

## LAG TIME IN ANTIBIOTIC ADMINISTRATION IN PATIENTS WITH SIGNS OF SIRS/SEPSIS AND ITS IMPACT ON MORTALITY AND LENGTH OF ICU STAY

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### ABSTRACT

#### Background

Severe sepsis and septic shock are one of the leading causes for hospitalisation and in-hospital mortality. The surviving sepsis guidelines campaign<sup>5</sup> developed in 2004 incorporated evidence based guidelines to reduce mortality from sepsis and septic shock. These include initiation of broad spectrum antimicrobials within 1 hr of recognition of sepsis. We set out to assess the compliance to time of antimicrobial administration guidelines in our hospital and whether the choice of antimicrobials were appropriate, its impact on mortality and length of stay in hospital.

#### Materials and Methods

The study was a retrospective observational study done in Columbia Asia Hospital, Bangalore. The study involved 127 patients admitted to ER/ICU with signs of SIRS/SEPSIS between January 2010 and December 2010. 52 patients were excluded from study since they had received antibiotics before admission. 75 patients were included in the study.

#### Result

Median time of antibiotic administration in our patients was 2.3 hours. Though mortality and length of stay was higher in the group which received antibiotics after 2 hours there was no statistical significance. In our study 23 (30%) of the patients got inappropriate antibiotics. Of the 12 deaths, 6 were in patients who received inappropriate antibiotics. There was no statistical significance.

#### Conclusion

Our study showed a lag time of 2.3 hours for antibiotic administration in sepsis patients. Though numbers are small to draw any definitive conclusions, mortality and length of stay can be significantly reduced, if the antibiotics are administered at the earliest after the diagnosis of sepsis is made.

**KEYWORDS:** Severe Sepsis and septic Shock are one of the Leading Causes for Hospitalisation and In-Hospital Mortality

### INTRODUCTION

Severe sepsis and septic shock are one of the leading causes for hospitalisation and in-hospital mortality. Despite improvements in health care, mortality rate from septic shock is 30% in the west and as high as 60% in developing

world<sup>1,2</sup>.

The surviving sepsis guidelines campaign<sup>5</sup> developed in 2004 incorporated evidence based guidelines to reduce mortality from sepsis and septic shock. These include initiation of broad spectrum antimicrobials within 1 hr of recognition of sepsis. There is an emphasis on administration of appropriate antibiotic cover for the presumptive organism, which is found to have significant impact on ICU outcome.

Unfortunately these guidelines are not immediately incorporated. Most of the time the delay in administering antimicrobials due to either a delay in recognition of the disease state or in the institution of therapy.

We set out to assess the compliance to time of antimicrobial administration guidelines in our hospital and whether the choice of antimicrobials were appropriate, its impact on mortality and length of stay in hospital.

## AIM OF STUDY

- To assess the lag time in antibiotic administration in patients with signs of SIRS/SEPSIS, admitted to ER/ICU.
- Impact on mortality
- Length of ICU stay

## MATERIALS AND METHODS

The study was a retrospective observational study done in Columbia Asia Hospital, Bangalore. The study involved 127 patients admitted to ER/ICU with signs of SIRS/SEPSIS. 52 patients were excluded from study since they had received antibiotics before admission. 75 patients were included in the study.

SIRS was defined according to the criteria put forth by the Society of Critical Care Medicine<sup>3,4</sup>, i.e patients presenting with any two of the following clinical signs [tachypnoea, sinus tachycardia, body temperature  $<35^{\circ}\text{c}$  or  $>38^{\circ}\text{c}$ , TC  $<4000$  or  $>11000$ ]. Sepsis was defined as presence of 2 or more SIRS criteria in the setting of a documented or presumed infection. Severe sepsis was defined by concomitant organ dysfunction and septic shock in the presence of accompanying sustained hypotension (SBP $<90\text{mmHg}$  or MBP $<65\text{ mmHg}$ ).

All patients with signs of SIRS, sepsis, septic shock were included in the study. Patients referred from other hospital, post operative and those shifted from ward, who had received antibiotics prior to shifting to ER/ICU were excluded from the study.

## REVIEW OF LITERATURE

The surviving sepsis guidelines 2004 recommends that appropriate antimicrobial therapy should be administered within 1 hour of recognition of sepsis. Various studies were done to assess the lag time in antibiotic administration and its impact on mortality and length of stay in hospital.

Kumar et al<sup>5</sup> did a retrospective cohort study involving 2731 patients with septic shock. This study was undertaken to quantify the association between mortality and time to administration of effective antibiotics following hypotension in septic shock patients. The median time of effective antibiotic administration was six hours. Survival was 79.9% if antibiotics were administered in the first hour, and 42% by the sixth hour. Each hour delay of antibiotics was associated with a mean decrease in survival of 7.6%.

Shahla et al<sup>6</sup> did a prospective observational study in 111 patients. Average time from triage to actual antibiotic administration was 2.48±1.86 hours. The timing of antibiotic administration was significantly associated with survival.

