Diverticular Disease: Risk Factors and Predictors of the Outcome

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Background: Diverticular disease is a common disease which has a considerable burden on health care facilities. Its incidence increases with age and has multifactorial pathogenesis.

Objective: To evaluate the predictability of relevant risk factors and the disease process.

Design: A Retrospective Study.

Setting: King Hamad University Hospital, Bahrain.

Method: All patients who were admitted with diverticular disease from 2016 to 2019 were included in the study. We documented the first attack of the disease to test the relevant parameters against the severity and outcome. Disease severity was categorized according to Sallinen VJ et al and P<0.05 was considered significant.

Result: One hundred thirty-four patients were included in the study; 76 (56.7%) males and 58 (43.3%) females. The median age was 59.5. One hundred fifteen (85.8%) patients presented with diverticulitis symptoms and 19 (14.2%) with diverticular bleeding. Diverticulitis affected the left colon in 85 (63.4%) patients and 8 (5.9%) on the right colon.

Diabetes was associated with advanced stages 4 and 5, P=0.010. In patients with diverticular bleeding, the bleeding stopped spontaneously in 12 (9%), while colonoscopic intervention was required in 7 (5.2%).

Conclusion: Diverticulitis affects the left colon while diverticular bleeding commonly occurs in the right colon. Tobacco smoking, aspirin and antithrombotic medications are risk factors for diverticular bleeding. Diabetes is associated with advanced severe diverticulitis presenting with peritonitis.

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Diverticular disease of the colon is a common disease with an incidence ranging from 5% in the fourth decade of life to as high as 60% in those over 70 years of age[1-3]. Historically, diverticulosis was known as the disease of the industrial revolution, since there was no evidence of this disease before the 1900s. In the late 1800s, the process of roller-milling of wheat was introduced, and it consisted of removing two-thirds of the fiber content of wheat.

Diverticular disease was described in the first decade of the 1900s[4]. Since then, many studies supported the role of reduced dietary fibers in the pathogenesis of diverticular disease[5,6]. However, it proved to be a complex disease process and much of the accepted theories have been challenged[7].

Changes in the colonic wall, increased intraluminal pressure and motility, genetic and hereditary factors, and colonic microbiota have been implicated in the pathogenesis of the diverticular disease[8-16].

Most of the affected individuals remain asymptomatic. However, 10–35% will develop symptoms of diverticular disease (pain, nausea, vomiting, fever, constipation, or less commonly, diarrhea, rarely bleeding). Of these patients, 85–90% will develop symptomatic uncomplicated diverticular disease (SUDD) and 10–15% will develop acute diverticulitis, with or without complications, which include abscesses, fistula, bleeding and perforation[9,17].

In Western countries, false diverticula are seen in the descending colon and the sigmoid, while in Asian countries, right-sided true diverticulosis is more prevalent[18,19]. The different locations

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of diverticulosis leads to different presentations; left-sided diverticulosis tends to present as an inflammatory process while the right-sided diverticula as bleeding[20,21].

Dietary factors, obesity, physical inactivity, smoking, alcohol, non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids have been claimed to predispose to the disease[22-27]. Studies suggest that hemoglobin (HGB), vitamin D and C-reactive protein (CRP) could be predictive of the disease severity[28-31].

The aim of this study is to evaluate risk factors of diverticular disease and to evaluate the predictability of the disease.

METHOD

All patients who were admitted with the diagnosis of diverticular disease from 2016 to 2019 were included in the study. The following were documented: age, gender, nature of the presentation, fever, site and stage, comorbidities, alcohol, smoking and BMI, HGB, WBC, CRP, vitamin D level, use of NSAIDs, aspirin, antithrombotic, corticosteroids and the management. The correlation between the risk factors and the development of disease was statistically tested. Disease severity was classified according to Sallinen VJ et al classification[32].

Different variables were analyzed using the appropriate statistical tests. P<0.05 was considered significant. The data was analyzed using SPSS version 22 and Microsoft Excel 2016.

