



REVIEW ARTICLE

Seasonality of Acute Cholecystitis: A Review of Global Patterns

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Abstract

Background: Acute Cholecystitis occurs throughout the year, but some months are associated with higher incidences. The aim of this study is to review prior research, summarise the current knowledge and controversies related to seasonal variability of acute cholecystitis and to examine whether acute cholecystitis has a seasonal pattern.

Material and methods: Studies analysing the seasonal variation of acute cholecystitis were identified from PubMed, Cochrane library and Google Scholar from 1990 to July 2021 with key words. The search was restricted to articles published in English. The references of the identified papers for further relevant publications were also reviewed.

Result: Twelve studies were conducted between the period from 1990 to 2021 from 7 countries around the world (Saudi Arabia, England, Pakistan, Iran, USA, Taiwan and Germany) were reviewed. Acute cholecystitis predominantly peaks during summer season in the revised literature from the studied countries apart from Germany. Cholecystitis occurred more frequently in females in England, Saudi Arabia, Pakistan, Iran and Taiwan. Few studies analysed the association of acute cholecystitis and age; in England and Taiwan it was more common among older patients.

Conclusion: Acute cholecystitis is more common in the summer months. Resource allocation towards the summer months to target seasonal peaks in acute cholecystitis should be considered.

Keywords

Cholecystitis, Epidemiology, Therapy, Seasons, Periodicity

cholecystitis in a particular time of the year is still not clear, several researchers have suggested that the behavioural and environmental risk factors such as temperature, humidity, dietary habits, and hydration can trigger gallstone formation and subsequent acute cholecystitis [1]. Other predisposing factors such as age, sex, genetic, and microbial activities associated with humidity changes are also being suggested by some researchers [2]. To explain the seasonal trend of acute cholecystitis, it is usual to consider that the main cause of acute cholecystitis is intrinsic. Better understanding of the underlying causes could provide insights into the relationship between the physical environment and disease risk, which is particularly important in the context of global ecological change in general, and climate change in particular. The understanding and predictive value of peaks in the incidence of cholecystitis would also assist in judicious allocation of the resources.

The primary aim of this study is to review the literature on seasonal variation in acute cholecystitis in a global setting. We hypothesised that a seasonal variation in incidence does exist. A secondary aim of this study is to summarise current knowledge on the cause of this phenomena by exploring basic biology, immunology and epidemiology.

Material and Methods

A literature search was conducted to identify papers analysing any seasonal variation in the incidence of acute cholecystitis. The studies were identified from a Medline, Cochrane library and Google Scholar search of studies published between 01/01/1990-31/07/2021. The Medical Subject Headings (MeSH) terms were

Introduction

As with many communicable and noncommunicable diseases the incidence of acute cholecystitis rises and falls in an annual seasonal pattern. Although the exact mechanism underlying the fluctuation of

Table 1: Type of study done.

References	Study period	Patients no.	Country	Season peak
[1]	2005-2014	161	Saudi Arabia	Summer
[2]	2014-2016	912	Saudi Arabia	No season
[3]	2010-2019	396 879	England	Summer
[4]	2013-2016	1,417	England	Summer
[5]	1988-2018	3924	Pakistan	Summer
[6]	1999-2004	864	Iran	Summer
[7]	2003-2011	75,585	USA	Autumn
[8]	2004-2011	3,95,838	USA	Summer
[9]	1996-2008	1,92,833	Taiwan	Summer
[10]	2001-2005	398	Germany	No season
[11]	2006-2016	1013	Germany	No season

used in the search including: “Cholecystitis, Acute/diagnosis” OR “Cholecystitis, Acute/epidemiology” OR “Cholecystitis, Acute/surgery” OR “Cholecystitis, Acute/therapy” AND “Seasons” AND “Periodicity”. In addition, the reference lists of the identified studies were manually reviewed to identify relevant articles. Studies were selected based on the following inclusion criteria: 1) Written in the English or German language; 2) Conducted continuously for 1 year or more; 3) The primary outcome was a clinical, ultra-sonographic and laboratory confirmed diagnosis of the diseases of interest in human subjects; 4) Studies used data on patients in primary or secondary care settings stratified by months, weeks, or season; 5) Data collected included the demographic characteristics of the patient, diagnostic and therapeutic interventions, primary and secondary diagnoses on hospital admission or discharge code according to the International Classification of Diseases.

