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Pharmacotherapy of upper gastrointestinal bleeding along with its utility at tertiary care hospital

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ABSTRACT

Acute upper gastrointestinal bleeding (AUGIB) is the most common GI emergency observed with mortality of 6-10% overall. The authors aimed to assess the pharmacotherapy of upper gastrointestinal bleeding along with its drug utility and their performance. A total of 120 patients were enrolled meeting the criteria and observed that the main cause of upper gastrointestinal bleeding was found to be esophageal varices followed by duodenal ulcers.The major contributing factor for UGI bleed was alcohol and smoking. The study revealed that males are predominantly being affected with UGI bleed; probable reasons may be habitual behaviour of the patients. Majority of the population who are affected were associated with comorbidities like hypertension, cirrhosis, jaundice, hepatitis, ulcers and diabetes mellitus. Portal hypertension was the major complication seen among the study population, followed by Jaundice and Ascites.The most common cause of portal hypertension is cirrhosis of liver. As an initial evaluation modality of all our UGI bleed patients were done with UGI endoscopy for both therapeutic and diagnostic purposes. The most commonly prescribed drugs were anti-secretory agents [pantoprazole], mucosal protectants [sucralfate], vasoactive agents [terlipressin], antibiotics [rifampicin, ceftriaxone, metronidazole]. It is observed in the study with high dose of alcohol consumption results into serious complications and increasing mortality and morbidity. In the modern era of medical management, it would be better to deal with rational drug prescription in association with clinical pharmacologist suggestions during medical rounds by clinician.

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INTRODUCTION

Upper gastrointestinal bleeding is gastrointestinal bleeding in the upper gastrointestinal tract, commonly defined as bleeding arising from the esophagus, stomach, or duodenum. Blood may be observed in vomit (hematemesis) or in altered form in the stool (melena). Depending on the severity of the blood loss, there may be symptoms of insufficient circulating blood volume and shock.As a result,upper gastrointestinal bleeding is considered a medical emergency and typically requires hospital care for urgent diagnosis and treatment.Upper gastrointestinal bleeding can be caused by peptic ulcers, gastric erosions, esophageal varices, and

some rarer causes such as gastric cancer (Khamaysi and Gralnek, 2013; Pericleous *et al.*, 2013; Esrailian and Gralnek, 2005).

Gastrointestinal bleeding from the upper tract occurs in 50 to 150 per 100, 0000 adults per year. It is more common than lower gastrointestinal bleeding, which is estimated to occur at the rate of 20 to 30 per 100,000 per year. The risk of bleeding is more common in males and increase with age (Hearnshaw *et al.*, 2010).

Upper gastrointestinal bleed or perforation still carries a finite risk of death. Data published since 2009 suggest that mortality in patients suffering from an upper gastrointestinal bleed or perforation has fallen to 1 in 13 overall but remains higher at about 1 in 5 in those exposed to NSAID's or aspirin. Mortality rates from upper gastrointestinal bleed are 6 to 10% overall (Laine *et al.*, 2018; Lanas, 2010).

Early upper endoscopy [within 24h] is recommended in most patients because it confirms the diagnosis and allows for endoscopic treatment, including epinephrine injection, thermocoagulation, applications of clips and banding. Although administration of proton pump inhibitors does not decrease mortality, risk of bleeding or need for surgery. Despite successful endoscopic therapy, rebleeding can occur in 10-20% of patients; a second attempt at endoscopic therapy is recommended in these patients. Arteriography with embolization or surgery may be needed if there is persistent and severe bleeding (Tripathi *et al.*, 2015; Hearnshaw *et al.*, 2011; Worthley and Fraser, 2005).

Aim

To assess the pharmacotherapy of upper gastrointestinal bleeding along with its drug utility and their performance.

Objectives

1. To evaluate the treatment approach used in patients of acute upper gastrointestinal bleeding.

2. To determine the utility of the drugs.

3. To evaluate prescribing pattern according to WHO list of essential drugs.

4. To find the causes of upper GI Bleed.

5. To assess Severity stratification.

MATERIALS AND METHODS

Study protocol

It is a prospective, observational study conducted for a period of 6 months. Patients who have meet the study criteria were included in the study. The required data was collected for evaluating pharmacological therapy of upper gastrointestinal bleeding and their utility and effectiveness.

