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Original Article

Implementation of Sepsis Bundles in Intensive Care Units of Bangladesh: A Prospective Observational Study

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Abstract

Objective: *To assess compliance of Intensive Care Units (ICUs) of Bangladesh to the components of resuscitation & management bundles of Surviving Sepsis Campaign (SSC). Secondary objective was to assess the impact of compliance on mortality and to determine how its compliance & mortality compared with other Asian and Western countries.*

Design: *Prospective Cohort study.*

Setting: *14 ICUs of Bangladesh.*

Participants: *65 adult patients with severe sepsis admitted into these ICUs in July 2009. The organizational characteristics of the participating centers, the patients' baseline characteristics, the achievement of target within the resuscitation & management bundle & outcome data were recorded.*

Outcome: *Compliance with the Surviving Sepsis Campaign's resuscitation (6 hrs) & management (24 hrs) bundles.*

Results: *Hospital mortality in ICU patients of Bangladesh suffering from severe sepsis was 49·2%. It was significantly higher than countries reported. Compliance to entire components of both resuscitation & management bundles were reported to be zero in ICUs of Bangladesh. Compliance of individual components of the bundles did not predict improved survival.*

Conclusion: *In ICUs of Bangladesh, high mortality of severe sepsis and failure of compliance of SSC bundle guidelines to have positive impact on survival were presumably attributed to delayed diagnosis, poor adherence to & delayed application of SSC guidelines on sepsis bundles.*

Key Word: *Severe sepsis, septic shock, Intensive care units, compliance, mortality.*

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Introduction

Sepsis is defined in association of a panoply of nonspecific inflammatory responses with evidence or suspicion of a microorganism.[1] The definition of severe sepsis and septic shock has been formulated since early 1990s, and has been accepted worldwide since then.[2,3] So when sepsis is associated with hypo-perfusion or single organ dysfunction, it becomes severe sepsis. When hypoperfusion in severe sepsis persists in spite of adequate fluid resuscitation and requiring vasopressors, it is called septic shock.[3]

The Surviving Sepsis Campaign (SSC) guidelines for the management of severe sepsis and septic shock were initially published in 2004[4] and were later updated in 2008.[5] The SSC guidelines outline two bundles (popularly known as sepsis bundles) namely a 6hours Resuscitation Bundle and a 24 hour Management Bundle with the aim of reducing severe sepsis mortality through the prompt and appropriate therapy during the initial hour of diagnosis of severe sepsis. The six hours bundle includes early blood culture, antibiotics and various aspects of early goal directed treatment for hemodynamic derangement.[6] The 24 hour bundle includes low dose steroid, glucose control, recombinant human activated protein C (drotrecogin alfa) & guidelines on ventilator support. Studies have shown that implementation of these bundles with improved compliance was found to be associated with reduced hospital mortality.[7,8,9] However baseline compliance for completing the elements of the resuscitation and management bundles were reported to be low.[7,8,10]

Compliance and impact of compliance on Asian intensive care units and hospitals with recommendation within the two sepsis bundles have been unexplored until MOSAICS study group published their findings involving 16 Asian countries (including Bangladesh) with 150 participating ICUs (14 from Bangladesh) enrolling 1285 (65 from Bangladesh) adult patients.[10] This study described the compliance status on Asian countries across the board but did not address the status of compliance and outcomes of compliance of ICUs of individual participating countries.

It has been observed that rational efforts to promote the SSC guideline do not exist in most Asia where cost is an important burden in implementation of potentially expensive bundles.[11,12] Bangladesh is no exception in this regard. It is a low income country as per World Bank analytical income classification 2009.[13] As such intensive care services in Bangladesh are very much under developed according to a survey done in 2007.[14]

With above consideration in mind we have made a domestic sub analysis of MOSAICS study[10] using the participating ICUs of Bangladesh. We have also aimed to determine the nature of compliance on the two sepsis bundles outlined in the recommendation of SSC[4,5] and assess the impact of compliance on mortality. In doing so we used the data of the participating ICU's of Bangladesh collected during the MOSAICS study period[10] and have came up with the findings and observations which were never addressed before for a low income Asian economy like Bangladesh.

Methods

Study design: This is a prospective cohort study that took place during the period of July 1, 2009 to July 31, 2009. It involved 65 patients in 14 ICU's of capital of Bangladesh. According to one study 90% of the ICU's of Bangladesh were located in its capital.[14]

While selecting the study ICUs we used a snowball method to identify units who would be interested to participate.

