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Complicated intra-abdominal infections: a prospective validation study of the WSES Sepsis Severity Score

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ABSTRACT

Introduction: The World Society of Emergency Surgery (WSES) has recently developed and validated a sepsis severity score for complicated intra-abdominal infections (cIAIs). We aimed to prospectively study the validity of this score in our local setting and compare it with global findings.

Methods: In a prospective study of 100 consecutive adult patients with cIAIs treated at Al-Ain Hospital, United Arab Emirates, from October 2014 to January 2016, we studied the demography of patients, disease, risk factors, WSES Sepsis Severity Score, management, hospital stay and mortality. Our findings were compared with those from a recent global multicentre prospective study from 53 countries (n = 4,496).

Results: Compared with global data, our patients had significantly more men ($p < 0.0001$) and were younger ($p < 0.0001$), had more appendicitis and perforated peptic ulcers ($p < 0.0001$), significantly lower sepsis severity score ($p < 0.0001$) and more delays in surgical intervention ($p = 0.001$). Nevertheless, they had similar adequate source control ($p = 0.54$) and surgical reinterventions ($p = 0.63$). Overall, our patients had significantly lower mortality rate (our study: 1.0% vs. global data: 9.3%; $p = 0.001$). A direct logistic regression model showed that the WSES Sepsis Severity Score significantly predicted mortality ($p < 0.0001$) but not our hospital's setting compared with other hospitals ($p = 0.18$).

Conclusion: Although patient demography and our hospital's setting significantly differed from other international hospitals, the WSES Sepsis Severity Score was very accurate in predicting mortality among our patients, which supports its generalisability for all patient populations worldwide.

Keywords: global, intra-abdominal infection, scoring, sepsis, severity

INTRODUCTION

Complicated intra-abdominal infections (cIAIs) are defined as infections that extend beyond organs, causing localised or diffuse peritonitis.[1] They can be serious, with profound morbidity and mortality. Although the mainstay treatment of cIAIs is source control and appropriate antibiotic therapy,[2] other factors can affect outcome. These include age of patient, severity of sepsis and its extent, organ failure on presentation, type of acquired infection, comorbidities and immunosuppression.[3-5]

The World Society of Emergency Surgery (WSES) performed a global prospective observational study on patients with cIAIs[6,7] and has developed a sepsis severity scoring system that could be used worldwide. Another recent WSES global study has validated this score[8] and found it to be highly accurate, easy to compute and practical for patients with cIAIs.

Important factors to be considered in this context include the local hospital setting, nature of local pathology, standards of healthcare administered, underlying health status of patient and economic variables. The United Arab Emirates (UAE) is unique from this perspective, as it is an extremely rapidly developing high-income country. Swift economic progress has meant that a number of fast-paced commercial projects have come up in quick time, employing and accommodating a large number of young, foreign men.[9] People from over 200 countries live in the UAE,[10] thus lending great diversity to the pathologies treated in our hospitals. Given this heterogeneity, we were interested to compare the data from patients with cIAIs in our hospital setting with the global sepsis data. The present study thus aimed to prospectively assess the validity of the WSES Sepsis Severity Score in our local setting and compare our results with global findings.

METHODS

Al-Ain Hospital, Al-Ain, UAE, is a major specialised acute care hospital, with 35 specialist departments and a capacity of over 400 beds.[11] The hospital is located in Al-Ain City, which has a population of more than 700,000 at present.[12] The study included all patients who were aged 18 years or over, had cIAIs, and had undergone interventional drainage or surgery for disease management at our hospital during a 15-month period from October 2014 to January 2016.

Ethical approval for this study was obtained from the Al-Ain Hospital Research and Ethics Governance Committee (ethical approval no.: AAH/EC-09-14-014). The study did not affect the routine healthcare provided to our patients and met the standards outlined in the Declaration of Helsinki. All patients who were admitted to Al-Ain Hospital sign a general consent form permitting the use of their anonymous data for audit and research purposes.

Management was considered delayed if the patient had localised or diffuse peritonitis for more than 24 hours before intervention. The patient was considered to have healthcare-associated infections if he/she were exposed to healthcare facility (although it may not have been the cause of infection).[13] Immunosuppression included immunosuppressant agents, chemotherapy, chronic glucocorticoids therapy, human immunodeficiency virus or lymphatic disease in the active phase. Severe sepsis and septic shock were defined according to the Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock.[14]

Overall, 100 consecutive patients were studied. Data was prospectively collected by the first author on a daily basis. Data collected included patient demography and disease, source and type of infection, severity of sepsis, associated diseases, delay in management, adequate control of source of infection, use of empirical antibiotics, need for reintervention, hospital stay and mortality. The WSES Sepsis Severity Score was calculated according to the Appendix.[8] Its value ranged between 0 and 18.

