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Seasonal Variation in Acute Cholecystitis: An Analysis of Cholecystectomies Spanning Three Decades



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ABSTRACT

Background: Seasonal variation in the occurrence of medical illnesses reflects the effect of the environment, provides insight into pathogenesis, and can assist health care administrators in allocating resources accordingly. Seasonal variation has been reported in various infectious and surgical diseases, but has been rarely studied in acute cholecystitis. Our objective was to study seasonal variation in acute cholecystitis at our institution.

Methods: We performed a retrospective analysis of patients who underwent cholecystectomy for acute cholecystitis from January 1988 to December 2018. Chi-square goodness-of-fit test was used to analyze seasonality of acute cholecystitis adjusting for variation in number of days between seasons. The number of days for seasons were taken as 92, 92, 91, and 90.25 for spring, summer, fall, and winter, respectively.

Results: Overall, 3924 patients underwent cholecystectomy for acute cholecystitis during the study period. The frequency of cholecystectomies performed varied between months (minimum February $n = 259$, maximum July $n = 372$, $P < 0.001$) and seasons (minimum winter $n = 789$, maximum summer $n = 1101$ $P < 0.001$). Age and gender distribution across months and seasons was similar ($P > 0.05$).

Conclusions: Our findings confirm seasonal variation in occurrence of acute cholecystitis with summer season witnessing the most and the winter season encountering the least patients with acute cholecystitis. Validation of our findings through prospectively collected data at national level is the way forward.

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Introduction

Seasonal variation has been described for many communicable, noncommunicable, and surgical diseases.^{1–6} These observations allow better understanding of the causative factors revealing the complex interaction of seasons with human behavioral and physiological changes and their environments.⁷ They also provide insight into the impact of seasons

on health care economics and expenditures,⁸ hence providing crucial data for health care forecasting.⁹

Surgical diseases that have been reported to vary with seasons include surgical site infection, cellulitis, acute appendicitis, and acute diverticulitis, all reported to occur more commonly in summer.^{1,4–6} However, seasonal variation in acute cholecystitis has been rarely studied. An analysis of the National Inpatient Sample database from the United

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States revealed that it was more common in summer compared with winters.⁶

Acute cholecystitis is one of the most common emergency conditions affecting thousands of patients annually. In 2012 alone, 215,995 patients in the United States of America were diagnosed with acute cholecystitis resulting in a direct cost of US \$9.3 billion.¹⁰ Gallstones are the major etiological factor common to many benign biliary tract diseases. Although the pathogenesis for gallstone formation is complex and multifactorial, bacterial infection from intestinal organism such as enterobacteriaceae is considered to be an important pathogenic factor for acute cholecystitis.^{11,12}

Better understanding of the relationship between seasons and occurrence of acute cholecystitis will provide new insight into its pathogenesis and assist epidemiologists, health care administrators, and planners to devise population-based interventions for this common emergency general surgical condition. We therefore performed a retrospective analysis of the seasonal variation of the histopathology-based primary inpatient diagnosis of acute cholecystitis at our hospital.

Methods

We conducted a retrospective study of adult patients who underwent cholecystectomy from January 1988 to December 2018. The study was conducted at the Aga Khan University Hospital in Karachi. The institutional Ethics Review Committee approved the project and exempted it from informed consent. Diagnosis of acute cholecystitis was based on histopathology findings which are used for coding primary inpatient diagnosis at our institution according to the International Classification of Disease system. Patients were identified utilizing version 9 of International Classification of Disease codes 574.0, 574.3, 574.6, and 574.8. The four seasons were defined as spring (March, April, and May), summer (June, July, and August), fall (September, October, and November), and winter (December, January, and February).

SPSS version 21 was used for analysis. Qualitative variables are reported as frequencies and percentages, whereas mean \pm standard deviation was used for quantitative variables. Chi-square goodness-of-fit test was used to assess seasonality of acute cholecystitis adjusting for variation in number of days between seasons. The number of days for seasons was taken as 92, 92, 91, and 90.25 for spring, summer, fall, and winter, respectively. Age and gender were tested for significant impact on seasonality using ANOVA and chi-square test, respectively. *P* value of less than 0.05 was considered significant.

