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PROFESSIONAL PAPER

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Risk Factors of Gangrenous Cholecystitis in General Surgery Patient Admitted for Cholecystectomy in King Abdul-Aziz University Hospital (KAUH), Saudi Arabia

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ABSTRACT

Introduction: Gangrenous cholecystitis (GC) is known as perforation and necrosis of the gallbladder wall caused by ischemia ensuing to vascular insufficiency. Gangrenous cholecystitis is associated with a high risk of morbidity. **Aim:** With a percentage of patients needing emergent help, our objective is to determine the risk factor of GC in KAUH. **Methods:** Retrospective review of 334 patients who underwent cholecystectomy during 2016 to 2018 In king Abdul-Aziz University Hospital (KAUH). The data was gained from the medical record of KAUH. The variables are defined as follows: age, gender, AST, ALT, WBC, DM, bilirubin and stone. In order to determine the risk factors that influence (GC). the data entry done by using Google forms while the analysis was done by using SPSS version 21. **Results:** Of 334 patients who underwent cholecystectomy, 57 patient (17.1%) had histologically confirmed gangrenous cholecystitis. Most of them female, 13 variables were identified that were associated with GC by univariate analysis: age 46.8 years, stone (82.5%), bilirubin is normal 9.9, mean white blood cell count 7.8, diabetes, fever, nausea, vomiting, CT finding, asparate aminotransferase, alanine aminotransferase and alkaline phosphatase. **Conclusion:** Patient age was a clear factor for developing GC, male gender was a factor but no correlation was found, normal range of WBC, total bilirubin was in a normal level, vomiting and fever and nausea was less compared to other researchers, at last computed Tomography was not supportive and do not give any importance in detecting GC.

Keywords: Cholecystitis, Gangrene, Cholecystectomy, General Surgery, Risk Factors.

1. INTRODUCTION

The gallbladder is a thin-walled, pear shaped pouch located in the visceral surface of the liver, it stores and concentrates bile secreted from the liver. The bile helps to digest and absorb fats in the small intestine (1).

Gallbladder pathology varies from acute or chronic cholecystitis, cholelithiasis, cholesterosis and gallbladder cancer (2, 3). Acute cholecystitis is commonly due to cystic duct obstruction by stones and less commonly secondary to tumours, infections or being acalculous (4, 5).

Patient with acute cholecystitis usually complain of upper right quadrant pain (RUQ), fever, anorexia, nausea and vomiting. If not treated properly different complications such as mucocele formation, emphysematous cholecystitis, pericholecystic abscess and gangrenous cholecystitis (GC) might develop (3, 6, 7).

The definition of gangrenous cholecystitis (GC) is as perforation and necrosis in the wall of gallbladder caused by ischemia ensuing to end stage vascular insufficiency (8).

In studies done by Shakespeare and Hunt, with 500,000 cholecystectomies for acute and chronic cholecystitis, the incidence of GC varies from 2% to 29.6% of all cases of acute cholecystitis with significant morbidity and mortality (6, 9).

Variables that were associated with GC include age, gender, heart rate (HR), higher blood pressure, cardiovascular diseases, longer delay time prior to hospital admission and presence of diabetes mellitus (10). Conversion from laparoscopic surgery to open surgery, surgical site infection (SSI), as well as white blood cell count (WBC), level of Liver enzyme and gallbladder wall thickening (GBWT) were identified as risk factors affecting mortality (5, 11).

2. AIM

This study aims to determine the risk factor and the incidence of GC in King Abdul-Aziz University Hospital (KAUH) Jeddah, Saudi Arabia, to correlate between intimate factors that increase risk for having GC upon presentation and the necessitates for urgent surgical intervention.

3. METHODS

This study was approved by institutional review board (IRB) of King Abdul-Aziz University hospital (KAUH), Jeddah. A retrospective record review was conducted of Case files from 334 penitents who underwent cholecystectomy procedure in the Department of General Surgery, Faculty of Medicine, at KAU University, between 2016 to 2018. Sex, age, time of hospital admission, accompanying disease, laboratory findings at the admission (white blood cells (WBC), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, alanine aminotransferase (ALT)) and, findings in abdominal computed tomography (CT), length of hospital stay, and mortality rate were recorded for each patient. The group of patients excluded from the study was composed of patients who went for a conservative medical therapy.

The definitive diagnosis of GC was established based on physical examination (pain in the upper right abdominal quadrant, fever), laboratory findings, radiologic findings, and detection of full-thickness necrotic areas along with infiltration by neutrophils and Mononuclear cells.

Statistical analysis

Statistical analysis was performed using the SPSS v21 software package, during the evaluation of the study Results. The Quantitative data were defined as mean 6 SD. P values, 0.05 were accepted to be significant.