Physician representing each ICU was called site investigator and he was recognized by his institution as an intensivist even without a specialty certification or degree in critical care/ intensive care medicine and must have been treating the whole patient not a single organ or system. Participation by the site investigators was voluntary and unfunded.

The primary objective of the study was to document the compliance of Bangladeshi ICUs to the recommendations within the SSC resuscitation & management bundles.

The secondary objectives were to document outcomes of severe sepsis in ICUs of Bangladesh, to evaluate if compliance of those ICUs to the recommendations within SSC bundles would lead to improved clinical outcome, to compare the outcome of the study with those of MOSAICS study[10] to see where Bangladeshi ICUs stand in comparison to the Asian ICUs in general & other participating ICUs of low income countries in MOSAICS study in particular.

Inclusion criteria for study ICUs included medical (including respiratory), surgical, mixed medical & surgical ICUs and ICUs having six or more beds.

Predominantly pediatric or neurological ICUs or coronary care unit were excluded from the study.

Inclusion criteria for the study patients involved all consecutive patients with severe sepsis who were admitted to the study ICUs between 1st of July 2009 at 00:00 hours (midnight) and 31st July 2009 at 23:59 hours.

Patients who were already in ICUs prior to 1st of July 2009 at 00:00 hour were not included. Patient less than 21 years and patients who were directly transferred to study ICUs from another hospital or another ICU with diagnosis of severe sepsis were excluded from the study. For all patients who were discharged from the ICU & readmitted to the ICU again during the study period, only the first admitted during the study period was included.

The definition of severe sepsis was adapted from the 2001 International Sepsis definition Conference and the Surviving Sepsis Campaign.[3,5]

Overall compliance was defined when all relevant individual targets were met for entire resuscitation and management bundles.

Data Collection

Prior to the study, written permissions were obtained from institutional review board/ ethical review committee or its equivalent of the participating hospitals by the site investigators. The need for informed consent was waived in view of the observational & anonymous nature of the study.

Before beginning data collection, site investigators were invited to several meetings to discuss the details of the study design. Those were followed by several orientation sessions for the data collectors who were handed over data collection forms. Each of them was designated by his respective site investigator. Online filling of data collection forms was not done as majority of participating hospitals did not have the facilities. No attempt was made to educate the data collectors in the participating ICUs on the Sepsis bundles.

Each data collector from respective participating ICU was given two kinds of data collection forms. The first form known as ICU questionnaire was completed before enrolment of the patients. The questionnaire recorded organizational characteristics, including the type of intensive care unit (open or closed), specialty (medical, surgical, mixed), number of beds, 24 hour intensivist cover, number of intensivist, ratio of nurses to beds, any accredited intensive care fellowship program/postgraduate course in critical care, type of hospital (government; private; university etc.). Data on the facilities, equipment and protocols in the ICUs were also collected. The second form recorded the clinical and demographic characteristics of all patients including age, sex, Acute physiology and Chronic Health Evaluation II (APACHE II) score, primary source of severe sepsis and organ dysfunction at sepsis presentation, number of organ failure, mortality in ICU and hospital, length of stay in ICU and hospital, duration of invasive mechanical ventilation (time from starting ventilation to successful extubation or breathing with a tracheostomy mask for a continuous period of e" 48 hours).This form also recorded, when clinically appropriate, the achievement of targets in resuscitation bundle (lactate measurement, blood cultures, broad spectrum antibiotics, fluid with or without vasopressors, central venous pressure, and central venous oxygen saturation) within six hours after presentation. Pulmonary artery catheterization for mixed venous oxygen saturation was not available in any of our study ICU. This form also recorded achievements of targets in management bundles (low dose steroid, glucose control, and lung protective ventilation within 24 hours). Drotrecogin alfa (activated protein C) was not available in Bangladesh during the time of study.

The onset of severe sepsis (time zero) was determined according to the patients location within the hospital when severe sepsis was diagnosed. For patients who developed severe sepsis in medical and surgical ward or any other non emergency department, time zero was determined by searching the clinical documentation for the time of diagnosis of severe sepsis. In patients who developed severe sepsis in the ICU time zero was determined by searching the clinical documentation for the time of diagnosis of severe sepsis. If no time and date could be found by these methods, the default time of presentation was the time of admission for the ICU. In Bangladesh no emergency department (ED) in the study hospitals had facility for documenting diagnosis of severe sepsis and no ED had protocol for implementing the 6 hour & 24 hour bundles during the study period.

