World J Surg (2021) 45:2337–2346
https://doi.org/10.1007/s00268-021-06093-5

SURGERY IN LOW AND MIDDLE INCOME COUNTRIES

Factors Affecting Patient Outcomes in Acute Appendicitis in Rural Areas: An Observational Cohort Study

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Accepted: 15 March 2021 / Published online: 3 April 2021

Abstract

Background The most common surgical emergency both in developed and non-developed countries is acute appendicitis and it has a time-dependent clinical course. In this observational cohort study, we aim to investigate the factors affecting patient outcomes in acute appendicitis at a rural hospital.

Methods This observational cohort study was held between November 2012 and May 2014 at a rural hospital. Patients' pre-operative, perioperative, and post-operative data were collected prospectively. Patients were followed-up for 12-months.

Results A total of 151 patients were recorded. Factors significantly associated with complicated cases (abscess/perforation) were referral region as remote towns (OR:7.94, 95%CI [3.46–18.23]; $p < 0.001$), referral season as winter (OR:2.47, %95CI [1.14–5.36]; $p = 0.022$), pre-operative hospital delay (OR:6.52, 95%CI [3.49–12.20]; $p < 0.001$), and duration of referral (OR:1.01, 95%CI [1.00–1.01]; $p < 0.001$). In the multivariate analysis, only pre-operative hospital delay remained as a significant factor (OR:5.87, 95%CI [2.85 – 12.07]; p < 0.001).

Factors affecting length of hospital stay (LoHS) were referral region as remote towns (95%CI, $\beta = 3.10$ [2.28–3.93], $t = 1.91$; $p < 0.001$), abscess/perforation (95%CI, $\beta = 4.70$ [4.04–5.36], $t = 14.05$; $p < 0.001$), pre-operative hospital delay (95%CI, $\beta = 1.25$ [0.87–1.62], $t = 6.58$; $p < 0.001$), and duration of referral (95%CI, $\beta = 0.011$ [0.01–0.14], $t = 7.34$; $p < 0.001$). In the multivariate analysis, all four factors stayed significant. The rate of complicated appendicitis was significantly high in winter than other seasons for patients referring from remote towns (75% vs 33%, $p < 0.001$).

Conclusions This observational cohort study is the only study specifically focused on the effect of season and region on abscess/perforation rates, LoHS, and accessibility to hospital in patients with acute appendicitis.

Introduction

Acute appendicitis is, indisputably, the most common surgical emergency both in developed and non-developed countries [1]. Even though it is common, the diagnosis can be challenging due to various types of clinical signs and symptoms. Classic clinical presentation occurs only in one third of cases [2]. Its clinical course starts with an inflammation. Then perforation and followed by local or diffuse abdominal sepsis. At this point, as the risk of perforation and abdominal sepsis is time-dependent, early

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diagnosis and management of acute appendicitis are crucial in order to lower morbidity and mortality rates [1]. The risk of perforation rises after twelve hours from the initial onset of symptoms but it significantly rises after 48 h [3, 4]. The perforation rate is around 15–30% for developed countries and as high as 40–60% for developing or non-developed countries.

The global incidence of appendicitis is 100 in North America, 105 in Eastern Europe, and 150 in Western Europe in 100.000 person per year [5]. The incidence is 160/100.000 person per year for Turkey but there is no available data about regional incidence differences of appendicitis including Bitlis region. Although there is a trend towards non-surgical management for acute appendicitis in developed countries, it is still managed surgically in developing or non-developed countries due to the late referral to clinics [6]. Besides, the differential diagnosis between complicated and non-complicated appendicitis can only be made after admission to the hospital and after performing some diagnostic tests and imaging. This is one of the main problem about the conservative management of acute appendicitis in rural areas. In this prospective observational cohort study, we aim to evaluate the seasonal and regional factors affecting complicated appendicitis (abscess/perforation) rates and length of hospital stay at a rural state hospital.