Francis M et al<sup>7</sup> did a retrospective chart review of patients with sepsis, a total of 213 patients were reviewed, median time of drug administration from the time of diagnosis was 163 minutes.

R Appelboam et al<sup>8</sup> studied 375 patients, they found that the median time of antibiotic administration in their ICU setup was 4 hours. Mortality was found to be higher in the delayed group.

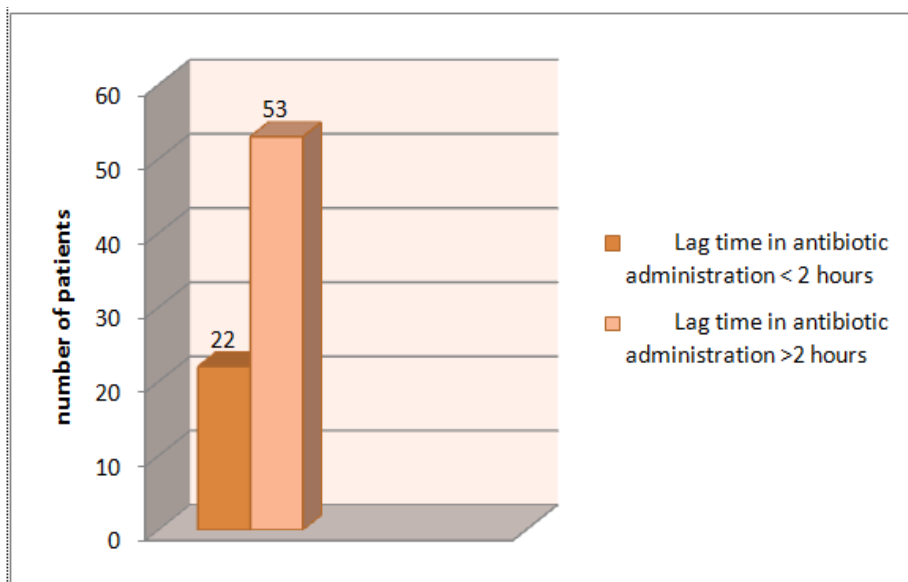
R Frost et al<sup>9</sup> did a prospective study in 33 patients wherein they found the median time in antibiotic administration to be 4.32 hours. Patients who received antibiotics early had better outcome compared to those who received late. Kollef et al<sup>10</sup> in their land mark paper on 2000 patients with both community acquired and nosocomial infections, demonstrated that inadequate antimicrobial treatment of infections was the most important independent determinant of hospital mortality of entire patient cohort.

**RESULTS**

The study involved retrospective chart review of 127 patients, 52 patients were excluded from the study since they had received antibiotics prior to admission to ICU/ER. 75 patients were included in the study.

**LAG TIME IN ANTIBIOTIC ADMINISTRATION**

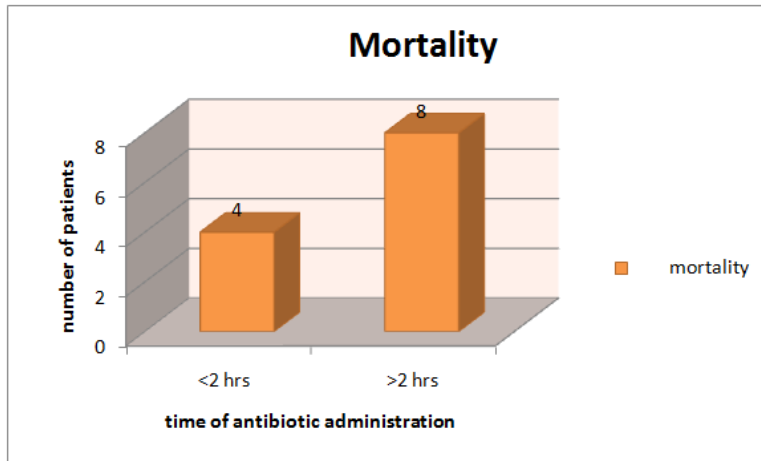
	Lag Time in Antibiotic Administration	
	< 2 hours	>2 hours
Number of Patients	22	53



Of the 75 patients studied the lag time in antibiotic administration was >2 hours in 53 patients and <2 hours in 22 patients. Median duration of antibiotic administration was 2.3 hours. Mean lag time was 2.81±1.88 hours.

**IMPACT ON MORTALITY**

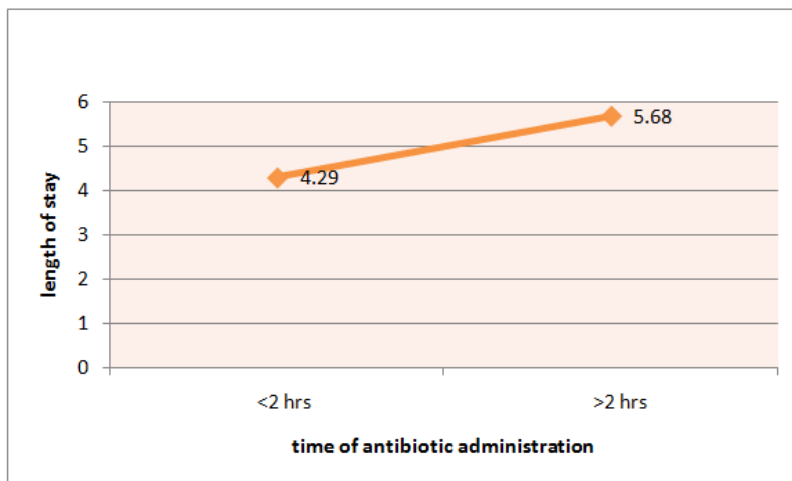
75	<2hrs n = 22	>2hrs n = 53	<i>p</i>
Mortality	4	8	0.73