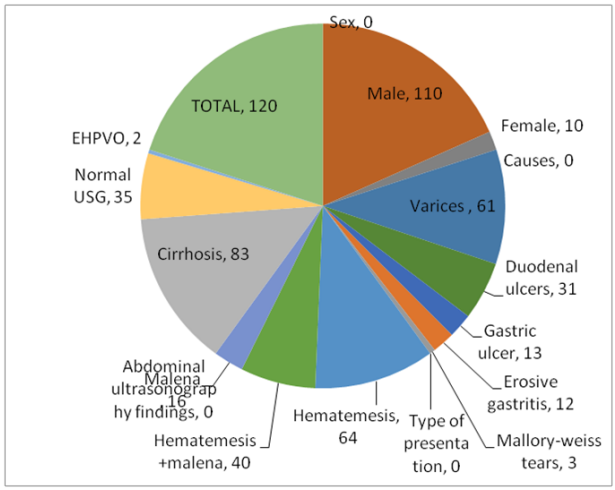

Figure 1: Comprehensive table of various characteristics of patients with UGI bleed

Study design

It is a prospective observational study/cross-sectional study.

Study site

The study was conducted at Gandhi Hospital, Hyderabad, Telangana, India.

Study period

For a period of 6 months.

Study population

120 patients were taken.

Study criteria

Inclusion criteria

1. Patients with complications of upper gastrointestinal bleeding are included.

2. Patients with a history of GI bleeding.

3. Patients, both male and female above 5 years of age.

4. Patients exposed to at least one or more of the risk factors are to be included, and patients who are not in ICU or not on Ventilatory support.

Exclusion criteria

1. Patients who were not willing to participate in the study or no scope for follow up.

2. Patients who refuse to take medications.

3. Pregnant, lactating women and pediatric patients.

RESULTS

The total sample size was120. And the software used - SPSS version 20 and graph pad prism 8.3.1.P-value < 0.05 is considered significant since the confidence interval is 95%.