4. RESULTS

Total number of 334 patients underwent cholecystectomy over the course of this study, 277 were found to have non-gangrenous cholecystitis and 57 were found to have GC. The risk of developing GC is higher in males compared to females, 23.9% & 14.6% respectively. The mean age of GC compared with to with non-gangrenous cholecystitis is 46.82 and 41.05, respectively (Table 1).

In GC, only 7 patients (15.6%) were found to have DM unlike the 273 patients with non-gangrenous cholecystitis, none of whom had DM as shown in Table 2 as risk factor in addition to smoking and alcohol intake.

Liver function tests were found to be in normal range in those patient with GC, ALP ($\mu = 87.82$), ALT ($\mu = 31.44$) and AST ($\mu = 25.37$). Mean WBC and serum bilirubin was less than 11000/mm³ & 20.5 μ mol/L respectively (Table 3).

On Table 4 the types of cholecystitis show the majority

		Gangrenous or not			
		Yes		No	
Gender	Male	21	23.9%	67	76.1%
	Female	36	14.6%	210	85.4%
Nationality	Saudi	37	15.7%	199	84.3%
	Non Saudi	20	20.4%	78	79.6%
.....		Mean	Stander div	Mean	Stander div
Age		46.825	14.2943	41.051	14.4216
BMI		52.7078	32.60156	32.8269	35.52995

Table 1. Ratio of mean between G and non GC

		Gangrenous or not			
		Yes		No	
Diabetes mellitus	Yes	7	15.6%	38	84.4%
	No	49	17.1%	237	82.9%
	Missing	1	33.3%	2	66.7%
Smoking	Yes	5	20.8%	19	79.2%
	No	52	16.8%	257	83.2%
	Missing	0	0.0%	1	100.0%
Alcohol consumption	yes	0	0.0%	1	100%
	No	53	16.2%	275	83.8%
	Missing	4	66.7%	2	33.3%
Temperature 38 C or above	Yes	1	33.3%	2	66.7%
	No	55	17.0%	268	83.0%
	Missing	1	12.5%	7	87.5%
Nausea	Yes	4	6.3%	60	93.8%
	No	53	19.7%	216	80.3%
	Missing	0	0.0%	1	100.0%
Vomiting	Yes	8	11.4%	62	88.6%
	No	49	18.6%	215	81.4%
	Missing	0	0.0%	1	100.0%

Table 2. Ratio of GC and non GC with risk of DM

Lab result	Gangrenous or not	N	Mean	Std. Deviation
WBC	Yes	57	183.108947	1323.3666502
	No	277	7.553217	3.1909072
AST	Yes	51	25.373	22.6654
	No	251	71.024	632.3963
ALT	Yes	52	31.442	26.2637
	No	250	48.272	89.6491
ALP	Yes	52	87.827	46.5777
	No	254	97.558	95.4758
Bilirubin	Yes	57	9.054	8.1743
	No	277	10.333	32.4543

Table 3. Mean WBC and serum bilirubin in our sample

		Gangrenous or not		Total
		yes	no	
Pancreatitis	Count	0	7	7
	Percentage	0.0%	2.5%	2.1%
Gall bile cancer	Count	0	3	3
	Percentage	0.0%	1.1%	0.9%
Gall bile inflammation	Count	6	46	52
	Percentage	10.5%	16.6%	15.6%
Gall bile stones	Count	47	209	256
	Percentage	82.5%	75.4%	76.6%
Other	Count	4	10	14
	Percentage	7.0%	3.6%	4.2%
missing	Count	0	2	2
	Percentage	0.0%	0.7%	0.6%

Table 4. Types of Cholecystitis in our sample

of the data having stones second to that gall bile inflammation. Radiological findings were analyzed on the bases of CT thickening. Positive findings were detected in a total of 4 patients, 2 of whom had GC (50%). Similarly, those with non-gangrenous cholecystitis were also two patients (50%). Irregular CT or absent gallbladder was positive only

Table 5. Radiological finding		Gangrenous or not			
		Yes		No	
		Count	Row N %	Count	Row N %
CT Wall thickening and edema	Yes	2	50.0%	2	50.0%
	No	55	16.7%	275	83.3%
	Missing	0	0.0%	0	100.0%
CT Irregular or absent gallbladder wall	Yes	1	100.0%	0	0.0%
	No	56	16.8%	277	83.2%
	Missing	0	0.0%	0	100.0%
CT gallbladder wall or lumen gas	yes	0	0.0%	0	100.0%
	No	57	17.1%	277	82.9%
	Missing	0	0.0%	0	100.0%
CT focal irregularity or defect in the gallbladder wall	Yes	0	0.0%	0	100.0%
	No	57	17.1%	276	82.9%
	Missing	0	0.0%	0	100.0%
CT intraluminal membranes	yes	0	0.0%	0	100.0%
	No	57	17.1%	277	82.9%
	Missing	0	0.0%	1	100.0%
CT absence of mural enhancement	yes	0	0.0%	0	100.0%
	No	57	17.1%	276	82.9%
	Missing	0	0.0%	1	100.0%
CT pericholecystic abscess	Yes	0	0.0%	1	100.0%
	No	57	17.2%	274	82.8%
	Missing	0	0.0%	2	100.0%

Table 5. Patients diagnosed with GC

in 1 patient that was diagnosed with GC (100%) (Table 5).