Material and methods

Patient cohort and data collection

This observational cohort study was planned to evaluate patients with a clinical diagnosis of acute appendicitis who referred to Bitlis State Hospital from November 2012 to May 2014. Patients' pre-operative, perioperative, and post-operative data were collected prospectively on a chart specifically designed for appendicitis cases. "Pre-operative hospital delay" was defined as time between first onset of symptoms and deciding to refer or being referred to the state hospital. "Referral duration" was defined as the duration of time between deciding to refer or being referred to the state hospital and admission to the emergency unit of the state hospital which is also called "transportation time". "Length of hospital stay" (LoHS) was defined as time between the end of operation and patient discharge from hospital. At this point, as a result of governmental health care cost policies, we aim to hospitalize every patient for 24 h if there is no post-operative complications. 24-h limit is a routine practice in our clinics for laparoscopic procedures.

Patients were followed-up for 12 months until May 2015. We define the study period of November 2012–May 2015 depending on the compulsory health care service for the government of the individual physician. Complication that occurred ≤ 30 days after operation defined as early complication and between > 30 days and 12 months defined as late complication. Surgical procedure was anticipated as laparoscopic surgery (conventional or single-incision) for every patient and open surgery if needed. This is an observational study. The local ethical committee has confirmed that no ethical approval is required.

Regional and seasonal information

Bitlis is located in the eastern part of Turkey that has an average altitude of 1700 m (range between 1500 and 4000 m). In general, it is a mountainside. According to the Turkish General Directorate of Meteorological Service, Bitlis has the longest average number of days with snow fall (33 days) and average number of days with snow cover (120 days) in Turkey. The highest average snowfall in a year (2 m) and the highest snowfall ever (5.8 m) was also recorded in Bitlis [https://mgm.gov.tr/]. There are 338.023 inhabitants (Downtown: 66.732; Tatvan: 86.514; Güroymak: 46.269; Ahlat: 38.121; Adilcevaz: 31.196; Hizan: 36.663; Mutki: 32.528) in Bitlis. Bitlis is 76th in provincial development ranking and 79th for income per person in a year (~$3.500) over 81 cities [http://tuik.gov.tr/Start.do].

Downtown, Tatvan, Güroymak, Ahlat, and Adilcevaz are on the main roads easily connected to state hospital with divided highways. Accessibility to hospital even in wintertime is easy from these towns and under an hour. Hizan and Mutki are not on the main roads and the road to these towns are passing through mountain roads and valleys (Fig. 1) (Google maps Bitlis City, Bitlis, Turkey. Retrieved December 28, 2020 from https://www.google.com.tr/maps/place/Bitlis/). It normally takes more than an hour in summer time to get to the state hospital from remote towns. However, in wintertime, it is very struggling because of the snowfall. In some parts of these towns, the roads are not paved and many inhabitants are living apart from town centre because they usually involved in agriculture and animal husbandry. There is a primary and secondary care health service in every town and a tertiary care health centre near downtown, which is called Bitlis State Hospital.

Statistical analysis

To assess differences in categorical and continuous variables, Pearson's Chi-squared test (Continuity Correction and Fisher's Exact Test), independent samples t-test, and ANOVA tests were used. We perform univariate and multivariate logistic regression analysis to define factors associated with abscess/perforation rates and linear regression analysis to define factors associated with LoHS