RESULT

One hundred thirty-four patients diagnosed with diverticular disease were included in the study; 76 (56.7%) were males and 58 (43.3%) were females. The median age was 59.5 (25 – 89). One hundred fifteen (85.8%) patients presented with symptoms of diverticulitis without bleeding and 19 (14.2%) with bleeding.

Diverticulitis affected the left colon in 85 (73.9%) patients and the right colon in 8 (7%) patients. Diverticular bleeding originated from the right colon in 10 (52.6%) patients and from the left colon in 5 (26.3%) patients, P≤0.001 and <0.001, respectively, see table 1. Pancolonic involvement was approximately 20% in both groups. As expected, the diverticulitis group without bleeding showed more intense inflammatory response with significantly higher CRP and WBC and fever compared to the diverticulitis with bleeding group, P=0.002, 0.022 and 0.025, respectively. The diverticulitis with bleeding group showed significantly lower hemoglobin levels at presentation, P≤0.001.

Tobacco smoking, aspirin, and antithrombotic medications were associated with diverticular bleeding, P=0.015, 0.005 and 0.005, respectively.

The severity of diverticulitis in the group without bleeding was classified according to Salinnen staging and assessed against the relevant factors, see table 2. Older age was associated with advanced stage, P=0.032. High WBC and CRP and low hemoglobin was associated with advanced stages of diverticulitis, P≤0.001, <0.001 and 0.001, respectively.

Table 1: Diverticulitis with Bleeding Compared to Diverticulitis without Bleeding

	Total (n=134)	Diverticulitis without Bleeding (n=115)	Diverticulitis with Bleeding (n=19)		
Gender					
Male	76 (56.7%)	64 (55.7%)	12 (63.2%)	χ^2= 0.374	0.541
Female	58 (43.3%)	51 (44.3%)	7 (36.8%)		
Age (years)					
Median (Min– Max)	59.5 (25 – 89)	59 (25 – 89)	63 (44 – 81)	t=1.294	0.198
Mean ± SD	58.2 ± 13.5	57.6 ± 14.1	61.9 ± 9		
Fever	35 (26.1%)	34 (29.6%)	1 (5.3%)	χ^2=4.990*	0.025*
Extent					
Left	90 (67.2%)	85 (73.9%)	5 (26.3%)	χ^2=19.945*	<0.001*
Right	18(13.4%)	8(7%)	10(52.6%)	χ^2=29.254*	<0.001*
Pancolonic	26 (67.2%)	22 (19.1%)	4 (21.1%)	χ^2=0.039	0.764
Tobacco	39 (29.1%)	29 (25.2%)	10 (52.6%)	χ^2=5.939*	0.015*
Alcohol	18 (13.4%)	14 (12.2%)	4 (21.1%)	1.105	0.287
BMI					
Median (Min– Max)	30.6 (19.2 – 51.1)	30.6 (19.2 – 51.1)	30.6 (22 – 36)	t= 1.634	0.110
Mean ± SD	31.1 ± 6.2	31.4 ± 6.5	29.6 ± 3.8		
DM	68 (50.7%)	59 (51.3%)	9 (47.4%)	χ^2=0.101	0.751
HTN	76 (56.7%)	67 (58.3%)	9 (47.4%)	χ^2=0.788	0.375
CKD	7 (5.2%)	5 (4.3%)	2 (10.5%)	χ^2=1.257	0.259
IBD	0 (0%)	0 (0%)	0 (0%)	–	–
HGB					
Median (Min– Max)	13.3 (5.5 – 17)	13.3 (8 – 17)	10 (5.5 – 15.6)	t= 4.207*	<0.001*
Mean ± SD	13 ± 2.1	13.4 ± 1.8	10.6 ± 2.8		
CRP					
Median (Min– Max)	16.7 (0.6 – 272.5)	23 (0.6 – 272.5)	4.2 (1.9 – 126)	U= 605.50*	0.002*
Mean ± SD	47.8 ± 61.6	52.3 ± 63.6	20.6 ± 38.1		
Vitamin D					
Normal	105 (78.4%)	88 (76.5%)	17 (89.5%)	χ^2=1.613	0.365
Low	29 (21.6%)	27 (23.5%)	2 (10.5%)		
NSAIDs	15 (11.2%)	11 (9.6%)	4 (21.1%)	χ^2=2.813	0.336
ASA	28 (20.9%)	19 (16.5%)	9 (47.4%)	χ^2=9.387*	0.005*
Steroids	16 (11.9%)	13 (11.3%)	3 (15.8%)	χ^2=0.312	0.701