Our data was compared with that of a recent global multicentre prospective observational study by the WSES that studied patients with cIAIs from 132 medical institutions in 54 countries worldwide.[8] The WSES has kindly permitted us to use the crude data from its study in lieu of the global cohort. Data of 36 patients who were enrolled in the WSES study from our hospital was excluded from analysis and that of patients from the other 131 centres in 53 countries was retained for comparison (n = 4,496).

Sample size was calculated depending on the number of patients needed to achieve significant difference in mortality ($p < 0.05$) when compared with global data (n = 4,500; mortality: 9%) using Fisher's exact test. Expected mortality of cIAIs in our hospital was less than 3% and the calculated sample size for our study was 95 patients.

Data was entered into an MS Excel datasheet (2010, Microsoft Corporation, Redmond, Washington, USA) and then coded as numbers for statistical analysis. Data was analysed using IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY, USA). The WSES Sepsis Severity Score was calculated based on the statistical programme.

Univariate analysis was performed for comparing patients treated at our hospital (n = 100) with those treated at 131 centres globally from 53 countries (n = 4,496). This included Pearson's chi-square test or Fisher's exact test, as appropriate, for categorical data, and Mann-Whitney *U* test for continuous or ordinal data. Non-parametric statistical methods were used because they compare the ranks and not crude numbers. These should be used when the distribution of data is not normal, when sample size is small, or when variance of the groups is not equal.

Finally, the WSES Sepsis Severity Scores and hospital location (Al-Ain or others) were entered into a direct logistic regression model to ascertain whether treatment at our hospital had an effect on mortality of patients. A p-value ≤ 0.05 was considered to be statistically significant.

RESULTS

Table I shows the nationalities of patients treated for cIAIs at our hospital. They were from 17 different countries – 57 patients were manual workers, 14 were office employees/teachers, four were students, 17 were unemployed and profession was unknown for eight patients. The median age of our patients with cIAIs was 32 (range 18–75) years – 75 (75.0%) patients were men and 25 (25.0%) were women (Table II). 6 (6.0%) patients had healthcare-associated infections and 37 (37.0%) patients had generalised peritonitis. Only 2 (2.0%) patients had malignancy, 2 (2.0%) patients had serious cardiovascular disease and none were immunosuppressed. 7 (7.0%) patients were not insured; all were from the Indian subcontinent (nationalities: Bangladeshi, Indian and Pakistani), except for one patient, who was an Egyptian tourist.

Table I. Countries of origin of Al-Ain Hospital patients with complicated intra-abdominal infections (n = 100).

Country	No. (%)
Bangladesh	21 (21.0)
Pakistan	13 (13.0)
United Arab Emirates	13 (13.0)
Egypt	10 (10.0)
Syria	8 (8.0)
India	7 (7.0)
The Philippines	7 (7.0)
Jordan	4 (4.0)
Morocco	3 (3.0)
Oman	3 (3.0)
Sudan	3 (3.0)
Indonesia	2 (2.0)
Tunisia	2 (2.0)
Australia	1 (1.0)
Ethiopia	1 (1.0)
Germany	1 (1.0)
Yemen	1 (1.0)

Table II. Comparison of demographics of patients with complicated intra-abdominal infections from Al-Ain Hospital with global data.*

Variable	No. (%)		p-value‡
	Al-Ain Hospital (n = 100)	Global data (n = 4,496)	
Age (yr)†	32 (18–75)	51 (18–99)	< 0.0001
Gender			< 0.0001
Men	75 (75.0)	2,569 (57.1)	
Women	25 (25.0)	1,927 (42.9)	
Source of infection			< 0.0001
Appendicitis	61 (61.0)	1,534 (34.1)	
Cholecystitis	2 (2.0)	837 (18.6)	
Gastroduodenal perforation	20 (20.0)	485 (10.8)	
Postoperative	3 (3.0)	385 (8.6)	
Colonic non-diverticular perforation	3 (3.0)	268 (6.0)	
Small bowel perforation	1 (1.0)	242 (5.4)	
Diverticulitis	3 (3.0)	234 (5.2)	
Post-traumatic	3 (3.0)	114 (2.5)	
Pelvic inflammatory disease	0 (0)	50 (1.1)	
Other	4 (4.0)	347 (7.7)	
Diffuse peritonitis	37 (37.0)	1,611 (35.8)	0.83
Healthcare-associated infection	6 (6.0)	564 (12.5)	0.046
Immunosuppression	0 (0)	412 (9.2)	< 0.0001
Malignancy	2 (2.0)	560 (12.5)	0.001
Serious cardiovascular disease	2 (2.0)	782 (17.4)	0.001

