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Original Research Article

Decoding Sepsis: Unveiling the Secrets of Arterial Blood Gas Analysis in Septic Patients - A Prospective Study

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Abstract:

Background: Sepsis is one of the top causes of hospital-related mortality worldwide, and tropical countries bear a significant portion of the burden. Arterial Blood Gas Analysis (ABGA) is an essential investigation for sepsis patients in the intensive care unit (ICU) because it reveals the acid-base status and electrolyte levels, and this study aims to assess the ABGA parameters of sepsis patients and their relationship with mortality.

Methodology: A prospective observational study was conducted on 100 patients over the age of 18 who had sepsis in a tertiary care center's ICU. Each patient underwent a microbiological examination to isolate the causal pathogen, and all individuals received an APACHE II score. The relationship between the end outcome and the ABGA parameters, MODS, and APACHE II score was calculated.

Results: The majority of patients were older than 60, with a male preponderance. Twenty-six percent of individuals had MODS, and 61.53% died. Gram-negative bacteria were the most common cause, with Klebsiella infecting 22% of sepsis patients. The two most prevalent acid-base diseases were primary respiratory alkalosis with secondary metabolic acidosis and primary metabolic acidosis with secondary respiratory alkalosis.

Conclusions: Tropical sepsis is a condition unique to nations such as India, and it demands special attention since it differs from non-tropical sepsis in terms of pCO2, bicarbonate level, and anion gap. The onset of MODS and a rising APACHE II score were independent predictors of mortality in these patients.

Keywords: Sepsis, ABG analysis, ICU, infectious disease, Critical Care.

Introduction

Sepsis is characterized by an abnormal, dysregulated response by the host to infection, and it continues to impose a significant burden on healthcare systems worldwide. This syndrome includes a spectrum of clinical presentations, ranging from sepsis to severe sepsis and ultimately septic shock [1]. While its impact is widely recognized, the incidence of sepsis remains particularly significant in tropical regions, such as India, due to factors like high population density and varying healthcare infrastructures. Out of the 48.9 million sepsis cases and 11 million sepsis-related deaths worldwide, nearly a quarter of the cases and deaths were contributed by India alone [2]. Sepsis can lead to severe complications, including Multi-Organ Dysfunction Syndrome (MODS), and sequelae of septic shock, both of which lead to a significant increase in mortality and morbidity [3]. One essential aspect of sepsis management is understanding the profound physiological changes it induces, including acid-base disturbances. Arterial Blood Gas Analysis (ABGA) plays a pivotal role in evaluating these acid-base disorders and providing invaluable insights into a patient's pathophysiological status. In sepsis, acid-base disorders commonly observed include respiratory alkalosis, metabolic acidosis, and mixed respiratory and metabolic acidosis [4]. Respiratory alkalosis often results from hyperventilation driven by the body's attempt to correct hypoxemia, whereas metabolic acidosis is primarily attributed to the accumulation of lactate and other organic acids due to tissue hypoperfusion. Mixed respiratory and metabolic

acidosis can occur concurrently, further complicating the clinical picture [5]. Each of these acid-base disorders brings its unique set of complications, such as electrolyte imbalances, altered cardiovascular dynamics, and impaired tissue oxygenation. Understanding the implications of these disturbances is essential in guiding therapeutic decisions and optimizing patient outcomes [6].

Metabolic acidosis is an independent predictor of mortality in the intensive-care unit (ICU), while metabolic alkalosis has been shown to be related to an increased duration of ICU stay. Hence by extension, the presence of acid-base imbalances in septic patients might increase the risk of mortality [5-8]. Given the profound impact of sepsis and its associated acid-base disorders, it is imperative to investigate their implications on patient survival. This research aims to shed light on the acid-base status of septic patients providing critical insights for clinical decision-making.

Methodology

This prospective observational study was conducted at a tertiary care teaching hospital in Western India. A total of 100 patients admitted to the medical ICU from September 2018 to September 2019 were enrolled in this study. Ethical approval and written informed consent from all patients were taken. All patients above 18 years of age and having sepsis and/or severe sepsis were included in the study.

