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Emerg Med J 2010 27: 504-507 originally published online June 1, 2010
doi: 10.1136/emj.2009.075820

Circadian and seasonal rhythms of acute upper gastrointestinal bleeding in Beijing

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Accepted 11 June 2009
Published Online First 1 June 2010

ABSTRACT

Objective To investigate the circadian and seasonal patterns in the presentation of acute upper gastrointestinal bleeding (AUGIB) in Beijing, China.

Methods Medical records of the Beijing Emergency Medical Service System (EMSS) for 1 August 2005 to 31 July 2007 were reviewed; all patients diagnosed with AUGIB were included in the study.

Results 2580 patients were recorded in the EMSS system with a diagnosis of AUGIB during the study period. 1888 (73%) were male and 692 (27%) were female. Mean age was 53±20 years for male patients and 63±21 years for female patients. Significant differences in the presentation of AUGIB were noticed between seasons ($p<0.001$) and months ($p<0.001$). The number of cases in cold months (from December to April) was significantly higher than that in warm months (June to September). There was a significant circadian rhythm; there were fewer cases during daytime hours compared with night-time hours ($p<0.001$).

Conclusions The presentation of AUGIB in Beijing has a clear seasonal and circadian rhythm. Circadian and seasonal rhythms associated with AUGIB may aid in identifying modifiable risk factors in individuals and populations.

INTRODUCTION

Despite improvements in both diagnostic and therapeutic management, acute upper gastrointestinal bleeding (AUGIB) remains a challenging and common emergency. In the middle of the last century, the seasonal variation in the incidence of bleeding of peptic ulcer was suggested by Bandler.[1] During the following 50 years, seasonal and circadian rhythms of AUGIB have been investigated repeatedly, but results are variable. Herein, we present our findings on the pre-hospital epidemiology of AUGIB in Beijing with respect to both seasonal and circadian rhythm. While seasonal variation of AUGIB has been reported, the mechanisms of this variation remain unclear. A systemic review of previous investigations was done and potential pathological mechanisms discussed.

METHODS

Study population

To investigate the circadian and seasonal rhythm of the presentation of AUGIB in Beijing, electronic medical records from Beijing's Emergency Medical Service System (EMSS) were retrospectively reviewed between 1 August 2005 and 31 July 2007. This EMSS is a centralised pre-hospital network serving all of the Beijing metropolitan area. Each ambulance is staffed with an emergency trained physician. Pre-hospital diagnosis was usually made by an EMSS physician based on history and bedside physical examinations (eg, haematemesis). To be included in the study, all of the following had to be available from the pre-hospital medical records: diagnosis of AUGIB; age and sex of the patient; and time of occurrence of AUGIB. Dates and times were extracted from the records for the purpose of the present study. Demographic data (in the year 2006) of population ratio of age groups and gender groups were obtained from the website of the Beijing Statistical Information Net (http://www.bjstats.gov.cn/tjnj/2006-tjnj/).

Data collection and statistical analysis

Each case had a day, month, season and the hour of occurrence assigned to it for statistical analysis. Seasonal periods were divided as usual: spring (March to May), summer (June to August), autumn (September to November), and winter (December to February). χ^2 Test was used to examine the differences of occurrence of AUGIB between seasons, months, and time periods of a day. Because there was no predetermined prediction about the comparisons, 2-tails were used to measure significance during hypothesis testing. A $p<0.05$ was considered statistically significant. All analyses were carried out with the software SPSS (Statistical Package for Social Sciences) 11.5 (SPSS Inc.). All protocols and procedures were approved by the human studies research committee of Peking Union Medical College prior to the advent of the study.

RESULTS

Demographic distribution of AUGIB cases

A total of 355 418 electronic medical records in Beijing's EMSS during the study period were reviewed; 2580 patients met the inclusion criteria. As expected, AUGIB was more common in men than in women: 1888 (73.2%) and 692 (26.8%), respectively. The mean age of all patients was 56±21 years (63±21 years for women and 53±20 years for men).