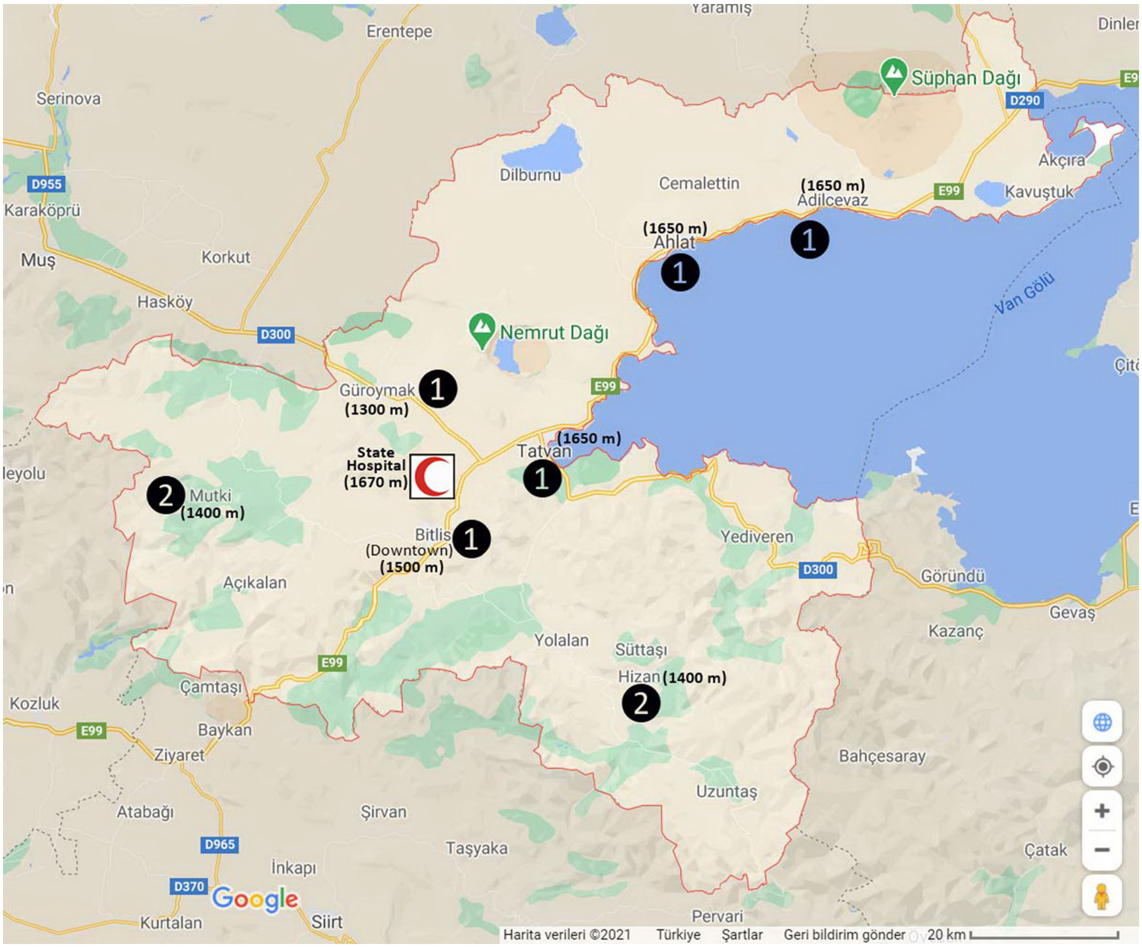

Fig. 1 Map of Bitlis city indicating location of the state hospital (crescent in square) and 7 towns (Downtown, Tatvan, Güroymak, Ahlat, Adilcevaz, Hizan, Mutki) of Bitlis city. ① Indicating close towns ② Indicating remote towns

and odds ratios (OR) are presented for each of the factor. All p-values were two-sided and a p-value of < 0.05 with a 95% confidence interval (CI) considered as significant. To analyse the effect of the season and referral region on patient outcomes like abscess/perforation as operation finding and LoHS, patient cohort was divided into binary groups. Mutki and Hizan are grouped as "Remote Towns" and Downtown, Tatvan, Güroymak, Ahlat, and Adilcevaz are grouped as "Close Towns" based on topography (Fig. 1). Because nationally winter season is considered four months in eastern, high altitude part of Turkey according to the Turkish General Directorate of Meteorological Service, season of the year was defined as "Winter Season" for December, January, February, and March, and "Other Seasons" for the rest of the months [https://mgm.gov.tr/]. As is known, operation findings of abscess and perforation may affect patient outcomes (early or late complications and prolonged LoHS due to antibiotic administration, pain relief or intra-abdominal drain). Therefore, we specifically aim to make a univariate and multivariate analyses for factors affecting LoHS and for the cases that have an operation finding of abscess/perforation vs. those without abscess/perforation (acute appendicitis, normal appendix).

Results

Patient demographics, clinic-pathologic features, operative/post-operative findings, and outcome measures of 151 patients are summarized in Tables 1 and 2. Every individual patient presented with at least one symptom and one sign in physical examination. Patients' white blood cell (WBC) counts and C-reactive protein (CRP) levels showed high sensitivity (96% and 96.9%, respectively) but low specificity (10.3% and 17.4%, respectively). Primary radiological diagnostic tool was ultrasound and it was conducted only for 78 patients (sensitivity 100%, specificity 25%). Computed tomography (CT) was conducted for 37 patients, and both sensitivity and specificity were 100%.