Results

Overall, 3924 patients underwent cholecystectomy for acute cholecystitis during the study period of 31 y. The mean age of the participants was 48.7 ± 13.95 y. Females accounted for 59.0% (2315) of the patients, whereas males were 41.0% (1609). The frequency of cholecystectomies performed varied from a

minimum of 259 in February to maximum of 372 in July. The variations in the frequency of cholecystectomies performed each month was statistically significant (*P* value < 0.001). Figure 1 depicts the monthwise frequencies of cholecystectomies performed for acute cholecystitis. The number of cholecystectomies performed ranged from 789 in winter to 1101 in summer season. Details of the number of cholecystectomies performed in the four seasons is as shown in Figure 2. After adjusting for variability in the number of days in each month, the seasonal variation in the frequency of cholecystectomies performed for acute cholecystitis was statistically significant across the four seasons (*P* value < 0.001). 1.39 times more cholecystectomies were performed for acute cholecystitis in the summer season compared with the winter season. The impact of gender and age on seasonality was not statistically significant (*P* value 0.25 and 0.11, respectively).

Discussion

In this study, acute cholecystitis was seen more commonly in summer than any other season. Although seasonal variation has been described for various other surgical diseases, it has been reported in only one other study so far for acute cholecystitis.⁶ There appears to be a predilection of these surgical conditions for the summer seasons and warmer temperatures. In their study of emergency general surgical conditions of National Inpatient Sample, Zangbar *et al.*⁶ found acute cholecystitis, acute diverticulitis, and acute appendicitis to occur more frequently in summer than in winters. Adler *et al.*¹ from their study of 18,672 admissions for diverticulitis in the United States, Australia, and the United Kingdom found a significant association with the summer season. In a review of eight studies by Fares, acute appendicitis was seen to be more common in summer months.³ Surgical-site infections have also been reported to occur more frequently in summer.⁵ In a population-based study, Peterson *et al.*⁴ found a strong association of cellulitis with warm weather.

In the United States alone, over 1 million cholecystectomies are performed annually, most commonly for symptomatic gallstones.^{13,14} Acute cholecystitis is diagnosed in over 20% of histopathology examinations of gallbladder specimens.¹⁴ Biliary colic, also known as biliary pain, is a noninfectious and noninflammatory condition that occurs when cholecystokinin-induced gallbladder contraction causes gallstones to lodge against the neck of the gallbladder and cystic duct irritating the mucosal lining.¹⁵ This is most commonly diagnosed on histopathology specimens as chronic cholecystitis. On the other hand, bacterial infection with subsequent release of inflammatory mediators results in acute cholecystitis.¹¹ Various different bacteria have been isolated from specimens of bile and gallbladder of patients who suffered from acute cholecystitis.¹⁶ Enteric organisms are the main isolates with gram-negative rods such as enterobacteriaceae isolated in over 70% of patients followed by gram-positive organisms such as enterococcus.¹⁶

Multiple studies have reported seasonal variation in gram-positive¹⁷ and gram-negative¹⁸⁻²¹ bacterial infections as well.