The occurrence of AUGIB has a high prevalence in aged populations. Sixty-four per cent of AUGIB occurred in people older than 50 years, with a peak incidence during the 7th decade. The frequency of AUGIB clearly accelerates after the 6th decade. When the frequency of AUGIB was adjusted by the percentage of the decade to the total population, a definite increment of episodes was noted with increasing age. There was an approximate exponential increase ($R^2=0.965$, $p<0.001$) with curve

estimation regression when average age of each group was considered as the variable (figure 1).

The seasonal and circadian rhythm of AUGIB

Significant differences were found among the cases occurring per season (χ^2=102.715, p<0.001). A higher incidence of AUGIB was observed in winter and spring while the lowest incidence of AUGIB occurred in summer (figure 2A). Also, significant differences were found among the cases occurring between each month (χ^2=197.240, p<0.001). Overall, the peak number of cases occurred in January and the cases per month reached a nadir in August (figure 2B). Patient gender had no influence on the incidence of AUGIB in men and women during any given month. Patterns for male and female patients were the same with regard to monthly variation (r=0.97, p<0.001 and r=0.75, p<0.001, respectively). The peak month of female cases occurred in January with a nadir in September. For men, the highest incidence was in April with the nadir in August.

With respect to circadian rhythm, during the six 4-hour periods of a 24-hour clock, a lower number of cases were recorded during daytime hours than at night (χ^2=84.594, p<0.001) (figure 2C). The occurrence of AUGIB was significantly higher between 16:00 to 04:00 than that between 04:00 to 16:00, with a peak incidence between 20:00 and 24:00.

DISCUSSION

Several investigations have observed the circadian and seasonal patterns of AUGIB, but most data were from mixed populations of acute and scheduled inpatients of single or multiple hospitals. Our study is unique in that our data are from the entire Beijing metropolitan area with cases initially tracked from pre-hospital records of Beijing's EMSS.

The resident population in Beijing is approximately 16 million people, with the Han ethnic population accounting for about 95% of the population. During the study period, there were no significant social events such as SARS or the Olympic Games which could lead migration or other significant changes in the composition of the population in Beijing. Since upper gastrointestinal bleeding (UGIB) is generally thought to have an incidence of about 50–100 per 100 000 people per year[2] and we identified 2580 cases of AUGIB, our sample might represent between 8% and 15% of total AUGIB cases in Beijing in the study period.

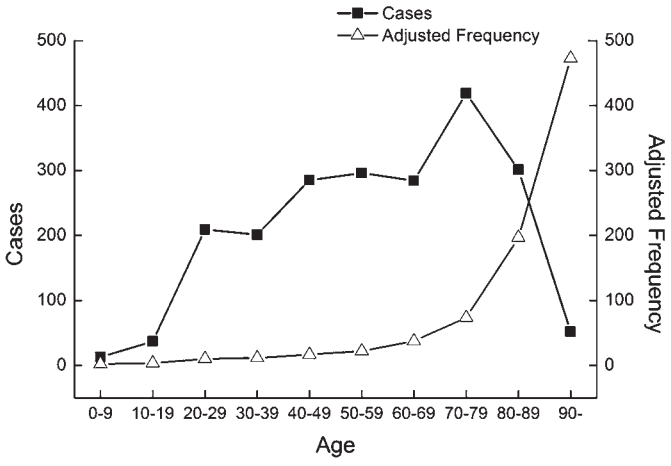

Figure 1 Cases illustrated as a function of each decade of age for the study population of 2580 patients. Adjusted frequency of acute upper gastrointestinal bleeding (AUGIB) for each decade shows a non-linear increase as age increases (approximate exponential increases). Adjusted frequency, cases of each decade of age/population ratio of the decade of age to total population, corresponding to relative incidence number of AUGIB in unit number of population of the respective age range for the study population.