As the majority of the data in this review came from countries in the Northern Hemisphere, seasons were defined based on their occurrence in the Northern Hemisphere: Winter (December-February), Spring (March-May), Summer (June-August) and Autumn (September-November).

Results

A total of 124 studies were identified from the initial Pubmed and Google Scholar search. After screening titles and abstracts, 113 studies were excluded and 11 retrospective studies were included which met the inclusion criteria.

Results from 11 studies using patient’s data ranging from 1990 to 2021 from 7 countries around the world, showed that the incidence of acute cholecystitis acquired from number of hospital admissions and discharge diagnoses (ICD-10: K80.00, K80.1, K80.2, K80.3, K80.4, K80.5, K80.8, K81.0, K81.1, K81.9, K82.2, K82.3, K83.0, K85.1 and ICD.9: 574.0, 574.00, 574.01, 574.3, 574.30, 574.31, 574.6, 574.60, 574.61, 574.8, 574.80, 574.81, 575.0, and 575.12) is highest during Summer season

(Table 1) [1-11]. There is no significant seasonal variation found in Germany [10,11]. One study from the United States of America (USA) noted the high number of hospital admission for acute cholecystitis in Autumn months [7]. Cholecystitis occurred more frequently in females in England, Saudi Arabia, Pakistan, Iran and Taiwan [2,3,5,6,9]. Only limited studies analysed the association of acute cholecystitis and age; in England and Taiwan it was more common among older patients [3,9].

Discussion

A summer peak in the seasonal variation of acute cholecystitis has been identified in 6 countries [1,3-6,8,9]. Although the exact cause is unknown several factors have been suggested to give a plausible explanation.

Dietary factors have been implicated in the pathogenesis of cholelithiasis. A high intake of saturated fat has been linked to an increased risk of gallstone formation. The increasing number of “fast food” restaurants where mainly high-carbohydrate, low-fiber diets, confectionaries and sweets are served, when individuals were most likely to be outside in summer [2], can act as a trigger for gallstone formation and subsequent acute cholecystitis. A positive association between intake of sugars, refined grains, and soft drinks and risk of gallstone formation has been reported consistently [12-15]. The ingestion of refined sugars has been shown to be associated with higher cholesterol synthesis in the liver secondary to increased insulin in response to high sugar consumption, whereas low fiber intakes have been associated with an increase in the risk of gallstone formation because of the resultant increase in secondary bile acid secretions due to decreased colonic motility [12]. Furthermore, a low fiber and high sugar diets can lead to constipation and subsequent crystal formation in the bile [16]. Prolongation of intestinal transit has been proposed as the mechanism for the increase in the proportion of deoxycholic acid in bile. Increases in biliary deoxycholic acid have long

been implicated in the pathogenesis of cholesterol rich gallstones [17]. Alcohol has been linked to an increased risk of constipation. Interestingly, summer time has been observed to be associated with the highest alcohol consumption [17]. This could be contributed in emergency presentation of acute cholecystitis in Summer.

Dehydration during summer can further augment the risk of acute cholecystitis—by causing bile stasis due to decreased gallbladder emptying. The concentrated bile salts produce stones which in turn can cause inflammation of the gallbladder mucosa [18]. Dehydration inadvertently also causes constipation which could also precipitate gallstone formation as explained above.