The six hours resuscitation bundle was adopted from original SSC standard severe sepsis resuscitation bundle (Table-I).

The elements of 24 hours management bundle were modified from original SSC standard severe sepsis management bundles as follows (Table-I).

Table-I

Target (1^{st} six hours)	Relevant clinical scenario
Measure lactate	All patients
Blood culture before antibiotics	All patients
Broad spectrum antibiotics within 1 hour of admission (ED excluded)	All patients
Fluids (20 ml/kg of crystalloids or equivalent with or without vasopressors)	Hypotension or lactate e"4 mmol/L with or without septic shock (hypotension despite initial fluids vasopressors required)
CVP > 8mmHg	Septic shock or lactate > 4 mmol/L
$ScvO_2$ > 70%	Septic shock or lactate > 4 mmol/L
Target (1^{st} 24 hours)	
Low dose steroids administered or considered	Septic shock
Glucose > 4.5 and d" 10.0 mmol/L at 1^{st} 24 hours	All patients
Tidal volume d" 6 ml/kg predicted body weight	ALI / ARDS

CVP= Central venous pressure, $ScvO_2$ = Central venous oxygen saturation
ALI = Acute lung injury, ARDS=Acute respiratory distress syndrome

For maintenance of adequate glucose control, upper limit of glucose of 10·0 mmol/L was decided based on the NICE-SUGAR study and latest recommendation from SSC[15,16] and the lower limit was set at 4·5 mmol/L according to Van Den Berghe et al's protocol for avoiding adverse effects of hypoglycaemia.[17] The glucose target was considered unmet if any measurements fell outside this range. We defined acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) as per American European Consensus Conference[18] and considered target for ALI/ ARDS as being met if the most frequently delivered tidal volume was d"6ml/kg predicted body weight.[19] Measurement of plateau pressure was abandoned as it was not feasible in our study ICUs. We decided that failure to achieve a target could be due to failure to attempt the measurement or there could be a failed attempt equated with failure to achieve a target.

We checked all collected hard copy data for outliers that might suggest entry errors and also checked for missing data. In both circumstances we checked with the site investigators for necessary rectification.

Outcome measures

All patients were followed until discharge from or death in the hospital. The primary outcome measure was compliance with resuscitation and management bundles. Patients who were discharged to another hospital were declared survivors, unless there was specific information considering death in the receiving hospital. Patients who were discharged home in a terminal state and who were expected to die within few hours or day were declared non survivors.[20] The secondary outcome measure was all cause hospital mortality.

Statistical analysis

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences), version 11·5. The test statistics used to analyze the data were Chi-square ($\div^2$) or Fisher's Exact Probability Test and Student's t-Test. Categorical or qualitative data were expressed as frequency with corresponding percentages and were compared between survivors and non-survivors using Chi-square ($\div^2$) or Fisher's Exact Test, while quantitative data were expressed as mean (with 95% confidence interval of mean) and standard deviation from the mean and were compared between groups using Student's t-Test. Level of significance was set at 5% or 0·05 and $p < 0·05$ was considered significant.

Results

The present study was intended to assess the compliance of Bangladeshi ICUs to Surviving Sepsis Campaign guidelines in the management of severe sepsis patients using two strategies: 6 hours resuscitation bundle and 24 hours management bundle. A total of 65 patients from 14 Intensive Care Units/Hospitals were selected for the purpose. Of the 65 patients, 18 (28%) were diagnosed as having severe sepsis and 47 (72%) septic shock. Thirty eight (58·5%) of 65 patients died and 27 (41·5%) survived. Most (78·9%) of the patients died within 28 days of admission and majority (84·2%) of the deaths occurred while they were in ICU and 6(15·8%) at home after discharge from ICU (Table II).