**From 131 centres globally. †Data presented as median (range). ‡p-value was calculated using Fisher's exact test, Pearson's chi-square test or Mann-Whitney* U *test, as appropriate.*

The most common sources of intra-abdominal infections in our setting were acute appendicitis (61.0%) followed by perforated duodenal ulcers (20.0%). When compared with the global data, our patients had significantly more men ($p < 0.0001$), were significantly younger ($p < 0.0001$), had higher incidence of appendicitis and perforated peptic ulcers ($p < 0.0001$), and had less malignancy ($p = 0.001$), immunosuppression ($p < 0.0001$), serious cardiovascular disease ($p = 0.001$) and healthcare-associated infections ($p = 0.046$). However, generalised/diffuse peritonitis was similar to the global data ($p = 0.83$).

Table III shows the severity markers and management of our patients. When compared with the global data, our patients had significantly less severe sepsis and septic shock ($p <$

0.005), lower WSES Sepsis Severity Score ($p < 0.0001$) and more delays in surgical intervention ($p = 0.001$). Nevertheless, we had significantly higher application of empirical antimicrobial therapy ($p = 0.03$), and comparable adequate source control ($p = 0.54$) and surgical reinterventions ($p = 0.63$), including relaparotomies. Overall, we had significantly shorter median hospital stay (our study: 4 [1–52] days vs. global data: 7 [1–164] days; $p < 0.0001$) and lower mortality rate (our study: 1.0% vs. global data: 9.3%; $p = 0.001$).

Table III. Comparison of severity markers and management of patients with complicated intra-abdominal infections from Al-Ain Hospital with global data.*

Variable	Median (range)/No. (%)		p-value†
	Al-Ain Hospital (n = 100)	Global data (n = 4,496)	
Sepsis status on admission			< 0.005
No sepsis	41 (41.0)	1,919 (42.7)	
Sepsis	53 (53.0)	1,788 (39.8)	
Severe sepsis	5 (5.0)	560 (12.5)	
Septic shock	1 (1.0)	229 (5.1)	
WSES Sepsis Severity Score on admission	3 (0–11)	3 (0–17)	< 0.0001
0–3	88 (88.0)	2,907 (64.7)	
4–6	10 (10.0)	829 (18.5)	
≥ 7	2 (2.0)	750 (16.7)	
Empirical antimicrobial therapy	100 (100)	4,317 (96.0)	0.03
Delay in initial intervention (> 24 hr)	69 (69.0)	2,336 (52.0)	0.001
Adequate source control	92 (92.0)	3,825‡ (93.4)	0.54
Reintervention	9 (9.0)	493 (11.0)	0.63
Hospital stay (day)	4 (1–52)	7 (1–164)	< 0.0001
Mortality	1 (1.0)	416 (9.3)	0.001

**From 131 centres globally. †p-value was calculated using Fisher's exact test, Pearson's chi-square test or Mann-Whitney* U *test, as appropriate. ‡Data was missing for 400 patients. WSES: World Society of Emergency Surgery*

To ascertain whether the hospital setting influenced mortality among patients with cIAIs, the effect of both the WSES Sepsis Severity Score and our hospital setting on mortality was tested using a direct logistic regression model (Table IV). The model was highly significant ($p < 0.0001$, Nagelkerke's $R^2 = 0.5$). The odds of death increased by 0.78 upon an increase of 1 on the WSES Sepsis Severity Score, which was highly significant ($p < 0.0001$).

Although the odds of death decreased by 0.76 in our hospital compared with global data, this was not significant (p = 0.18), indicating that the decrease in mortality could be explained by the decrease in the sepsis scores of our patients.

Table IV. The direct logistic regression model including the WSES Sepsis Severity Score and Al-Ain Hospital (compared with other 131 global centres) in predicting mortality of patients having complicated intra-abdominal infection.

Variable	B	SE	Wald test	p-value	OR (95% CI)
WSES Sepsis Severity Score	0.58	0.02	647.4	< 0.0001	1.78 (1.70–1.86)
Al-Ain Hospital	−1.44	1.09	1.77	0.18	0.24 (0.03–1.98)
Constant	−4.21	1.11	14.46	< 0.0001	0.02

B: coefficient; CI: confidence interval; OR: odds ratio; SE: standard error; WSES: World Society of Emergency Surgery

DISCUSSION

We found that among our patients with cIAIs, there were significantly more men and younger patients. Our patients also had varied sources of cIAIs, significantly lower sepsis severity scores and more delays in surgical intervention when compared with the global data. Overall, we had significantly lower death rates. However, the lower mortality rate seen in our patients was explained by their lower WSES Sepsis Severity Scores rather than our hospital's setting when compared with other hospitals.