Those below 18 years of age, or those unable to meet the qSOFA criteria for sepsis were excluded. Detailed history taking and thorough clinical examination were done to reach a provisional diagnosis. The final diagnosis was made with the assistance of investigations such as complete blood count, renal function tests, liver function tests, urine examination, chest X-ray, USG Abdomen, CT scan, and MRI according to the case. ABGA and serum electrolytes were measured in all patients. According to the clinical spectrum of the disease, microbiological investigations were carried out to establish the etiology of sepsis. The severity of sepsis was scored within 24 hours of diagnosis using the Acute Physiology and Chronic Health Evaluation (APACHE) II score. APACHE II score is the gold standard for risk assessment of critically ill patients [9].

Sepsis was defined as systemic inflammatory response syndrome (SIRS) with suspected or proven microbial etiology. SIRS includes the presence of at least two of the following - body temperature >38°C or <36°C, heart rate >90/min, respiratory rate >20 breaths/min, leukocyte count >12,000/mm3 or <4,000/mm3, or with >10% immature neutrophils. Severe sepsis was defined as sepsis associated with organ dysfunction. MODS was defined as the dysfunction of more than one organ, requiring intervention to maintain homeostasis [3]. Sepsis caused by Plasmodium species, Dengue virus, Arboviruses, Rickettsia, and Leptospira was considered to be tropical sepsis. Specimen collection for blood culture and ABG analysis were done ideally [10]. Interventions including antimicrobial therapy were decided by the treating physicians. All patients were followed up until death or discharge from the ICU.

Data collection, compilation, and entry were done using Microsoft Excel 2007. The mean, median, mode, and standard deviation were analyzed to establish the measure of central tendency. To determine the association between two variables, the standard t-test and chi-square test were used. Epi Info software was used for statistical analysis.

Results

Out of the 100 patients enrolled in this study, 68 were males and 32 were females. The majority of the patients were aged >60 (38%). The age group of 41-50 years had the least (10%) number of patients. The distribution of males and females in different age groups was similar (Figure 1).