Table II

Distribution of patients by outcome

	Frequency	Percentage
CVP measured (n = 65)	45	69·2
Achievement of CVP (n = 42)	32	76·2
$S_{cv}O_2$ measured (n = 65)	11	16·9
Achievement of $S_{cv}O_2$ (n = 11)	10	90·9
Fate of patientDiedSurvived	3827	58·541·5
Mortality (n = 38)Within 28 days		
After 28 days	3008	78·921·1
Place of death (n = 38)In ICU		
At home	3206	84·215·8

Pneumonia was the leading source of infection (58·5%). The mean APACHE II score was 18·8 ± 7·4. Circulatory dysfunction was the commonest organ dysfunction with hypotension (78·5%) and septic shock (70·8%). Over two-thirds (67·7%) of the patients were given antibiotics before obtaining blood sample for culture. 83·1% of the patients received antibiotic in first 3hours of admission and 73·8% received resuscitation with I/V fluid at the rate of 20 ml/kg of body weight. None of the patients on mechanical ventilation (n = 45) received low tidal volume (d" 6 ml/kg PBW). About 70% of the patients Central Venous Pressure (CVP) was measured and of them 62% achieved CVP target (e" 8 mmHg).

Demographic characteristics of the study subjects showed that non-survivors were relatively old (mean age 55.6 years) than the survivors (mean age 52.3 years) ($p = 0.451$). No significant difference was observed between the groups in terms of gender. A significantly higher proportion of non-survivors (86.8%) were admitted with medical problems than that of their survivor counterparts (63%) ($p = 0.024$). However, type of ICU (closed or open) and diagnosis at admission (septic shock or severe sepsis) did not influence fate of the patients ($p = 0·951$ and $p = 0·156$ respectively) (Table III).

Table III

Baseline demographics, patient and ICU characteristics

Baseline characteristics	Group Survivors(n = 27)	Mean difference Non-survivors(n = 38)	p-value (95% CI)	
Age (years)	52·3 ± 19·7	55·6 ± 15·6	3·3(-5·4 –12·1)	0·451
SexMaleFemale	10 (37·0)17 (63·0)	19 (50·0)19 (50·0)	-——	0·300
Type of patientMedicalSurgical	17 (63·0)10 (37·0)	33 (86·8)5 (13·2)	——-	0·024
Type of ICUClosedOpen	13 (48·1)14 (51·9)	18 (47·4)20 (52·6)	——-	0·951
DiagnosisSeptic shockSevere sepsis	17 (63·0)10 (37·0)	30 (78·9)8 (21·1)	——-	0·156

Figures in the parentheses denote corresponding percentage.

In terms of source/focus of infection (Table IV), lung was the significant source of infection among the non-survivors (68·4%) than among the survivors (44·4%) (p = 0·047). Soft-tissue infection was also significantly higher in the former group (21·1%) compared to that in the later group (3·7%) (p = 0·046).

There was no significant difference between survivors and non-survivors with respect to organ dysfunction, although incidence of septic shock was significantly higher among the non-survivors (81·6%) compared to the survivors (55·6%). The mean APACHE II score was also much higher in the former group than in the later group (p = 0·008) (Table V).

Table IV

Association between source of infection & survival of patients

Source of infection	Group Survivors (n = 27)	Non-survivors (n = 38)	p-value
Lung (pneumonia)	12 (44·4)	26 (68·4)	0·047
Urinary tract (UTI)	7 (25·9)	11 (28·9)	0·788
Abdomen (except urinary tract)	8 (29·6)	9 (23·7)	0·591
CNS	4 (14·8)	4 (10·5)	0·440
Soft tissue	1 (3·7)	8 (21·1)	0·046
Bones & joints	1 (3·7)	1 (2·6)	0·662
Intravascular catheter	1 (3·7)	0 (0·0)	0·415
Primary bacteraemia	1 (3·7)	2 (5·3)	0·628
Other sources	2 (7·4)	8 (21·1)	0·249

Figures in the parentheses denote the corresponding percentage.

Table-V

Comparison of organ dysfunctions between survivors and non-survivors

Organ dysfunction	Group Survivors (n = 27)	Non-survivors (n = 38)	Mean difference (95% CI)	P-value
Hypotension	20 (74·1)	31 (81·6)	——	0·468
Hepatic dysfunction	5 (18·5)	8 (21·1)	——	0·801
Hyperlactataemia	4 (14·8)	4 (10·4)	——	0·440
Acute lung injury	10 (37·0)	15 (39·5)	——	0·842
Renal impairment	10 (37·0)	18 (47·4)	——	0·407
Thrombocytopenia	2 (7·4)	7 (18·4)	——	0·367
Coagulopathy	4 (14·8)	6 (15·8)	——	0·915
Other organ dysfunction	1 (3·7)	0 (0·0)	——	0·415
ARDS	8 (29·6)	10 (26·3)	——	0·769
Septic shock	15 (55·6)	31 (81·6)	——	0·023
APACHE II score	16·0 ± 6·6	20·8 ± 7·3	4·8(1·2 – 8·3)	0·008

Figures in the parentheses denote corresponding percentage.