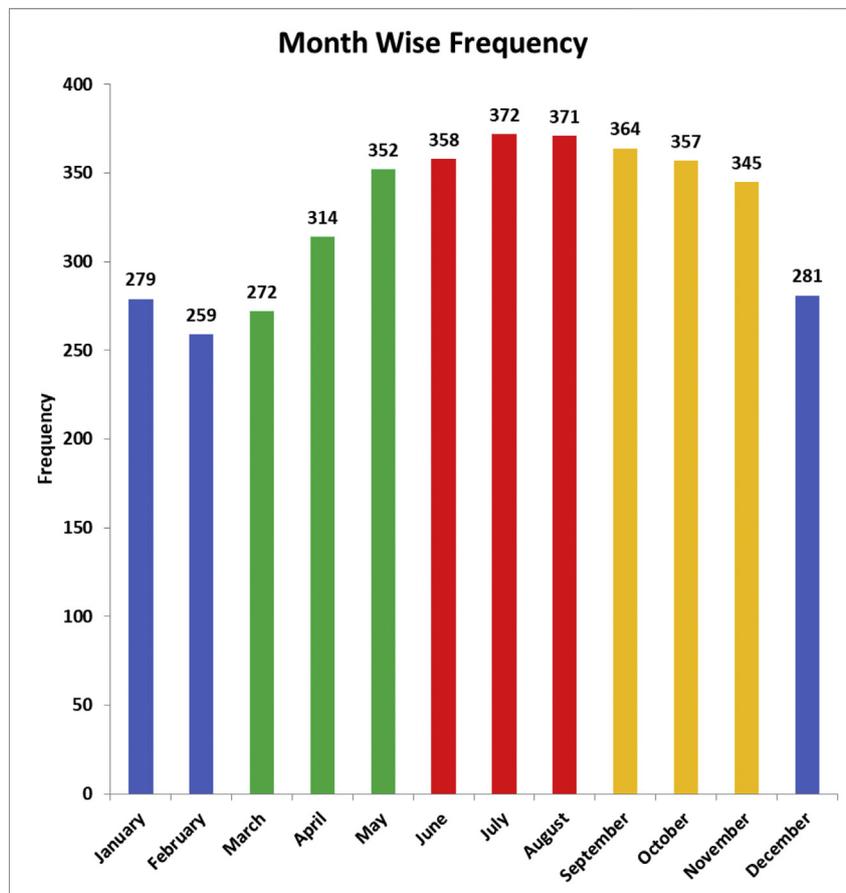


Fig. 1 – Monthwise frequency of cholecystectomies performed for acute cholecystitis over 31 y. $P < 0.001$ (chi-square goodness-of-fit test). (Color version of figure is available online.)

In a study of 188,949 isolates from 73 German Intensive Care Units, Schwab et al.²¹ found a 15% increase in incidence density of gram-negative organisms at temperature of greater than 20°C compared with less than 5°C. Eber et al.¹⁸ in a study of 211,697 inpatient blood stream infections from 132 US hospitals found that for every 5.6°C rise in mean monthly temperature, incidence of gram-negative blood stream infections from *Escherichia coli* and *Acinetobacter* increased by 3.5% and 10.8%, respectively. In England, Deeny et al.²² found that community-acquired blood stream infections from *E. coli* occurred more frequently in summer. Infectious diseases from gram-negative organisms such as urinary tract infections have also been found to occur more frequently in warm weather.²³

Considering the causal relationship of bacterial infection with acute cholecystitis, we can now propose a plausible explanation for the observed seasonal variation. Greater incidence of bacterial infections with a rise in temperature possibly lead more patients to have acute cholecystitis in summer. However, seasonality in infectious diseases is yet a poorly understood and an enigmatic phenomenon. Host behavioral and physiological changes, alterations in virulence of microorganisms, variations in incidence of foodborne illnesses, and changes in immune response are implicated.²⁴⁻²⁷ Thus, a combination of multiple factors is what possibly

results in an increased incidence of infectious diseases during the summer months. Better understanding of the underlying causes offers potential avenues for intervention and prevention of these diseases.

This is one of the two studies that has determined seasonal variation of acute cholecystitis and found a significant association with the summer months. The sample size is large and spans more than 3 decades. However there are certain limitations. Our data are based on inpatient primary diagnosis after cholecystectomy. It is important to note that all patients who develop acute cholecystitis may not have undergone operative management, and therefore, such cases are also not accounted for. This is especially important as the management of patients with acute cholecystitis previously has been with antibiotics and interval cholecystectomy, until recently when index cholecystectomy is performed for acute cholecystitis for most patients. Moreover, other factors that may influence the occurrence of acute cholecystitis such as body mass index and comorbidities such as diabetes mellitus have not been included.