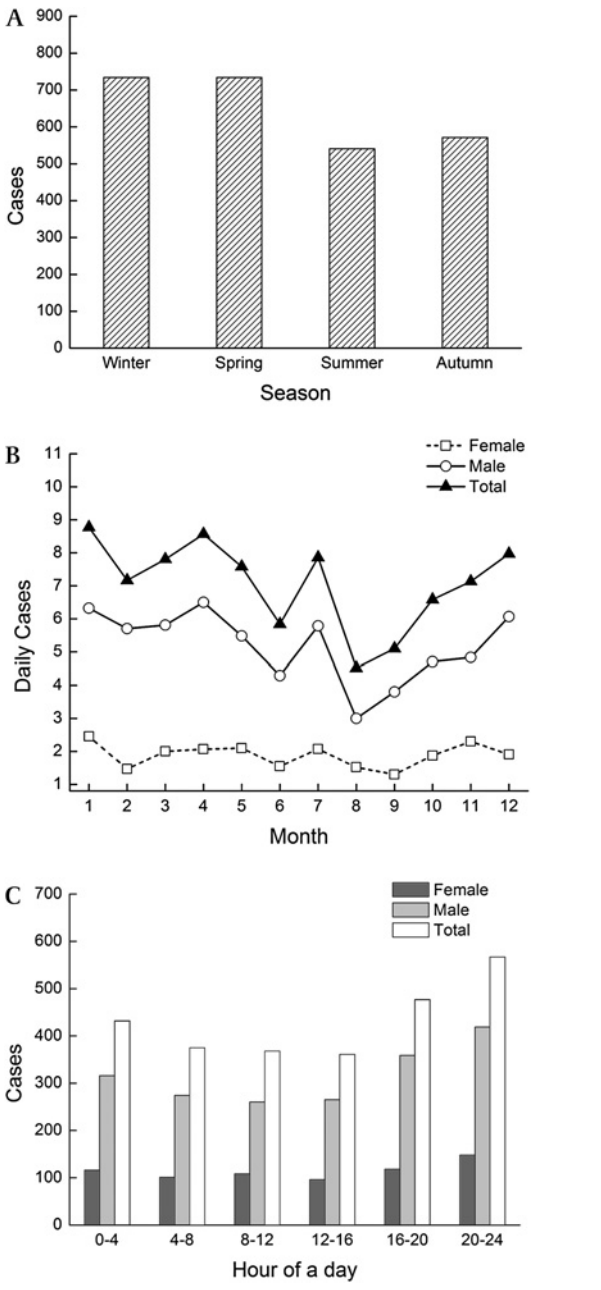

Figure 2 (A) Seasonal variation of acute upper gastrointestinal bleeding (AUGIB) incidence. (B) Monthly variation in the incidence cases of AUGIB. (C) Circadian variation in the incidence of cases for each 4-hour period on a 24-hour clock. Each column represents a 4-hour period. The case numbers were clearly lower during daytime hours and were higher at night.

In a previous report from 15 major hospitals in Beijing, the causes of 5191 cases of UGIB were reported with endoscopic examination. Peptic ulcer accounted for 48.7%, variceal bleeding for 25.4%, gastritis for 4.5%, and malignancy for 3.1%.[3] From the above proportion, we would expect that our results are reflective of the seasonal and circadian rhythm of bleeding for severe peptic ulcer disease and bleeding varix in the Beijing population. Nevertheless, mucosal damage is common in patients with hepatic cirrhosis.

Demographic distribution

In our study of 2580 AUGIB cases, male patients accounted for about three-quarters of all the AUGIB patients. This result is similar to prior studies carried out in other countries. The adjusted occurrence frequency of AUGIB during each decade of age showed that a rising relative risk of AUGIB with age is not unexpected.[2 4 5] Considering that the ascending curve has an approximately exponential increase (R^2=0.965, $p<0.001$), it is reasonable to focus on the occurrence of AUGIB in aged people and find modifiable factors that may reduce their risk of AUGIB.