Table VI

Comparison of compliance to components of two bundles between survivors and non-survivors

Compliance	Group		p-value
	Survivors(n = 27)	Non-survivors(n = 38)	
Compliance to resuscitation bundle			
Lactate measurement done	5/27 (18·5)	6/38 (15·8)	0·772
Blood cultures before antibiotics	18/27 (66·7)	26/38 (68·4)	0·882
Antibiotics given in first 6 hrs	23/27 (85·2)	31/38 (81·6)	0·963
I/V fluids given @ 20 ml/kg body-wt	20/27 (74·1)	28/38 (80·0)	0·580
Targeted CVP achieved	11/15 (73·3)	21/27 (77·8)	0·513
$S_{cv}O_2$ e" 70% achieved	5/5 (100·0)	5/6 (83·3)	0·545
Compliance to management bundle *			
Low-dose steroids administered	8/27 (29·6)	17/36 (47·2)	0·158
Glucose e" 4.5 to d" 10 mmol/L at 6-24 hrs	6/27 (22·2)	11/37 (29·7)	0·502
Low Tidal volume criteria for ARDS on MV	0 (0·0)	0 (0·0)	———

Figures in the parentheses denote corresponding percentage.

*Drotrecogin Alfa was not available in Bangladesh

Table VI illustrates the distribution of compliance to different components of resuscitation and management bundles. Compliance to all the individual components of resuscitation bundle was almost homogeneously distributed between survivor and non-survivor groups. None of the study subjects in either group met low tidal volume criteria for ARDS patients on mechanical ventilation. Compliance to entire resuscitation bundle was virtually absent. Compliance to 3–5 components of resuscitation bundle was met in 71% of the cases and that to 1–2 components in 27·4% cases. Compliance to none of the 6 components was only in 1·6% cases (Fig.1). Compliance to management bundle was very poor. As drotrecogin alfa was not available in Bangladesh, the management bundle consisted of 3 components. Lack of compliance to any of the three components was observed in 44·3% cases. Compliance to one component was observed in 45·9%, to two components in 9·8%. Compliance to entire management bundle was not found at all (Fig.2).

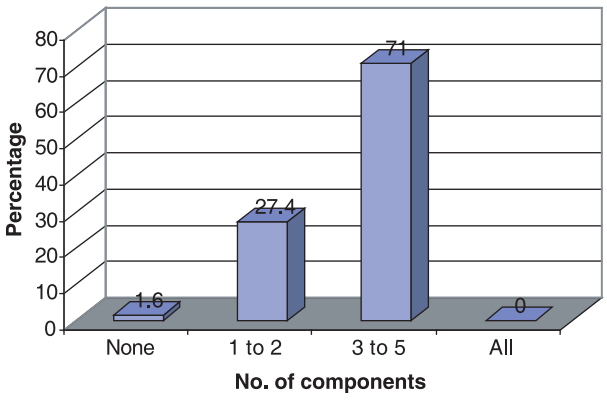

Fig.-1: *Stratification of patients by compliance to number of components of resuscitation bundle*

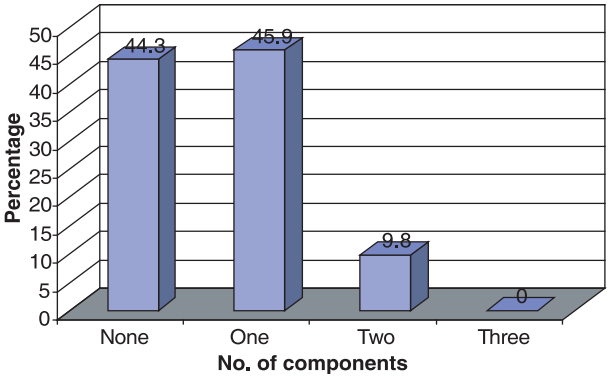

Fig. 2: *Stratification of patients by compliance to number of components of management bundle*

Table VII depicts the compliance status and its influence on outcome of patients. Survival was not found to be associated with compliance status to resuscitation and management bundles (p = 0.544 and p = 0.288 respectively).