Our findings of seasonal variation in acute cholecystitis provide important information for epidemiologists, public health experts and health care administrators who may devise population-based interventions and allocate resources for prevention and treatment accordingly.

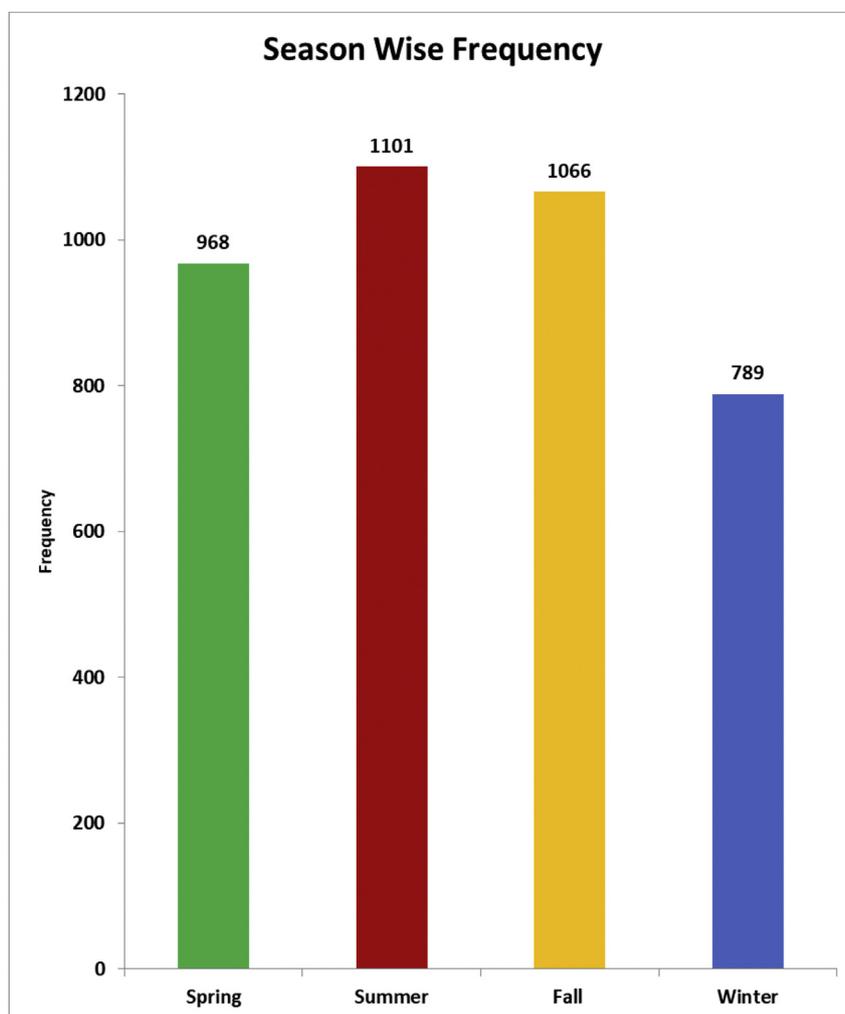


Fig. 2 – Seasonal variation in cholecystectomies performed for acute cholecystitis over 31 y. $P < 0.001$ (chi-square goodness-of-fit test). (Color version of figure is available online.)

Conclusion

Our findings confirm seasonal variation in the occurrence of acute cholecystitis with the summer season witnessing the most and the winter season encountering the least patients with acute cholecystitis. This study provides avenues for further research targeted toward primary prevention of acute cholecystitis.

Acknowledgment

Authors' contributions: Muhammad Sohaib Khan: Conceived, designed, executed and analyzed the project. Prepared and wrote the manuscript. Noman Shahzad: Designed the project, analyzed the data, and edited the manuscript. Sumaiyya Arshad: Executed the project, participated in manuscript preparation. Amir Hafeez Shariff: Supervised the design, execution and analysis of the project and performed critical review of the manuscript.

Disclosure

The authors reported no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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