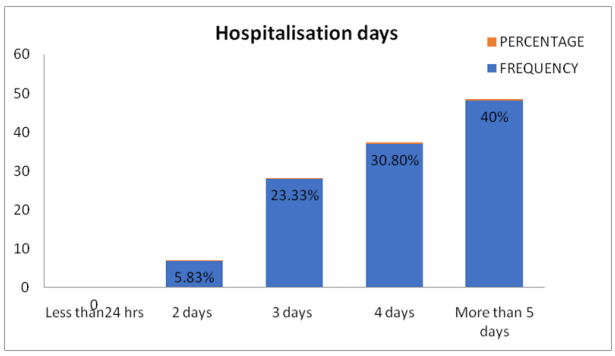

Figure 2: Days of hospitalisation of UGI bleed patients

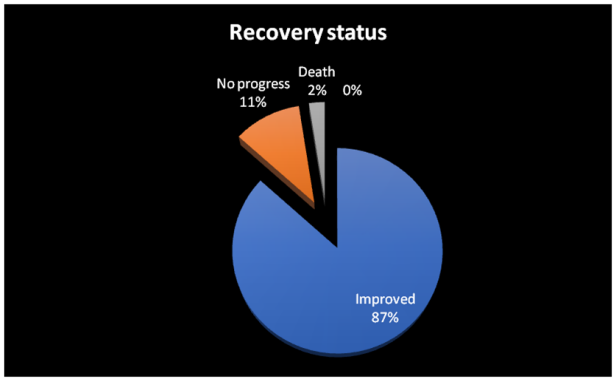

Figure 3: Recovery status of UGI bleed patients

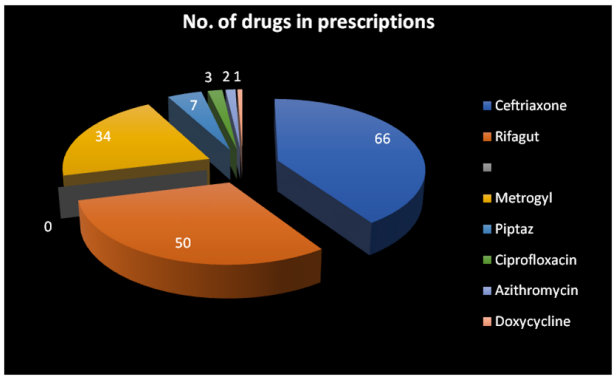

Figure 4: Distribution of antibiotics in UGI bleed patients

Table 1 shows the gender-wise distribution of UGI bleeds patients in the gastroenterology department. Among 120 total population, there are 110 male population followed by 10 female population. Table 2 shows the distribution of patients based on their age group. The patients age group between 5-10 years includes 1 patient, age group between 10-15years includes 2 patients, age group between 15-20years includes 10 patients and age group above 35years includes 70 patients. Table 3 shows the P-value calculated by independent t-test. A statistically significant difference was not found in the age between the genders. Table 4 shows the P-value calculated by the chi-square test. A statically significant difference was found in alcoholic status. Table 5 shows the P-value calculated by the chi-square test.A statically significant difference was found in smoking status. Table 6 shows the comorbidities of UGI bleed patients in which cirrhosis ranges about 35.8%; hypertension ranges about 29.1%. Table 7 shows the social history of UGI bleed patients in which the alcoholic patients' percentage ranges about 43.3%, smoking and alcoholic patients percentage ranges about 21.6%.

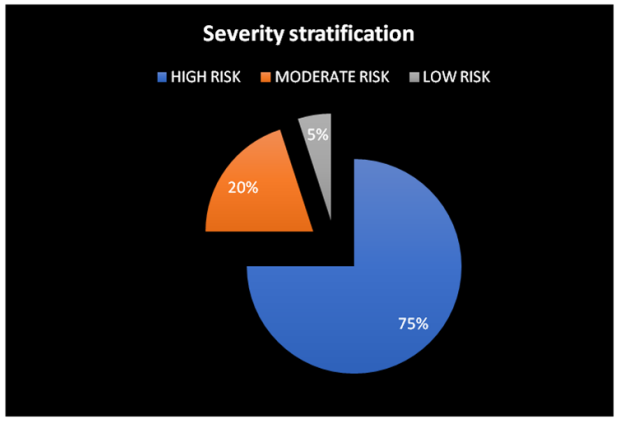

Figure 5: Severity stratification

Table 8 and Figure 1 pie-chart represents the various characteristics of patients with UGI bleed. The main causes observed through endoscopic findings, where oesophageal varices (50.8%) followed by duodenal ulcers (25.8%) were the main causes reported from the study. The type of clinical presentation reported with abdominal pain (75%), chest pain (66.6%), fever (58.3%), loss of sensorium (54.1%), hematemesis (53.3%), SOB (shortness of breath) (51.6%), hematemesis+ melena (33.3%), melena (13.3%).Cirrhosis (69.1%) is the major finding observed in abdominal USG.

Figure 2 graph represents the hospitalization days of the UGI bleed patients. The majority of the patients were hospitalized for more than five days. Table 9 shows the recovery status of the study population, where 86.6% of the study population were improved.

Figure 3 pie-chart represents the recovery status percentages of UGI Bleed patients in the gastroenterology department. Significant improvement was observed in a majority of the patients. Table 10 rep-

Table 1: Demographics of UGI bleed patients (gender-wise)

Gender	No. of patients	Percentage (%)
Male	110	91.6
Female	10	8.3
Total	120	100

Table 2: Age-wise demographics of UGI bleed patients

Age group	No. of patients	Percentage (%)
5-10 Years	1	0.83
10-15 Years	2	1.66
15-20 Years	10	8.33
20-25 Years	7	5.83
25-30 Years	12	10
30-35 Years	18	15
Above 35 Years	70	58.3

Table 3: Gender wise age distribution

Gender	Frequency	Minimum	Maximum	Mean±SD	P-Value
Male	110	9 Yrs	80 Yrs	66.33±11.868	0.0001
Female	10	11 Yrs	50 Yrs	23.66±12.89	

Table 4: Gender wise alcoholic distribution

Gender	Alcoholic status		P Value
	Alcoholic	Non-alcoholic	
Male	90	20	0.0001
Female	3	7	