Table VII

Association between compliance status and outcome of compliance

Compliance status	Group		p-value
	Survivors (n = 27)	Non-survivors (n = 35)	
Compliance to resuscitation bundle			
5 components	4 (14·8)	6 (17·1)	0·544
< 5 components	23 (85·2)	29 (82·9)	
Compliance to management bundle			
1-2 components	13 (48·1)	21 (60·0)	0·288
No component	14 (51·9)	14 (40·0)	

Figures in the parentheses denote corresponding percentage.

Discussion

Of the 14 ICUs that participated in our study, all of them were located in the capital of Bangladesh.

Total beds in these study ICUs (146) represented 2% of all beds of the study hospitals and accounted for 25% of entire ICU beds of the country. Our study patients (n = 65) represented 10·8% of all admission in the study ICUs during the study period. This is very similar to 10·9% in the Asian ICUs in the MOSAICS Study,[10] 11% in United States.[21]

We observed that, complete compliance with all the six components of the resuscitation bundle was nonexistent in Bangladeshi ICUs and 1·6% study patients had zero compliance to all of the individual components of the resuscitation bundle.

Similarly complete compliance with all those components of the management bundle (excluding drotrecogin alfa) was also absent in our study ICUs and 39·3% of study patients had zero compliance to all of the individual components of management bundle.

Non survivors in our study accounted for 58·4% of our patients and what is noteworthy is that compliance to different components of both bundles did not influence survival in our study.

Compliance with resuscitation bundle in our study was visibly insignificant compared to 10% in Spain,[7] 10·7% in France,[9] 14% in the United Kingdom,[22] and 31·3% in multinational study by SSC involving countries of Europe & North America.[8]

Similarly compliance to management bundle in our study was very poor compared to15·7% in Spain[7] and 36·1% in multinational survey.[8]

On reviewing the data of MOSAICS study[10], we were able to compare the achievements of bundle targets & hospital mortality among the three groups (Table VIII), which included the low income countries (Bangladesh, Nepal, and Vietnam) of MOSAICS study, entire Asian study countries (Low income, middle, and high income) of MOSAICS study and Bangladesh alone. There was no significant difference among the three study groups in terms of hospital mortality. Although Bangladesh showed certain strength in target achievement in components like CVP, SvO_2, blood culture before antibiotics, IV fluid & antibiotics, overall compliance in both bundles were poor in low income countries which included Bangladesh (p = 0·003 & p = < 0·001 in resuscitation & management bundles respectively.)

Table VIII

Achievements SSC bundle targets and hospital mortality among the low-income countries (Bangladesh, Nepal, and Vietnam) and among entire Asian Study countries (low-income, middle-income, and high-income) compared to those of Bangladesh alone.

Target	Group			p-value
	Bangladesh (n = 65)	Bangladesh, Nepal & Vietnam (n = 176)	Entire Asian study countries (n = 1285)	
Resuscitation bundle(1st 6 hours)				
Lactate measurement done	11/65 (16·9)	26/176 (14·8)	512/1285 (39·8)	< 0·001
Blood cultures before antibiotics	44/65 (67·7)	111/176 (63·1)	807/1285 (62·8)	0·629
Antibiotics given in first 3 hrs	54/65 (83·1)	134/176 (76·1)	844/1285 (65·7)	0·001
I/V fluids given @ 20 ml/kg body weight	41/51 (80·4)	110/134 (82·1)	816/999 (82·7)	0·965
CVP e" 8 mm Hg	32/42 (76·2)	52/132 (39·4)	359/874 (41·1)	< 0·001
$S_{cv}O_2$ e" 70% or S_VO_2 e" 65%	10/47 (21·3)	13/124(10·5)	99/837 (11·8)	0·130
Management bundle(1st 24 hours)				
Low-dose steroids administered	25/47 (53·2)	76/123 (61·7)	449/805(55·7)	0·411
Glucose e" 4.5 to d" 10 mmol/L at 24 hrs	17/64 (26·5)	56/175 (32)	350/1285 (27·2)	0·409
Tidal volume d" 6ml/kg PBW	0/45 (0·0)	10/101 (9·9)	74/630 (11·7)	0·047
Overall compliance: entire resuscitation bundle	0/65 (0·0)	4/176 (2·3)	98/1285 (7·6)	0·003
Overall compliance: entire management bundle	0/65 (0·0)	4/176 (2·3)	149/1285 (11·6)	< 0·001
Hospital mortality	32/65 (49·2)	82/176 (46·6)	572/1285 (44·5)	0·680

Figures in the parentheses denote corresponding percentage.