Circadian rhythm

A circadian rhythm of AUGIB in Beijing was observed, with a higher incidence at night and a lower incidence in daytime. The reason of this circadian rhythm is not entirely clear. Nevertheless, several physiological factors related to circadian rhythms may offer a satisfying partial, if not complete, explanation. For example, in patients with or without *Helicobacter pylori* infection, Saitoh *et al* noticed that intragastric acidity increased at night. This may be related to the increased occurrence of peptic ulcer bleeding during the night.[6]

Haemorrhage from gastro-oesophageal varices constitutes a large portion of Beijing AUGIB cases. The circadian distribution of variceal haemorrhage in cirrhotic patients has been reported in several studies.[7–10] These studies showed peak incidence of variceal bleeding at night, although two peaks of bleeding have also been reported.[7 10] García-Pagán *et al* reported circadian variation of portal pressure as a possible influence on the variceal haemorrhage in patients with cirrhosis. The bleeding peak of 22:00 to 23:00 of variceal bleeding was observed concurrent with the portal pressure increases.[9] Alvarez showed no significant changes of cardiac output and portal blood flow in a group of healthy subjects. However, there was a significant circadian rhythm for both portal blood flow and cardiac output with an acrophase at 00:50 in the cirrhotic group.[11] He then further showed that nocturnal propranolol administration can blunt this time-related increase in portal pressures in cirrhotic patients.[12] Furthermore, Piscaglia showed that in cirrhotic patients total fibrinolytic activity reached a peak at about 19:00, and remained at a high level until shortly after 22:00, which may provide another explanation for why variceal haemorrhages tend to occur at night.[13]

Monthly and seasonal rhythm

Our data on the monthly and seasonal variation of AUGIB shows a seasonal rhythm of AUGIB with a greater incidence in January and April, Beijing's coldest months, and the lowest incidence during summer. Many previous investigators have found similar seasonal variation in variously selected populations of patients with upper gastrointestinal pathology of acute or chronic nature.[1 4 5 14–29] These studies may contribute to a biometeorological explanation of the phenomenon. (1) Natelson showed that with cold stress test, the mucosal damage to the duodenum of mice increases, which indicates that the high incidence of duodenal ulcers in cold periods may be associated with the cold stress at the cellular and molecular level.[30] (2) Moshkowitz showed that in dyspeptic patients, *H pylori* infection significantly increased in winter and decreased in summer, which may contribute to the seasonal changes in duodenal ulcer.[31] (3) Xirasagar *et al* showed that the increase in arthritic and respiratory symptoms—with concomitant increase in the use of non-steroidal anti-inflammatory drugs—during winter may be associated with increased ulcerative bleeding.[32] (4) Cold-induced peripheral vasoconstriction may also lead to a shift in blood volume from the body surface to the splanchnic circulation.[33] Consequently portal blood flow increases, leading to aggravation of the portal hypertension and more variceal bleeding. Sato *et al* showed that seasonal changes are prominent, especially in cirrhotic patients with Child–Pugh grade C.[15]