Table 1 Demographic and clinic data of the patients

Variable	Patients (n = 151)	%
Sex		
Female	42	27.8
Male	109	72.2
Age		
Mean	25	SD: ± 7.49
Median (15–58)	23	
*Symptoms**		
Abdominal pain	145	96
RLQ Pain	132	87.4
Anorexia	110	72.8
Nausea	54	35.8
Vomiting	33	21.9
Fever	25	16.6
*Signs**		
Abdominal tenderness	131	86.8
RLQ tenderness	116	76.8
Rebound tenderness	108	71.5
Markle sign (heel-jar test)	104	68.9
Rovsing's sign	35	23.2
Rigidity	15	10
Leucocyte count (cells/μL)		
Mean	13,220	SD: ± 2781
Median	13,340	Range: 8520 – 21,020
Leucocytosis (> 10,500 cells/μL)		
No	34	22.5
Yes	117	77.5
CRP level (mg/dL)		
Mean	45.2	SD: ± 31.9
Median	42	Range: 2.8 – 141
CRP		
≤ 4 mg/dL	27	17.9
> 4 mg/dL	124	82.1
Alvarado scores		
5–6 (Possible AA)	12	7.9
7–8 (AA)	96	63.6
9–10 (Definite AA)	43	28.5
Alvarado score		
Mean	7.9	SD: ± 1.07
Median	8	Range: 5 – 10
USG (n = 78)		
Negative	2	2.6
Positive	76	97.4
CT (n = 37)		
Negative	0	0
Positive	37	100

*Individual patients may have multiple signs and symptoms

SD: Standard deviation, CRP: C-reactive protein, RLQ: Right lower quadrant, AA: Acute appendicitis, USG: Ultrasonography, CT: Computed-Tomography

Table 2 Operative and post-operative findings of the patients and outcome measures

Variable	Patients (n = 151)	%
Operation type		
Open	1	0.7
Laparoscopic	71	47
SILS	79	52.3
Operation finding		
Acute appendicitis	107	70.9
Abscess/perforation	36	23.8
Normal appendix	8	5.3
Post-operative complication		
No	143	94.8
Wound Infection (≤ 30 days)	4	2.6
Intra-abdominal abscess (≤ 30 days)	4	2.6
Geographic location (Home Town)		
Downtown	61	40.4
Güroymak	30	19.9
Tatvan	4	2.6
Ahlat	8	5.3
Adilcevaz	7	4.6
Mutki	32	21.2
Hizan	9	6
Referral season		
Winter	71	47
Other	80	53
Pre-operative hospital delay (days)		
Mean	1.52	SD: ± 1.01
Median (0.5–5)	1	
Duration of referral (minutes)		
Mean	79.7	SD: ± 123.92
Median (10–600)	30	
Length of hospital stay (days)		
Mean	2.42	SD: ± 2.66
Median (1–14)	1	

SILS single incision laparoscopic surgery

Operation type was laparoscopic surgery except one patient who presented with a generalized abdominal tenderness and operated by a midline incision. Operation finding of this patient was acute appendicitis that was caused by ascaris lumbricoides infestation. There was no conversion to conventional laparoscopy (n = 71) from single incision laparoscopic surgery (SILS) (n = 79), and no conversion from laparoscopy to open surgery. There was only eight patients with early complications (5.2%). There was no late complication or mortality.

The detailed distribution of complicated (abscess/perforation) and non-complicated (no abscess/perforation) cases per month is presented in Fig. 2 and it demonstrates that there is a distribution difference between close and remote towns. Furthermore, patients living in remote towns have significantly longer periods of pre-operative hospital delay (2.35 vs. 1.21 days; $p < 0.001$) and duration of referral (215.8 vs. 29 min; $p < 0.001$) compared to close towns.