Bangladesh being a low income Asian country[13] there is scarcity of financial resources in most ICUs.[14] Emergency services capable of diagnosis and delivering initial management of sepsis are very much nonexistent[23,24] & here there is a lack of facility for prompt emergency care similar to what is practiced in ED of the developed countries. As such burden of diagnosis & initiation of management of severe sepsis is shifted from ED to inpatient units and often to ICUs. This is because ED in Bangladesh typically plays the role of triage station for direct admission of sick patients to inpatient unit or ICU.[24]

As a result, there are varying degrees of delay in diagnosis of severe sepsis and consequently similar degrees of delay in initiation of management which is often inadequate & not following SSC guidelines properly. It is hypothesized that this delay causes organ dysfunction more than anticipated.

Becker et al suggested that delay in detection of sepsis could cause mortality rate to remain high even after implementation of the SSC bundle.[25] Admission to the ICU after development of organ failure (i.e. late admission) has a significant impact on outcome.[26,27] It has been shown that time from onset of organ dysfunction to diagnosis was strongly correlated with mortality rates; those ranged from 33·3% when treatment was initiated within first 24 hours after onset to 84·5% when treatment was delayed for 2 to 3 days. The risk of death was 8.73 times greater when severe sepsis was identified more than 48 hours after the onset of organ dysfunction, even if antibiotic therapy and fluid resuscitation were started immediately after diagnoses.[26]

Successful implementation of clinical practice guidelines usually improves quality of care. An understanding of the barriers stopping the implementation of critical care guideline is essential for developing interventions to improve practice.[28] Three major barriers have been reported to hinder application of guidelines: knowledge barrier (lack of awareness or of familiarity), attitude barriers (lack of agreement, self efficacy, and outcome expectancy or inertia of previous practice), and behavioral barriers (insufficient staff, lack of resources).[29]

In Bangladesh scarcity of training facility with resulting lack of trained manpower compounded by lack of financial resources have been responsible for both inadequate & poor quality of care for critically ill patients.[23]

We can use an early sepsis detection protocol used in study model of Brazil[30] where mortality due to severe sepsis was reported to be 56% before application of the model. The measures taken in this model were simple and inexpensive and could be adopted even if financial resources are limited. For the implementation of an early inpatient early-sepsis-risk detection protocol, the nursing staff of the hospital need to be trained and nurse must be assigned to the protocol.[26] Such early sepsis detection protocol may be a solution to delayed detection of sepsis in Bangladesh.

ICUs of Bangladesh can also use educational program to improve compliance in Sepsis bundles. In a Spanish study mortality improved from 42·5% to 38·7% after an educational program designed to increase compliance with Sepsis bundles.[7] In a French study, improved compliance was associated with decrease in mortality from 39·6% to 27·4%.[9] The multinational survey by S.S.C showed a reduction in mortality from 37% to 30·8% with increased compliance.[8]

Study limitation & conclusion

Our study was subject to selection bias as we used a snowball method to include suitable study ICUs. The sample size was small (n=65). It was too small compared to severe sepsis patient population of Bangladesh keeping in mind that our study ICUs represented one fourth of all ICU beds of Bangladesh. So an accurate epidemiology of severe sepsis in Bangladesh was difficult to obtain from this study.

In univariate analysis certain factors like medical patients (as opposed to surgical patients), pulmonary or soft tissue infection, and presence of septic shock or higher APACHE-II score emerged as predictor of non survival. However whether they were the independent predictor of non survival could not be ascertained as a valid binary regression analysis could not be possible because the size of the sample (n = 65) needed to be significantly larger.

We strongly suspect that delay in diagnosis of severe sepsis and subsequent delay in initiation of treatment and lack of implementing proper adherence to the treatment guidelines of the SSC were presumed to be the significant reason for the high mortality & poor compliance of Sepsis Bundles in management of severe sepsis in Bangladeshi ICUs.

Nonetheless our study is the first of its kind from Bangladesh where there are limited financial resources & man power in health care sector. It is an eye opener for our health care professionals treating severe sepsis patients and for the health care policy makers of Bangladesh who need to organize effort for promotion of treatment of severe sepsis nationwide.

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