5. DISCUSSION

Development of GC can negatively impact outcome, if got discovered or predicted early it will help in decreasing its morbidity, length of hospitalization, post-surgical complications and mainly mortality risk (4, 5). In our study we found out that the mean age of patient with gangrenous cholecystitis is 46.82 years old, in the past few years there was a lot of effort to create score system to help us in predict the risk factors for (GC), one of these scores is yacope system that found an increase in likelihood of a patient developing a GC after the age of 45 years which it is one of this system multivariable that help to predict GC (12).

Based on the literature the incidence of cholecystitis was higher in female than male, however the risk of developing GC is higher in males compared with females (3, 11). As seen in the result of our study (acute or GC) male percentage were (12%) and the female percentage (4.5%), unfortunately until this moment the reason is undetermined (11, 13). In our study results (12.3%) had diabetes mellitus compared to (19%) in Nikfarjam study. Because one of the main factor in (GC) is vascular compromise or injury, authors have suggested that the presence of atherosclerosis or micro vascular disease may increase a diabetic patient risk to gangrenous changes (13, 14).

Concerning the fever (1.8%), nausea (7%) and vomiting (14%) and the difference compared to other researches. In United States they found GC patient to be associated with fever (29%), nausea and vomiting (61%) (15). We believe that this difference may be caused by the antiemetic and antipyretic that the patients in KAUH receives prior to admission, for this reason, most of the patient did not develop fever, nausea and vomiting.

Our result shows the mean of WBC count was (7.82) which was found to be unexpectedly normal as regards to other patients with GC, A high degree of leucocytosis has been correlated with the infection severity in the gallbladder wall. Other study Reported that WBC count 15,000/mm³ predicted development of GC, whereas it was 17,000/mm³ (16). In there study's the leucocytosis is mainly caused by an infection and the immune response toward that infection but in our patients we found that almost (82.5%) of the cases are reported to be non-inflammatory (impacted stones)

causes reducing the WBC and the inflammatory response .

The total bilirubin was normal (9.925MCMOL/L), and liver enzymes ALT(31,442U/L),AST(25,373U/L), ALP(87,827U/L) were in normal ranges. ALT(7-55U/L), AST(8-48U/L), ALP (45-115U/L), based on another study the total bilirubin was elevated (25,650) and alcohol consumption was high (17). Studies show that high level of bilirubin due to hepatic necrosis as well as alcohol consumption that will lead to hepatocellular injury, both will increase chances of liver injury via GC related inflammation in the gallbladder bed lining that simulates an in increase liver enzymes. (18, 19). Alcohol consumption on our study was not recorded, Saudi Arabia is an Islamic country so the liver function test is normal on the other hand bilirubin was normal probably due to the early detection and treatment of the cases.

In GC, we found impacted stone in (82.5%) of patients who underwent laparoscopic cholecystectomy; this is compatible with another study which shows that (50%) of GC patients were complaining of stone which causes manageable pain and the no need to an emergent surgery increasing the percentage of chronic cholecystitis and lowering the percentage of inflammation and decreasing the inflammatory problems to (10.5%) lowering the pre and post operation complications (16). Stones cause sustained cystic duct obstruction that will lead to tension in the gallbladder wall and injury in the epithelium leading to GC in the long term (20, 21). This high percentage is may be due to high fatty meal consumption (22).

Önder reported that air in the gallbladder wall or lumen, irregular or absent gallbladder wall, intraluminal membranes, pericholecystic abscess, and lack of gallbladder wall enhancement are specific CT findings of acute cholecystitis complicated by GC (16). In our study we found insignificant results in (94,8%) which was compatible with a study done by Bennett GL (86,5%) (23), that's may be due how hard it's to report a specific CT findings of acute cholecystitis complicated that may lead to gangrene as air in the gallbladder wall , lack of gallbladder wall enhancement, pericholecystic abscess and intraluminal membranes (24) .

6. CONCLUSION

Patient age was a clear factor for us for developing GC, male gender was a factor but there was no correlation, because:

- Total bilirubin was in a normal level that's maybe due to early detection and treatment,
- Vomiting and fever and nausea was less compared to other researchers which may be correlated to the antipyretics and antiemetics the patients receive prior to admission,
- At last Computed Tomography (CT) was not supportive and do not give any importance in detecting GC,
- Normal range of WBC mainly caused by the high percentage of impacted stones.

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