In the univariate analysis, factors significantly associated with complicated cases (abscess/perforation) were referral region as remote towns (OR:7.94, 95% CI [3.46–18.23]; $p < 0.001$), referral season as winter (OR:2.47, %95 CI [1.14–5.36]; $p = 0.022$), pre-operative hospital delay in days (OR:6.52, 95% CI [3.49 – 12.20]; $p < 0.001$), and duration of referral in minutes (OR:1.01,

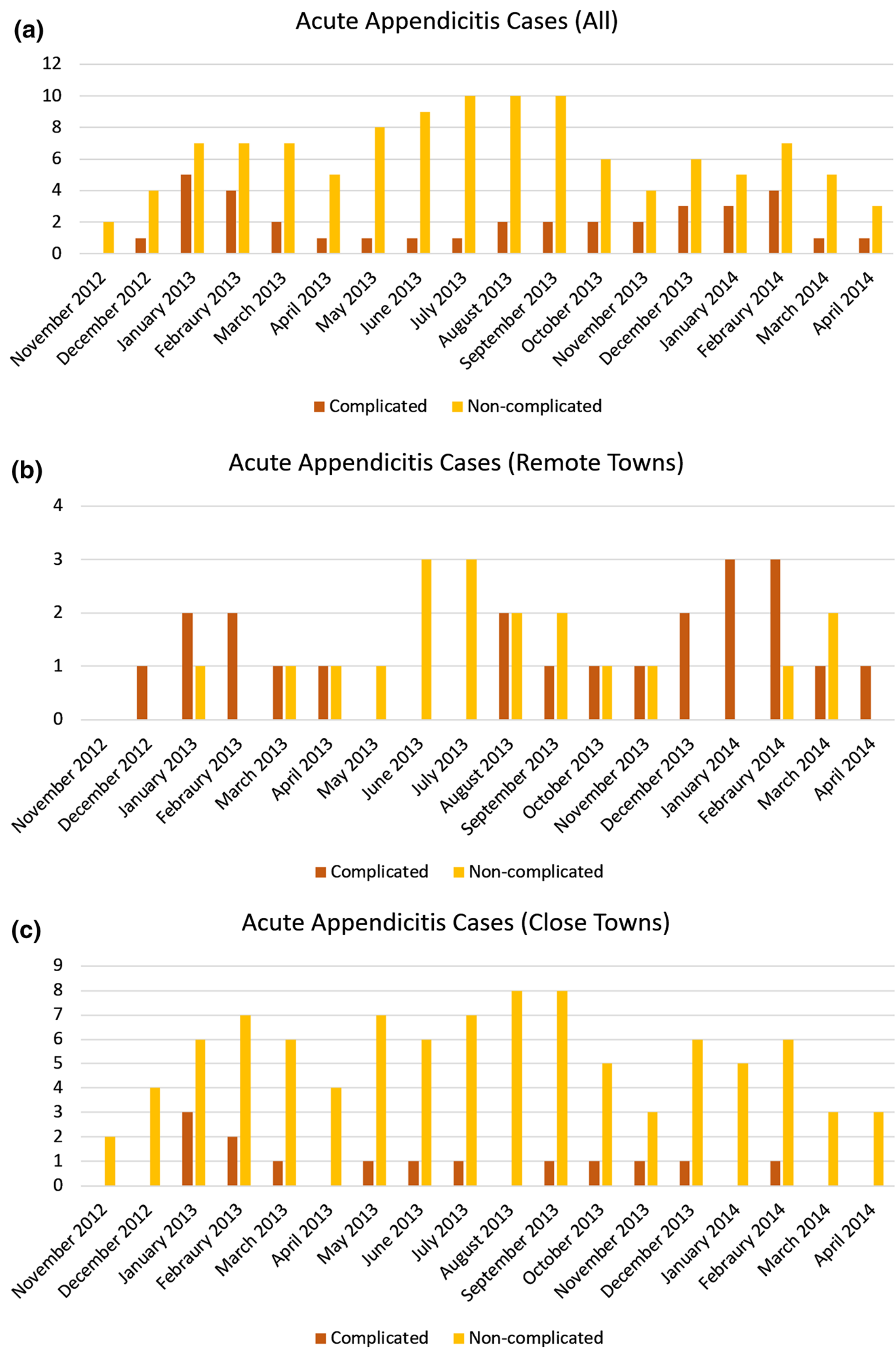

Fig. 2 Number of complicated (abscess/perforation) and non-complicated (no abscess/ perforation) cases per month. a All cases b Remote towns c Close towns

95% CI [1.00–1.01]; $p < 0.001$) (Table 3). In the multivariate analysis, only pre-operative hospital delay remained as a significant factor related with complicated cases (OR:5.87, 95% CI [2.85–12.07]; $p < 0.001$) (Table 4).

