequency of variceal bleeding in December (8.8%) and January (8.7%) compared to a nadir in June (7.8%). A retrospective data from Israel[12] found peak incidence during winter season with significant p-values (= 0.02). Thirteen point five percent cases presented during March while as only 5.7 % cases presented during June. Findings from a Beijing hospital[17] as well as from an European centre[14] also found that the cases of variceal bleeding were significantly higher in cold months (December to April) compared to warmer months (June to September). Exposure to low air temperature (LAT) was found to expose patients to a higher risk of variceal bleeding regardless of Child-Pugh

Table 1: Patient characteristics

Total population studied (AVUGIB cases)	530
First episode	222 (42 %)
Recurrent bleed	308 (58 %)
Gender	
Male n (%)	286 (54 %)
Female n (%)	244 (46 %)
Age in years (mean ±SD)	46.5 ± 12.7
Etiology of Variceal bleed	n (%)
NAFLD	233 (44 %)
HBV	74 (14 %)
HCV	47 (9 %)
ALD	16 (3 %)
EHPVO	32 (6 %)
Others	128 (24 %)

AVUGIB: Acute variceal upper gastrointestinal tract bleeding; NAFLD, non-alcoholic fatty liver disease; HBV, Hepatitis B virus HCV, Hepatitis C virus; ALD, Alcoholic liver disease; EHPVO Extrahepatic portal venous obstruction

Table 2: Distribution of the cases as per the four seasons

	Total	Winter	Spring	Summer	Autumn
Frequency (n)	530	73	169	158	130
Percentage (%)	100	13.77	31.88	29.81	24.52

Table 3: Distribution of the cases on monthly basis

Season	Month	Frequency (n)	Percentage (%)
Winter	January	18	3.39
	February	32	6.03
	March	23	4.33
Spring	April	39	7.35
	May	88	16.60
	June	42	7.92
Summer	July	70	13.20
	August	53	10.0
	September	35	6.60
Autumn	October	53	10.0
	November	21	3.96
	December	56	10.56
	Total	530	100

class score, aetiology of liver disease and concomitant HCC.[13]

Although the exact etiopathogenesis remains unknown for this higher risk of variceal bleed during winter months but various physiological and neuro-hormonal factors have been implicated. During winters, a rise in portal pressure and systemic pressures has been found[18] besides decreased secretion of vasopressin from the posterior pituitary.[19] Another possible factor could be an increased alcohol and calorie intake during festive winter season.

In our study we observed a different pattern of occurrence of variceal bleeding events. We had most of the cases in spring season followed by summer accounting for 32% and30% respectively. On monthly basis, May (16.6%) had the highest percentage of cases followed by July (13.2%). Winter season (January, February and March combined) accounted for 13.4% cases only. Cordero FM et al.,[20] also reported that portal hypertension related gastrointestinal bleeding was mostly seen in the months between April and June.

This uneven pattern could be explained on basis of multiple factors. Kashmir is the northern-most part of India covered with an extensive range of mountains. The temperature during winters goes very low with good amount of snowfall leading to closure of many roads during this season which makes access to health care facilities very difficult. Besides there are only two medical centres capable of managing variceal bleed holistically, ours being one of them. Thirdly, there is migration of population especially friable to warmer provinces during winters. Fourthly, increased alcohol intake during festive winter months does not exist as alcohol intake is a religious and social taboo here.

Bacterial infection is an important precipitating factor in many complications of cirrhosis, including variceal bleeding, hepatic encephalopathy, renal failure and coagulation status.[21] Variceal bleeding is a well-established risk factor for bacterial infection in patients with cirrhosis[22] and conversely sepsis has been found to increase the risk of variceal hemorrhage.[23] Multiple factors operate for increased risk of bacterial infection in cirrhosis like liver dysfunction, portosystemic shunting, increased levels of endotoxins, gut dysbiosis, increased bacterial translocation, cirrhosis-associated immune dysfunction, and genetic factors.[24,25] Endothelins (mostly endothelin-1) released during bacterial infection could also contribute to the initiation of variceal haemorrhage through the induction of cyclo-oxygenase products,[26] such as thromboxane A2 and prostaglandin F2a.

During late autumn and almost whole of the winter season most of the fragile population including patients with chronic diseases like cirrhotic tend to remain indoors. This accounts for the low level of exposure to various pathogens resulting in low levels of endotoxemia.

CONCLUSIONS

We believe unique demographic and socio-cultural factors combined with non-uniform health care facilities are responsible for this unique pattern of variceal bleeding in this part of the world. We recommend optimisation

of management strategies for prophylaxis of variceal bleed such as optimising beta-blocker therapy and variceal ligation could lead to decrease in variceal bleeding and decreased morbidity and mortality in these patients.

ACKNOWLEDGEMENT

The authors are thankful to the record keeping section at the Gastrointestinal Endoscopy section at GMC Srinagar which is a tertiary care hospital in Srinagar, India.

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SAS, BAK, SAK - Concept and design of the study; prepared first draft of manuscript; **SAS, SAK, MYM, NAS, BAK, ZAW -** Interpreted the results; reviewed the literature and manuscript preparation; **SAS, MYM -** Concept, coordination, review of literature and manuscript preparation; **SAS, BAK, SAK -** Statistically analysed and interpreted, preparation of manuscript and revision of the manuscript. All the authors approved the final version of the article for publication.

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Source of Support: Nil, **Conflict of Interest:** None declared.