Bacterial infections are associated with acute cholecystitis due to the release of inflammatory mediators [12]. The most frequent pathogens in biliary infection are gram-negative anaerobes, dominated by *Escherichia coli*, *Klebsiella* spp., *Acinetobacter baumannii* complex and *Enterobacter* spp. [19,20]. Summer peaks of infection by gram-negative bacterial infections have been reported [21,22]. This may give plausible explanation to the predominance of acute cholecystitis notification cases in summer. A higher incidence of bacterial infections associated with a rise in temperature during the Summer months could perhaps explain the higher incidence of acute cholecystitis which is associated with bacterial pathogens.

Inflammatory bowel disease (IBD) is commonly associated with increased risk of cholelithiasis, particularly in patients with Crohn's disease (CD), the etiology is not clear. Terminal ileum dysfunction due to resection or chronic inflammation is thought to contribute to disturbed enterohepatic circulation of bile acid, leading to its depletion. The decrease in the bile acid pool may cause precipitation of cholesterol, initially as crystal and subsequently as cholesterol stones [23]. An additional potential mechanism could be colonization of the terminal ileum by anaerobic bacteria, resulting in deconjugation of bile acids to products that are less well absorbed and have an irritating effect on the mucosa of the gallbladder. Interestingly, the peak of incidence rate of Crohn diseases in most of the countries were found during the spring and summer seasons [24]. How often the Inflammatory bowel disease are responsible for seasonal pattern of acute cholecystitis is unclear. Further studies are required to confirm this hypothesis.

On the other hand, the role of cholecystokinin (CCK) in the expression of seasonal variation of acute cholecystitis has been proposed by several authors [10,25]. Cholecystokinin is a peripheral hormone released by the proximal small bowel in response to fatty and amino acids in a meal, this in turn stimulates the gallbladder to contract and release stored bile into the intestine. If a gallstone is present, it may

lodge against the neck of the gallbladder or cystic duct causing mucosal irritation, which leads cholecystitis. Interestingly, cholecystokinin has been found to exhibit seasonal changes with highest concentrations generally occurring in summer and lowest in winter [25].

In many regions of the world, it is well-established that dietary patterns, body weights and daily energy expenditures vary with the seasons. A marked seasonal rhythm of dietary intakes and weight gain is seen during the Autumn and Winter months [26,27]. In contrast, weight loss is typically observed during the late Summer [26]. Moreover, a variety of studies have noted that cholesterol levels are higher in winter than in summer. In a recent study during Winter, acute cholecystitis rates were at their lowest suggesting that seasonal trends in weight gain, lipid levels and diet may not be the cause [28]. Furthermore, delay in seeking health care in winter and spring season may be the cause and can give plausible explanation to the predominance of acute cholecystitis notification cases in summer months. Authors in Taiwan presented the Traditional Chinese New Year as a factor that may prevent patients from seeking surgical Care. These cultural conditions may predispose Taiwanese to having the lowest incidence of cholecystectomy during February (around the Chinese New Year) [9]. In the contrast, almost no seasonal variations exist in Germany, this may be due to differences in the incidence of cholecystitis or alternatively, to differences in admission policy and patient wish. There are patients who are wished to defer surgery for personal or social reasons, such summer vacation.

Conclusion

Seasonal patterns of acute cholecystitis are quite clearly demonstrated by the epidemiological data; showing a peak during the summer months in all countries included in the study except Germany. The exact reason why acute cholecystitis cases present in summer more than other seasons is still not clear, several extrinsic factors such as, bacterial infection, constipation, dehydration, alcohol consumption and low fiber diet during summer months could contribute to the higher incidence of acute cholecystitis. Further prospective studies are required to define more accurately the possible association between these factors and the seasonal occurrence of acute cholecystitis.

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Nil.

Conflicts of Interest

Authors have no competing interest to declare.

Authors Contribution

All authors contributed to the study conception and design. Literature search and data collection and analysis were performed by Auda Fares, Adnan Taib and Resul

Toprak. The first draft of the manuscript was written by Auda Fares and revised and correction final draft by Adnan Taib all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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