Factors significantly affecting LoHS were referral region as remote towns (95% CI, $\beta = 3.10$ [2.28–3.93], $t = 1.91$; $p < 0.001$), having abscess/perforation as operation finding (95% CI, $\beta = 4.70$ [4.04–5.36], $t = 14.05$; $p < 0.001$), pre-operative hospital delay (95% CI, $\beta = 1.25$ [0.87–1.62], $t = 6.58$; $p < 0.001$), and duration of referral (95% CI, $\beta = 0.011$ [0.01–0.14], $t = 7.34$; $p < 0.001$) (Table 3). In the multivariate analysis, all four factors stayed significant (Table 4). When we analyse the seasonal changes in abscess and perforation rates

Table 3 Univariate analysis of factors effecting abscess and perforation rates (a) and length of hospital stay (b)

Variables	Category	OR (95% CI)	*p value*
(a)			
Sex	Female	Reference (1)	*0.666*
	Male	1.21 (0.51–2.84)	
Age	< 25	Reference (1)	*0.294*
	≥ 25	1.50 (0.70–3.19)	
Referral Region	Close Towns	Reference (1)	*< 0.001*
	Remote Towns	7.94 (3.46–18.23)	
Referral Season	Other	Reference (1)	*0.022*
	Winter	2.47 (1.14–5.36)	
Pre-operative hospital delay (days)	-	6.52 (3.49–12.20)	*< 0.001*
Duration of referral (minutes)	-	1.01 (1.00–1.01)	*< 0.001*

Variables	Category	Unstandardized coefficients		Standardized coefficients		*p value*
		β (95% CI)	Std. Error	BETA	t	
(b)						
Sex	Female	Reference (1)	0.48	0.05	0.60	*0.550*
	Male	0.29 (-0.67–1.25)				
Age	< 25	Reference (1)	0.44	0.07	0.91	*0.364*
	≥ 25	0.40 (-0.47–1.28)				
Referral region	Close Towns	Reference (1)	0.42	0.52	7.44	*< 0.001*
	Remote Towns	3.10 (2.28–3.93)				
Referral season	Other	Reference (1)	0.43	0.16	1.91	0.058
	Winter	0.82 (-0.03–1.67)				
Abscess/perforation	No	Reference (1)	0.33	0.76	14.05	*< 0.001*
	Yes	4.70 (4.04–5.36)				
Pre-operative hospital delay (days)	–	1.25 (0.87–1.62)	0.19	0.47	6.58	*< 0.001*
Duration of referral (minutes)	–	0.011 (0.01–0.14)	0.00	0.52	7.34	*< 0.001*

Logistic regression, Method =Enter. OR: Odds ratio, CI: Confidence interval, Linear regression, Method =Enter. β: Regression coefficient, BETA: Standardized Regression coefficient

(a) Univariate analysis of factors effecting abscess and perforation rates

(b) Univariate analysis of factors effecting length of hospital stay

depending on referral region, we demonstrated that the rate of complicated appendicitis was significantly high in winter than other seasons for patients referring from remote towns (75% vs 33%, $p < 0.001$) (Fig. 3).

Discussion

The management of acute appendicitis is generally different in developed, developing or non-developed countries [7–9]. Although non-operative management is recently getting more and more adopted in various clinics, surgery is still the primary option specifically in developing or non-developed countries [10]. This fact is also the same for urban and rural regions of a country. As acute appendicitis is a time-dependent disease, the late presentation is associated with more complicated cases with higher morbidity and mortality rates specifically in rural and underdeveloped regions [6, 11, 12]. It is also associated with prolonged hospital stays, higher number of reoperations, and higher health costs [13–15]. Average duration from the beginning of the symptoms to admission to an emergency unit is ≤ 15 h in developed countries [16]. As for developing or non-developed countries, the duration is reported at least 72 h [6]. The risk of perforation is low during the first 36 h [17]. Pittman-Waller et al. reported a median delay of 16.5 h for nonperforated cases as compared to 39.8 h for perforated cases in a study of 5755 appendectomies [13]. Furthermore, this delay was significantly associated with higher rates of complications (61.7% vs. 6.5%), increased