Table 5: Gender wise smoking distribution

Gender	Smoking status		P VALUE
	Smokers	Non-smokers	
Male	89	21	0.0112
Female	1	9	

Table 6: Comorbidities of UGI bleed patients

Comorbidities	No. of patients	Percentage (%)
Cirrhosis	43	35.8
HTN	35	29.1
DM-2	18	15
Jaundice	5	4.1
Hepatitis	3	2.5
Ulcers	2	1.6

Table 7: Type of social history of UGI bleed patients

Type	No. of patients	Percentage (%)
Alcoholic	52	43.3
Smoking and alcoholic	26	21.6
Non- alcoholic	21	17.5
Smoking	21	17.5

Table 8: Comprehensive table of various characteristics of patients with UGI bleed

Different variables	No. of patients(n)	Percentage (%)
	Sex	
Male	110	91.6
Female	10	8.3
Causes		
Varices	61	50.8
Duodenal ulcers	31	25.8
Gastric ulcer	13	13
Erosive gastritis	12	10
Mallory-Weiss tears	3	2.5
Vascular malformations	0	0
	Type of presentation	
Abdominal pain	90	75
Chest pain	80	66.6
Fever	70	58.3
Loss of sensorium	65	54.1
Hematemesis	64	53.3
SOB	62	51.6
Hematemesis+malena	40	33.3
Malena	16	13.3
	Abdominal ultrasonography findings	
Cirrhosis	83	69.1
Normal USG	35	29.1
EHPVO	2	1.6
Total	120	

Table 9: Recovery status

Recovery status	No.of patients(n)	Percentage (%)
Improved	104	86.6%
Other compilations	13	10.83%
Deaths	3	2.5%
Total	120	100

Table 10: Drug distribution based on the severity

Drugs	Severity					
	High		Moderate		Mild	
	No. of patients	percentage	No. of patients	percentage	No. of patients	percentage
PPI	85	70.8%	20	16.6%	04	3.3%
Antacids	3	2.5%	4	3.3%	1	0.83%
H2 blockers	1	0.83%	0	0%	0	0%
Mucosal protectants	0	0%	0	0%	1	0.83%

Table 11: Distribution of antibiotics in UGI bleed patients

Drugs	No.of drugs in prescriptions
Ceftriaxone	66
Rifagut	50
Metrogyl	34
Piptaz	07
Ciprofloxacin	03
Azithromycin	02
Doxycycline	01

Table 12: Blood urea nitrogen[BUN]

Threshold (mg/dl)	No.of patients(n)	Percentage
6.5-7.9	03	2.5%
8.0-9.9	04	3.3%
10-24.9	23	19.1%
>25	90	75%

Table 13: Hemoglobin

Threshold [g/dl]	No. of patients(n)	Percentage
12-13	24	20%
10-11.9	16	13.3%
<10	80	66.6%

Table 14: Systolic blood pressure

Threshold [mmHg]	No.of patients(n)	Percentage
100-109	95	79.16%
90-99	15	12.5%
<90	10	8.3%

Table 15: Various characteristics of UGI bleed patients

Variables		No. of patients (n)	Percentage
Melena	Present	56	46.6%
	Absent	64	53.3%
Hepatic disease	Present	74	61.6%
	Absent	46	38.3%
Cardiac failure	Present	03	2.5%
	Absent	117	97.5%

resents the drug distribution in UGI bleed patients based on their severity, in which most of the patient population were treated with proton pump inhibitors. Table 11 shows the distribution of antibiotics in UGI bleed patients in which most of the study population were treated with ceftriaxone, metrogyl and rifagut. Figure 4 pie-chart represents the distribution of antibiotics in the UGI Bleed patients.

Figure 5 pie-chart represents the severity stratification of the UGI bleed patients, where 75% of the patients were categorized under high risk.

Table 12 shows the abnormalities of blood urea nitrogen [BUN], where 75% of patients were observed with >25mg/dl, which is to be considered. Table 13 shows the abnormalities of haemoglobin levels where 66.6% of patients were observed with <10 g/dl, which represents the severity. Table 14 represents the systolic blood pressures of UGI bleed patients. About 79.16% of the patient's systolic blood pressure range were found between 100-109 mmHg. Table 15 shows the various characteristics of UGI bleed, in which the presence of hepatic disease in the study population was found to be 61.6%, and the presence of cardiac failure in the study population was found to be 2.5%.