χ^2: Chi-square test t: Student t-test U: Mann Whitney test
p: p-value for comparing between the two studied groups
*: Statistically significant at p ≤ 0.05

Fever was associated with advanced stages, P≤0.001. DM was associated with advanced stages reaching up to 100% of patients presenting with stages 4 and 5, P=0.010. Other significant predictors of severity included tobacco smoking and alcohol, P=0.039 and 0.001, respectively. Use of steroids and antithrombotic medications was associated with severe stages of diverticulitis, P≤0.001 and 0.017, respectively.

Table 2: Salinnen Staging in Diverticulitis without Bleeding Group (n=115)

	Salinnen stage			Test of sig.	p
	1 (n = 77)	2 – 3 (n = 30)	4 – 5 (n = 8)		
Age (years)					
Median (Min. –Max.)	59 (27 – 82)	55.5 (25 – 84)	64 (61 – 89)	F=3.550*	0.032*
Mean ± SD.	56.7 ± 14.2	56.7 ± 13.3	70.1 ± 11.1		
Gender					
Male	39 (50.6%)	19 (63.3%)	6 (75 %)	χ^2= 2.580	0.286
Female	38 (49.4%)	11 (36.7%)	2 (25%)		
Extent					
Left	53 (68.8%)	25 (83.3%)	7 (87.5%)	χ^2=3.178	0.204
Pancolic	18 (23.4%)	3 (10%)	1 (12.5%)	χ^2=2.741	0.254
Right	6 (7.8%)	2 (6.7%)	0 (0%)	χ^2=0.213	1.000

χ^2: **Chi-square test** **F: F test (ANOVA)** H: H for **Kruskal Wallis test** P:P-value for the association between **Salinnen stage** and different parameters

*: Statistically significant at P≤ 0.05

CRP levels at presentation and alcohol consumption were independent predictors of complicated diverticulitis, P=0.001 and 0.028 with CI 95% of 1.023 (1.009–1.037) and 9.141 (1.270–65.798), respectively.

Male gender, WBC, CRP levels, fever, alcohol consumption, diabetes, antithrombotic medication and steroids intake were associated with surgical intervention, P=0.042, <0.001, <0.001, <0.001, <0.001, 0.003, 010 and 0.002, respectively.

Seventy-eight of the no bleeding group were admitted and managed conservatively; their length of hospital stay correlated positively with presentation with fever, alcohol consumption, diabetes, antithrombotic medications, WBC and CRP, P≤0.001, 0.017, 0.022, 0.001, 0.003 and <0.001, respectively.

Assessment of the factors which predict disease recurrence revealed a positive correlation with young age and hemoglobin level P=0.029 and <0.001, respectively.

Sensitivity and specificity of WBC counts and CRP levels to predict complicated diverticulitis were assessed under the ROC curve which revealed a cut off values of 24 for CRP and 13.89 for WBC.

The bleeding group included 19 patients; in 12 (63.15%) patients, bleeding stopped spontaneously while colonoscopic intervention was required in 7 (36.8%) patients. Four (21%) patients received a blood transfusion; further analysis failed to reveal any positive correlation between the studied factors and the need for blood transfusion.

Thirteen (68.4%) patients from the bleeding group were managed as inpatients while the other 6 (31.6%) were discharged from accident and emergency. The length of hospital stay among the inpatients was correlated positively with tobacco smoking, HTN, CKD and CRP, P=0.008, 0.006, 0.026 and 0.003, respectively.

Finally, factors predicting recurrence of diverticular bleeding were tested and revealed a positive correlation with alcohol, NSAIDs and steroids, P=0.016, 0.016 and 0.004, respectively.