Table 4 Multivariate analysis of factors effecting abscess and perforation rates (a) and length of hospital stay (b)

Variables	Category	OR (95% CI)	*p value*			
(a)						
Referral Region	Close Towns	Reference (1)	*0.337*			
	Remote Towns	2.06 (0.47–8.99)				
Referral Season	Other	Reference (1)	*0.609*			
	Winter	1.41 (0.38–5.17)				
Pre-operative Hospital Delay (days)	–	5.87 (2.85–12.07)	*< 0.001*			
Duration of Referral (minutes)	–	1.00 (0.99–1.01)	0.794			
Variables	Category	Unstandardized coefficients		Standardized coefficients		*p value*
		β (95% CI)	Std. Error	BETA	*t*	
(b)						
Referral region	Close Towns	Reference (1)	0.41	0.19	2.76	*0.007*
	Remote Towns	1.14 (0.32–1.95)				
Abscess/perforation	No	Reference (1)	0.41	0.70	10.73	*< 0.001*
	Yes	4.37 (3.56–5.17)				
Pre-operative hospital delay (days)	–	0.42 (0.05–0.79)	0.19	0.16	2.26	*0.026*
Duration of referral (minutes)	–	0.004 (0.00–001)	0.002	0.17	7.28	*0.024*

Logistic regression, Method =Enter. OR: Odds ratio, CI: Confidence interval. Linear regression, Method =Enter. β: Regression coefficient, BETA: Standardized Regression coefficient, CI: Confidence interval

(a) Multivariate analysis of factors effecting abscess and perforation rates

(b) Multivariate analysis of factors effecting length of hospital stay

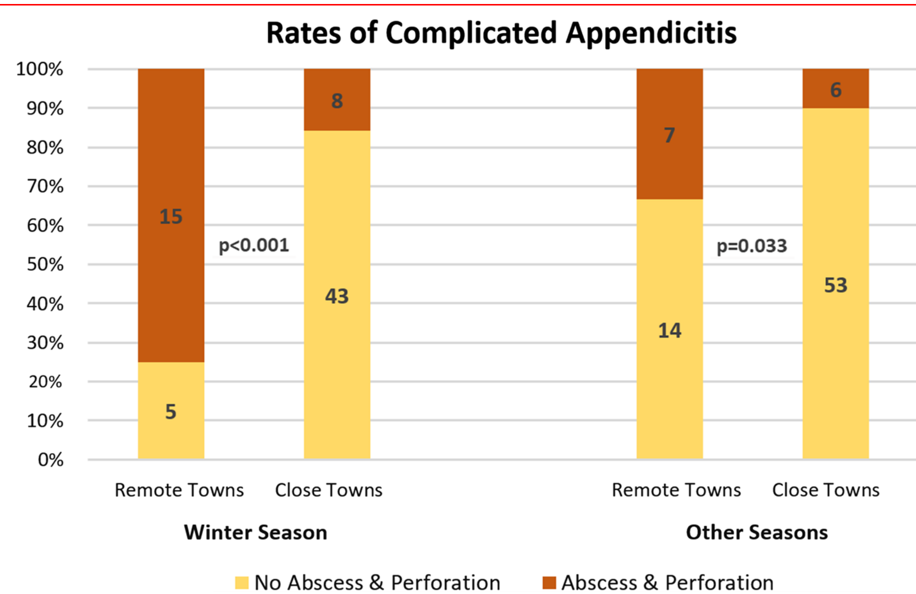

Fig. 3 Abscess and perforation rates depending on referral region in winter season and other seasons

LoHS (6.6 vs. 2.2 days), increased use of CT scans, and increased overall medical costs in patients with perforated appendicitis versus nonperforated appendicitis [13]. In this study, we also observed that abscess/perforation rate was a time-dependent fact. In the univariate analysis, it is significantly associated with pre-operative hospital delay (days) (OR:6.52, 95% CI [3.49 – 12.20]; $p < 0.001$) and duration of referral (minutes) (OR:1.01, 95% CI [1.00 – 1.01]; $p < 0.001$). Furthermore, pre-operative hospital delay was determined as an independent factor effecting abscess/perforation rate in multivariate analysis (OR:5.87, 95% CI [2.85–12.07]; $p < 0.001$). Similarly, LoHS was also significantly associated with pre-operative hospital delay (95% CI, $\beta = 1.25$ [0.87–1.62], $t = 6.58$; $p < 0.001$) and duration of referral (95% CI, $\beta = 0.011$ [0.01–0.14], $t = 7.34$; $p < 0.001$). Meaning that LoHS is naturally related with complicated cases (abscess/perforation). This is demonstrated in both univariate (95% CI, $\beta = 4.70$ [4.04–5.36], $t = 14.05$; $p < 0.001$) and multivariate analysis (95% CI, $\beta = 4.37$ [3.56–5.17], $t = 10.73$; $p < 0.001$).