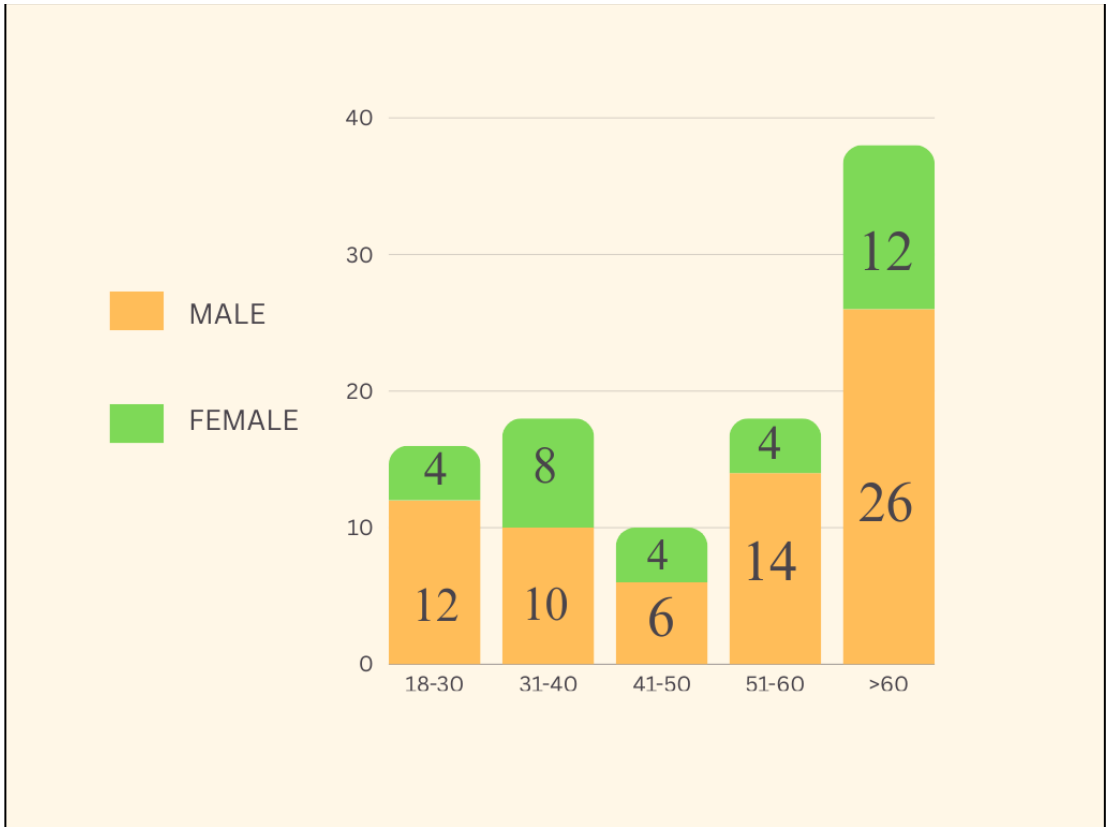

Figure 1: Bar graph showing age and sex-wise distribution of patients

In the present study, 26% of patients had involvement of multiple organs and developed MODS, while in the remaining 74% of patients, MODS was absent. 61.53% (n=16) of patients who developed MODS died. Among all the sepsis patients, infection by gram-negative bacteria was the most prevalent cause at 42%, followed by infection due to gram-positive bacteria at 26%. Only 20 patients had parasitic infections and very few patients had viral and fungal infections. The most common organisms causing infection leading to sepsis were Klebsiella (22%) followed by S. aureus (20%), while S. typhi was the causative agent in just 2 patients (Table 1). Eighteen and 38 patients of the total had an APACHE II score of >19 and <10, while most (44%) had a score between 10-19. The mean score was seen to be 14.5 ± 8.1.

Table 1: Distribution of patients according to the causative organism

Type of Organism	Frequency
Klebsiella	22
Dengue	8
E. coli	14
Enterococcus	6
P. falciparum	4
P. vivax	16
S. aureus	20
S. typhi	2
Candidiasis	4
Pseudomonas	4
Total	**100**

The number of patients admitted in the ICU reduced from 100 to 60 on day 2 and further dropped to 26 on day 5 following deaths and discharges. On the 1st day, 60 patients had a blood pH of <7.4, and 40 had a blood pH of ≥7.4. On Day 2, 90% of the remaining patients (n=60) had a pH of ≥7.4 while only 10% had a pH of <7.4. Similar findings were seen on the 5th day with 84.6% of patients of that day (n=26) with a pH of ≥7.4 and the remaining patients (n=4) having a pH <7.4. The level of arterial Na+ was observed in all patients on days 1, 2, and 5. It was seen that maximum patients had Na+ in the normal range (135-145 mEq/L) on all three days and an ascending trend was seen

among the number of patients having normal Na+ levels. Hyponatremia (Na+ <135 mEq/L) was seen among 40 patients on day 1 which reduced to 20 and 4 on days 2 and 5. On day 1, 18 patients had hypernatremia (Na+ >145 mEq/L) which reduced to 8 on day 2, and to 6 on day 5. The number of patients having normal K+ levels (3.5-5 mEq/L) on the day of admission and the following days was more compared to the patients having normal Na+ levels on those days. Sixty-two percent (n=62), 73.3% (n=44), and 84.6% (n=22) of patients had normal K+ levels on days 1, 2, and 5. A descending trend was seen among both, the number of patients having hypokalemia (K+ <3.5mEq/L) and the number of patients having hyperkalemia (K+ >5 mEq/L) (Figure 2).