DISCUSSION

Diverticular disease represents a problem of considerable magnitude which is a healthcare burden in the Western and developing countries[33-35].

Comparison of the risk factors in our study revealed a positive correlation between tobacco smoking, aspirin, and antithrombotic medications and diverticular bleeding.

A recent study showed that the independent risk factors for diverticular bleeding were alcohol consumption, smoking, NSAIDs, low-dose aspirin and non-aspirin antiplatelet drugs. Moreover, dual therapy carried a higher risk than monotherapy[36]. Consequently, patients on NSAIDs or antiplatelet medications should be carefully monitored for diverticular hemorrhage if they have diverticulosis[37].

Elder individuals were found to have more advanced stages of diverticulitis than younger individuals, a finding which refuted the old concept stating that diverticulitis in young age groups was considered a malignant form of the disease[38,39].

A meta-analysis found that NSAIDs was associated with diverticular perforation, other studies found that NSAIDs was associated with diverticular bleeding and perforation[40,41].

The results of this study showed that regular use of aspirin (greater than or equal to two times per week) had a risk of diverticular bleeding compared to non-users. This association was seen in non-aspirin NSAID users[42]. Recent American Gastroentorogical Association (AGA) guidelines recommend avoiding non-aspirin NSAIDs (but not avoiding therapeutic aspirin) in acute diverticulitis patients[43]. In our study, aspirin proved to be a risk factor for diverticular bleeding compared to the diverticulitis group.

In a study, smoking was not significantly associated with symptomatic diverticular disease; smokers suffered a higher risk of complicated diverticular disease[44]. Our findings supported this; tobacco smoking was found to increase the severity of diverticulitis.

High mean prediagnostic serum vitamin D (25-OH) levels in patients with uncomplicated diverticulosis was found and showed an association between low ultraviolet light exposure and diverticulitis[45].

A study showed that waist circumference and waist-to-hip ratio significantly increased the risks of diverticulitis and diverticular bleeding[46]. Rosemar et al found that BMI was an independent risk factor[42]. However, in our study, we did not find any correlation between vitamin D levels or obesity and the severity of diverticulitis.

Corticosteroid use is known to be associated with increased mortality risk after perforated diverticular disease[47]. Biondo et al found that the need for emergency surgery in patients on chronic steroid therapy was high (39.3%)[48].

Makela et al found a CRP cut-off value of 149.5 mg/l, which could distinguish complicated from non-complicated diverticulitis[31]. Moreover, he found that a CRP value of more than 150 mg/l and old age were independent risk factors for complicated diverticulitis. In our study, the cut-off point was 24, which determined complicated from uncomplicated forms of diverticulitis.

Clinically significant bleeding occurs in 3% to 15% of patients with colon diverticula, usually as a result of trauma to the vasa recta at the neck or dome of the diverticulum[49,50]. Bleeding resolves spontaneously in 75% to 80% of patients but recurs in 25% to 40% within 4 years[49]. In our study, 14.17% of patients presented with diverticular bleeding; bleeding stopped spontaneously in 12 patients while colonoscopic intervention was required to control bleeding in the remaining 7 (36.8%) patients.

At present, the risk factors for diverticular bleeding are identified. However, due to the lack of enough prospective studies, it is difficult to estimate which factors are most important[51].

In our study, the length of hospital stay among diverticular bleeding patients was correlated positively with tobacco smoking, HTN, CKD and CRP, while recurrence was correlated with alcohol, NSAIDs and steroids. Joaquim et al found that hemoglobin ≤ 11 g/dl, age >75 years, bilateral diverticula and chronic kidney disease were independent risk factors for diverticular bleeding[52]. Many studies refuted the contribution of aspirin intake, antithrombotics and atherosclerotic disease to the development of diverticular bleeding[53,54].

CONCLUSION

Diverticulitis affects the left colon while diverticular bleeding originates more from the right colon. Tobacco smoking, aspirin, and antithrombotic medications are risk factors for diverticular bleeding. Diabetes is associated with advanced severe diverticulitis presenting with peritonitis. CRP levels at presentation and alcohol consumption are independent predictors of complicated diverticulitis.

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