There are different barriers to care and delays to health seeking behaviour in rural and underdeveloped areas [18]. Rural poverty and geographic location are also related with affordability of transportation and health care [6, 19]. In rural areas, it is more evident that topography of the region and seasonal changes affects accessibility to health care. We analysed that patients living in remote towns have significantly longer periods of pre-operative hospital delay (2.35 vs. 1.21 days; $p < 0.001$) and duration of referral (215.8 vs. 29 min; $p < 0.001$) compared to close towns. Moreover, as the state hospital is located in mountainside with an average altitude of 1700 m, both pre-operative hospital delay and duration of referral are significantly longer in winter season ($p < 0.001$). Although we presented that duration of referral is significantly affecting abscess/perforation rates in univariate analysis, it is consequentially related with the time of travel from referral region (naturally remote towns will have longer referral time) and the time of travel during winter season because many roads in remote towns closes due to heavy snowfall.

We see that the distribution of complicated cases is different among remote towns and close towns and different between winter season and other seasons (Fig. 3). Moreover, in univariate analysis, higher rates of complicated appendicitis are related with admitting to state hospital from remote towns (OR:7.94, 95% CI [3.46 – 18.23]; p < 0.001) and during winter season (OR:2.47, %95 CI [1.14–5.36]; $p = 0.022$). We presented that these factors are not significant in multivariate analysis, but for the LoHS specifically referral region as remote town demonstrated significant effect in univariate and multivariate analysis. Besides, winter season is a factor that is significant in univariate analysis and near significant ($p = 0.058$) in multivariate analysis for prolonged LoHS. Thus, we demonstrated that abscess/perforation rate was significantly high for cases referred from remote towns both in winter ($p < 0.001$) and other seasons ($p = 0.033$) but specifically in winter season (Fig. 3). We should also be aware of other factors that may affect the pre-operative hospital delay like self-medication (anti-inflammatory and analgesic drugs), day of the week, and time of the day that symptoms occurs. However, we believe that not all these factors affect the relationship between pre-operative hospital delay and abscess/perforation rates so much.

There are some limitations of the study. First of all, this is a single centre cohort study. It would be better to include at least 2 major centres with a similar topographic condition in order to have a more homogenous and comparable data. Secondly, a cost analysis should be made to demonstrate the effect of these significant factors over general health expenses. Furthermore, it could be possible that a number of patients in remote towns with non-complicated acute appendicitis are more inclined to go to hospital in summer season rather than in winter that can result spontaneous resolution of the symptoms.

In summary, this observational cohort study is the only study specifically focused on the effect of season and region on abscess/perforation rates and LoHS in acute appendicitis. We found that the rate of abscess/perforation, which is one of the indicator for quality of health care in rural areas, is significantly high in winter season and high for patients referring from remote towns. This is also related to significant prolonged LoHS that can be translated in to higher costs. It must be carefully and seriously managed. One of the key element is trying to overcome the challenges of accessibility to health care. Identifying the reasons for pre-operative hospital delay is essential in order to develop strategies and quality improvement interventions to reduce morbidity, mortality, and health care costs.

Author Contributions EO is the sole investigator in this study. EO conceived the study, collected, managed and analysed the data. EO takes responsibility for the paper as a whole.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations

Conflict of interest The author declares that they have no conflict of interests.

Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Ethics Approval This is an observational study. The Istanbul University Istanbul Faculty of Medicine Research Ethics Committee has confirmed that no ethical approval is required.

Informed Consent Informed consent was obtained from all individual participants included in the study as a part of routine surgical procedures. Surgical and interventional treatment procedures were compliant with up-to-date and standard of care treatment modalities.

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