DISCUSSION

The study population includes 120patients diagnosed with upper gastrointestinal bleeding, out of which 110 were of male patients and 10 were female. The majority of the population belongs to the age group of above 35 years (58.3%), and the rest of them are 30-35 years(15%).The present study reveals that males were predominantly being affected with UGI bleed; probable reasons may be the habitual behaviour of the patients.

Among all the UGI bleed patients, the comorbidities associated with them were cirrhosis (35.8%), hypertension (HTN)(29.1%), diabetes mellitustype-2 (DM-2)(15%), jaundice(4.1%), hepatitis(2.5%), ulcers(1.6%). Above mentioned non-communicable diseases were being associated with smoking and alcohol consumption. Among all UGI bleed patients in the GE department evaluated to understand the specific causations and association suggested that alcoholic was 43.3%, non-alcoholic was 17.5%, both smoking and alcoholic was 21.6%, and only smoking was 17.5%.

In our study, predominant causes of UGI Bleed among all 120 patients those of descending order of occurrence; Esophageal varices 50.8%, duodenal ulcers 25.8%, gastric ulcers 10.8%, erosive gastritis 10%, Mallory-Weiss tears 2.5%. Portal hypertension was the major complication seen among the study population, followed by jaundice and as cites. The most common cause of portal hypertension is cirrhosis of the liver. In this, the important pathogenic mechanism is being scarring of liver tissue followed by repair of injury resulting in resistance to portal blood flow, which leads to an increase in portal blood pressure in the portal vein.

In this study, diabetes mellitus and hypertension were the most common co-morbidities which already existed in our patients prior to the diagnosis. In our evaluation as alcohol consumption is the commonest association in diabetes mellitus and hypertension.

The total hospital stay among all the bleeding patients were segregated into no. of days in respective to their severity; following severedisease-40%,moderate-30%, mild-25%. Among all 120 patients,104 patients were recovered, 13 patients were reported with other complications such as hepatic encephalopathy, and 3 patients were died. The hospital stay was based on their recovery status and their response to treatment.

On detailed observation of prescription pattern like an average number of drugs per prescription is 2.02, which is an acceptable pattern by WHO. In our observation of this study suggests that no such Prescription has taken place with generic drug prescriptions in our patients, as and when generic drug prescription done will further give us the rational use of drugs with regard to safety and efficacy.

Of 120 cases in the gastroenterology department,the most commonly administered drugs for high-risk patients were terlipressin and for moderate and mild were H_2-blockers, antacids, mucosal protectants. Terlipressin and pantoprazole were prescribed more because of its effectiveness in controlling the disease.In our study, among the total number of UGI bleed patients receiving antibiotics in an order of priority like ceftriaxone-66, rifaximin-50, metronidazole-34, piperacillin-7, ciprofloxacin-3, azithromycin-2. They are mostly used to reduce the infection.

As the symptomatic evaluation suggest that the commonest symptom is being abdominal pain-90, chest pain-80, fever-70, loss of sensorium-65, hematemesis-64, SOB-62, hematemesis and melena-40, only melena-16.

Among 120 patient population, the patients at high risk were found to be 75%, patients at moderate risk were found to be 20%, and patients at low risk were found to be 6%. Severity stratification was determined by following a full rock-all score.

CONCLUSION

This study highlights the need to minimize the percentage of antibiotics per prescription. Therefore, a strict protocol for prescribers and clinical pharmacologist is required to promote the rational use of antibiotics, which would not only prevent antibiotic resistance but also reduce the treatment expenditure in this modern era of medical management. Though the appropriateness of the antibiotics prescribed was evaluated, the need for the introduction of guidelines for prescribing antibiotics and the role of Hospital Antibiotic Policy must be made mandatory with implementation.

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Declarations

Author contribution

All authors contributed to research work, data collection, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Declaration of competing interest

The authors report no conflicts of interest in this work.

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