There were 12 mortalities, 4 out of 22 in <2 hour group and 8 out of 53 in >2 hour group. There was no statistical significance.

**IMPACT ON LENGTH OF STAY**

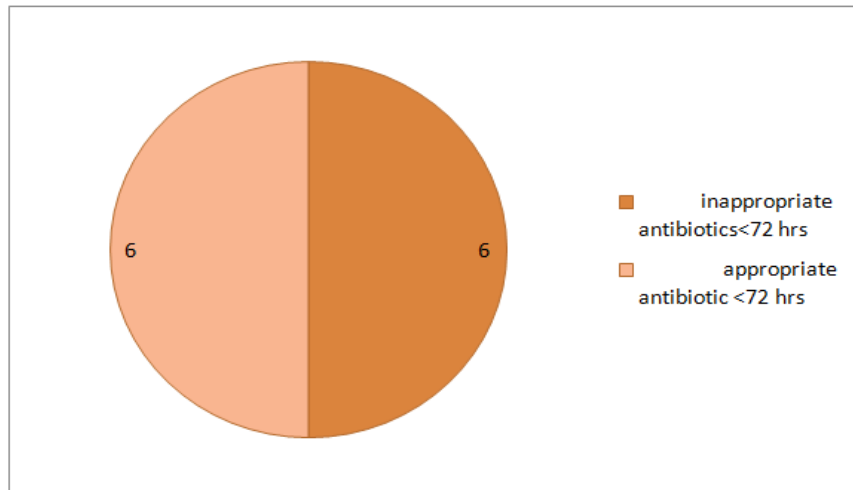
75	<2hrs n = 22	>2hrs n = 53	<i>p</i>
ICU-LOS	4.29±2.17	5.68±5.32	0.96



The length of stay in ICU was 4.29±2.17 days in <2 hour group compared to 5.68±5.32 days in >2 hour group, but there was no statistical significance.

**EFFECT OF INAPPROPRIATE ANTIBIOTIC ON MORTALITY**

75	Appropriate Antibiotic < 72hrs (n=52)	Inappropriate Antibiotic < 72hrs (n=23)	p
Mortality (n=12)	6	6	0.16



Among the 75 patients, 23 patients got inappropriate antibiotics and they were changed after culture reports. Of the 12 deaths, 6 of them were in patients who got inappropriate antibiotics and 6 with appropriate antibiotics. There was no statistical significance.

**DISCUSSIONS**

Our study was done to evaluate the degree of compliance to “Surviving Sepsis Guidelines” regarding time of antibiotic administration, and to know its impact on patient outcome and length of stay in our hospital.

Median time of antibiotic administration in our patients was 2.3 hours. In a study conducted by Kumar et al<sup>5</sup> in 2731 patients, median lag time was 6 hours. In another study by Shahla et al<sup>6</sup>, the average time of antibiotic administration was 2.3 hours.

Though mortality was higher in the group which received antibiotics after 2 hours there was no statistical significance, in the study by Kumar et al<sup>5</sup>, mortality increased by 7.6% for every hour of delay in antibiotic administration.

In our study 23 (30%) of the patients got inappropriate antibiotics. Of the 12 deaths, 6 were in patients who received inappropriate antibiotics. In study by Shahla et al<sup>6</sup> increased mortality was seen with inappropriate antibiotics. In another study by Kollef et al<sup>10</sup> mortality was significantly higher in patients who received inappropriate antibiotics.

**CONCLUSIONS**

Our study showed a lag time of 2.3 hours for antibiotic administration in sepsis patients. Our survival rates are well within international standards and our timing of initiation of antimicrobial therapy seems reasonable. Though numbers are small to draw any definitive conclusions, mortality and length of stay can be significantly reduced if the antibiotics are administered at the earliest after the diagnosis of sepsis is made. Emphasis should be given in choosing the appropriate antibiotics based on the local epidemiology patterns.

Most of the delays occur due to failure in recognition of disease, delay in prescription, delivery and administration of the drug.

Antibiotics are decided after initial evaluation, investigations, resuscitation and stabilization of the patient. In the midst of a busy resuscitation, the need for antibiotics or source control is often overlooked. Although ICU physicians tend to focus mainly on the initial resuscitation processes, optimal resuscitation should always involve concurrent rather than sequential measures. We need to consider timely administration of appropriate antibiotics as a key factor in patient outcome and adhere to the Surviving Sepsis Guidelines.

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