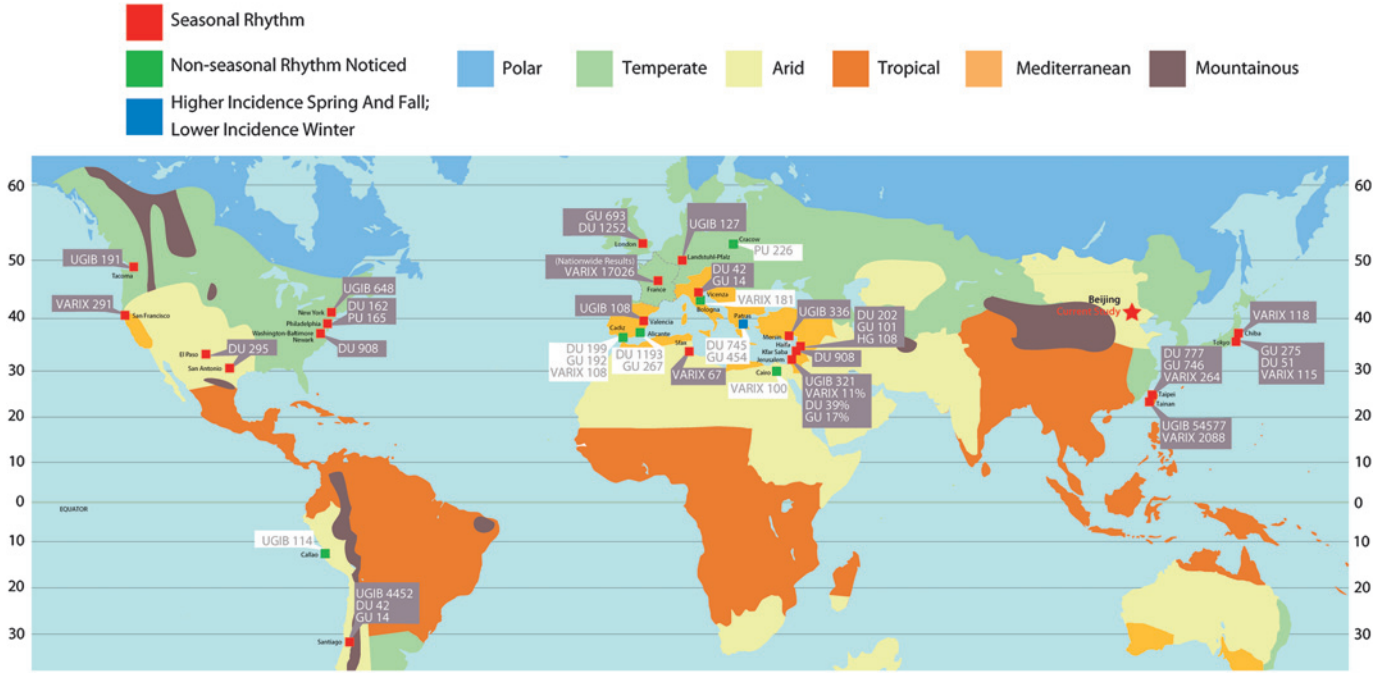

Figure 3 Rhythm of the presentation of upper gastrointestinal bleeding and its geographic distribution with respect to global climatic zones. The majority of studies worldwide have been carried out within a narrow range of latitudes. DU, duodenal ulcer; GU, gastric ulcer; UGIB, upper gastrointestinal bleeding.

We reviewed 26 studies focusing on the seasonal variation of bleeding from gastric ulcers, duodenal ulcers and/or varices.[1 4 5 10 14–29 34–39] These are shown graphically in the map (figure 3). Nineteen of them have comparable results to ours with respect to seasonal rhythms.[1 4 5 14–29] There is a paucity of studies from the southern hemisphere, but one study in Chile showed a similar seasonal variation, with a higher incidence from March to July, the autumn and winter of Chile.[23] Six studies showed no significant seasonal variation in the incidence of UGIB[10 34–38]; four of these were from Mediterranean countries and one from coastal Peru, where winters are mild and relatively warm.[37] A study from Greece showed different seasonal variation of duodenal ulcer, with a lower incidence in winter, and higher incidence in spring and autumn.[39]

One limitation of our study is that all the case documentation started with the emergency medical service, but many other patients reach the emergency department by their own means. Thus, our study is likely to have a selection bias towards more severe episodes of AUGIB. Although this is a limitation in terms of capturing the maximum number of cases, it can be argued that AUGIB is the presentation of most concern and easiest to assign causation in epidemiological studies of this problem in the pre-hospital setting. Another limitation is the absence endoscopic diagnoses in this study.

Our study shows that in the Beijing metropolitan area, the presentation of AUGIB has significant circadian and seasonal rhythms. While the physiological underpinnings of the circadian rhythms associated with AUGIB seem to be reasonably well explained, the seasonal factors are very poorly understood. We note with interest that almost all environmental studies of this important, life-threatening condition have been conducted in a narrow range of northern latitudes. Modifiable risk factors for disease in a larger cross-section of the global population will likely yield insights into population-based risk factors valuable for prediction, prevention and treatment.

Competing interests None.

Ethics approval This study was conducted with the approval of the Peking Union Medical College, Beijing.

Provenance and peer review Not commissioned; externally peer reviewed.

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