Following the discovery of oil in the UAE and the country's associated fast economic growth, its population dynamics has been greatly influenced by the large numbers of expatriate workers moving to it attracted by its numerous employment opportunities. Workers in the UAE come from over 200 countries[10] and are of various ethnic backgrounds. This sociocultural diversity and mix not only offers a unique experience but also poses distinctive challenges vis-à-vis the provision of healthcare services.[9] Its population is mainly young, with a male:female ratio of approximately 2:1 owing to the large influx of young foreign men.[9] This is reflected in the demography of our patients with cIAIs as well, with more men than women and a

younger patient population. Patients in the present study were from 17 different countries; 57.0% of them were manual workers and 87.0% were expatriates.

The source of infection was significantly different in our patients when compared to the global data, with more appendicitis and perforated duodenal ulcer in our setting. It was interesting to note the high percentage of perforated duodenal ulcers in our population. We have previously documented the higher incidence of perforated duodenal ulcers in Bangladeshi men, particularly during the fasting month of Ramadan.[15] Timely and adequate management of cIAIs usually achieves good results.[2] However, proper source control and appropriate antibiotic therapy are essential for favourable outcome of cIAIs. If this were not performed early and properly, high morbidity and mortality are to be expected among these patients. Although our patients had delayed management, we were surprised to find that this was not related to a lack of health insurance among patients – only 7.0% of patients lacked insurance in our cohort. We have noticed that in our clinical practice, individuals of certain nationalities have a higher tolerance for pain and present only when the pain persists, often reaching a stage of advanced complicated infection by the time of hospital presentation. The management of cIAIs at our hospital was similar to that in other parts of the world, with proper source control, appropriate use of antibiotics and reinterventions being performed, as necessary. Interestingly, our compliance for empirical antimicrobial therapy was extremely high (100.0%). We attribute this high level of compliance to the high quality standards necessitated by the Joint Commission International for accreditation purposes. Our hospital has been accredited by the Commission since 2010.

Clinical trials on patients with severe intra-abdominal infections may not be representative of the true mortality of such conditions. These studies usually indicate an increased survival rate due to restriction criteria involved.[16,17] It is important to highlight that our study validates the generalisability of the WSES Sepsis Severity Score, as it was

established in a heterogeneous multiethnic population from an urban general hospital. The global data had an overall mortality of 9.3% while our study had an overall mortality of 1.0%. Despite this disparity in mortality rates, our local settings did not affect patient mortality on logistic regression analysis. Our study population comprised mainly young, healthy workingmen, and perforated appendicitis and perforated peptic ulcer were the main pathologies. It was not surprising that the clinical outcome was good for our patients. Patient outcome and mortality were accurately predicted by the WSES Sepsis Severity Score for our patients, further supporting its generalisability and validity.

There were certain limitations to our study. First, our study represented data from a single hospital, which may not be generalisable to other hospitals in the country. Second, our hospital is a general hospital and does not have an oncology or transplantation centre, which explains the low incidence of malignancy and immunosuppression noticed among our patients. Third, as the number of compared groups was not equal, it should be expected that variance would be different. Parametric statistical methods are not advised for such cohorts and, consequently, we used non-parametric statistical methods that could address this limitation.

In conclusion, although the demography of our patients and the setting of our hospital significantly differed from that in other international hospitals, the WSES Sepsis Severity Score was very accurate in predicting mortality among our patients with cIAIs. This supports the generalisability of the WSES Sepsis Severity Score.

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Permission was obtained from World Society of Emergency Surgery (WSES) to use crude data from their recently published prospective study[6] for comparison with our local data. The authors thank the WSES for granting permission to use crude data from their database for this study.

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APPENDIX

The WSES Sepsis Severity Score (range 0–18) for patients with cIAIs.

Risk factor	**Score**
Age > 70 yr	2
Immunosuppression	3
Setting of acquisition	

Healthcare-associated infection	2
Clinical condition at admission	
Severe sepsis	3
Septic shock	5
Origin of cIAIs	
Colonic non-diverticular perforation peritonitis	2
Diverticular diffuse peritonitis	2
Postoperative diffuse peritonitis	2
Small bowel perforation peritonitis	3
Delay in source control	
Delayed initial intervention > 24 hr	3

cIAI: complicated intra-abdominal infection; WSES: World Society of Emergency Surgery