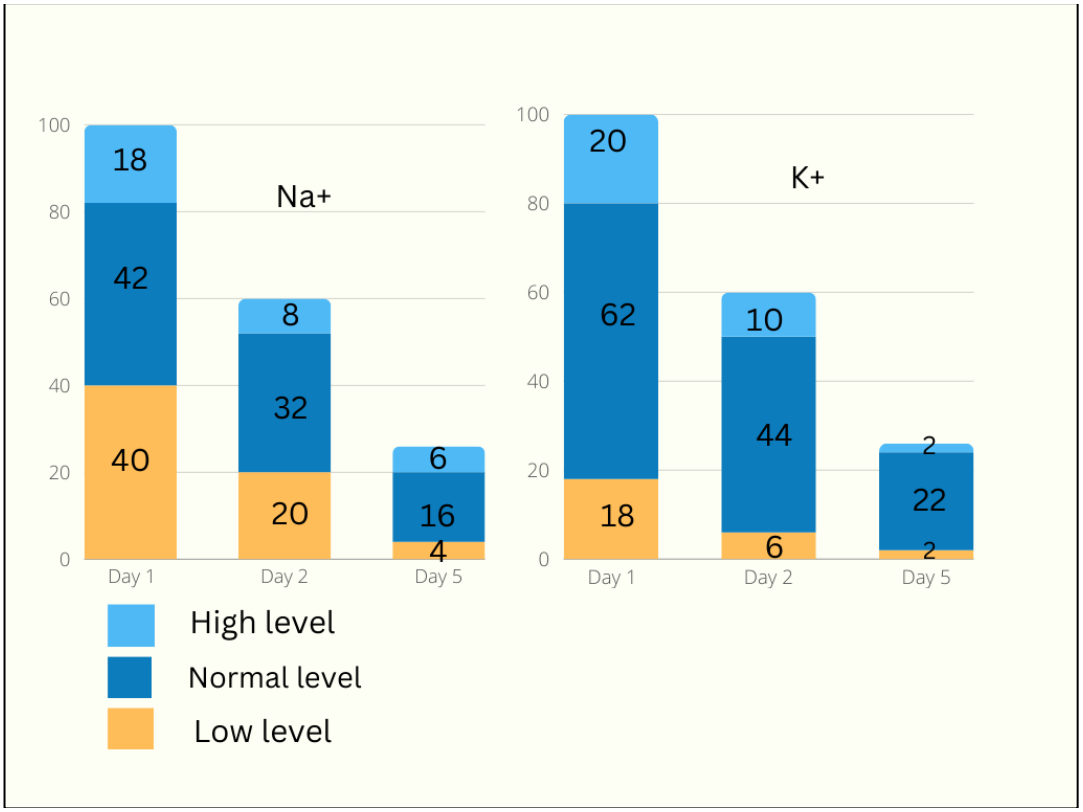

Figure 2: Profile of arterial Na+ and K+ in the patients

On the day of admission, partial pressure of CO2 (PCO2) was seen to be <35 mmHg in 56 patients while 22 patients had PCO2 of >45 mmHg, and 22 patients had PCO2 within the normal range (35-45 mmHg). The mean PCO2 was 37.1 ± 26.6 at the time of admission. On days 2 and 5, 83.3% (n=50) and 61.5% (n=16) of patients had PCO2 <35mmHg while 13.3% (n=8) and 23.1% (n=6) of patients had PCO2 >45mmHg.

The level of HCO3- was ≤ 22 mEq/L in 62% of patients on day 1 which fell to 26.7% (n=16) on day 2 and to 30.8% (n=8) on day 5. Only 38 patients had HCO3- level >22 mEq/L on day 1 which raised to 44 patients on day 2 and further the number reduced to 18 on day 5. The anion gap was seen to be normal (<16 mEq/L) among 68% of patients on day 1, 36.6% (n=22) of patients on day 2, and 53.8% (n=14) of patients on day 5 of admission. The number of patients who had a high anion gap (>16 mEq/L) increased from 32 on day 1 to 38 on day 2 but reduced to 12 on day 3. The incidence of primary acid-base disorder among sepsis patients in our study was found to be 4% while the majority (96%) of patients had mixed acid-base disorders. Among the patients with mixed acid-base disorders, primary respiratory alkalosis with secondary metabolic acidosis and primary metabolic acidosis with secondary respiratory alkalosis had the highest number of patients (n=26) which was followed by primary respiratory acidosis with secondary metabolic alkalosis (n=24).

The least number of patients were affected by primary metabolic alkalosis with secondary respiratory acidosis (n=2) and primary respiratory acidosis with primary metabolic alkalosis (n=2) (Figure 3). Over 75% of patients showed an improved outcome and 24 patients died during the course of the study. The fatality rate was found to be 24%.

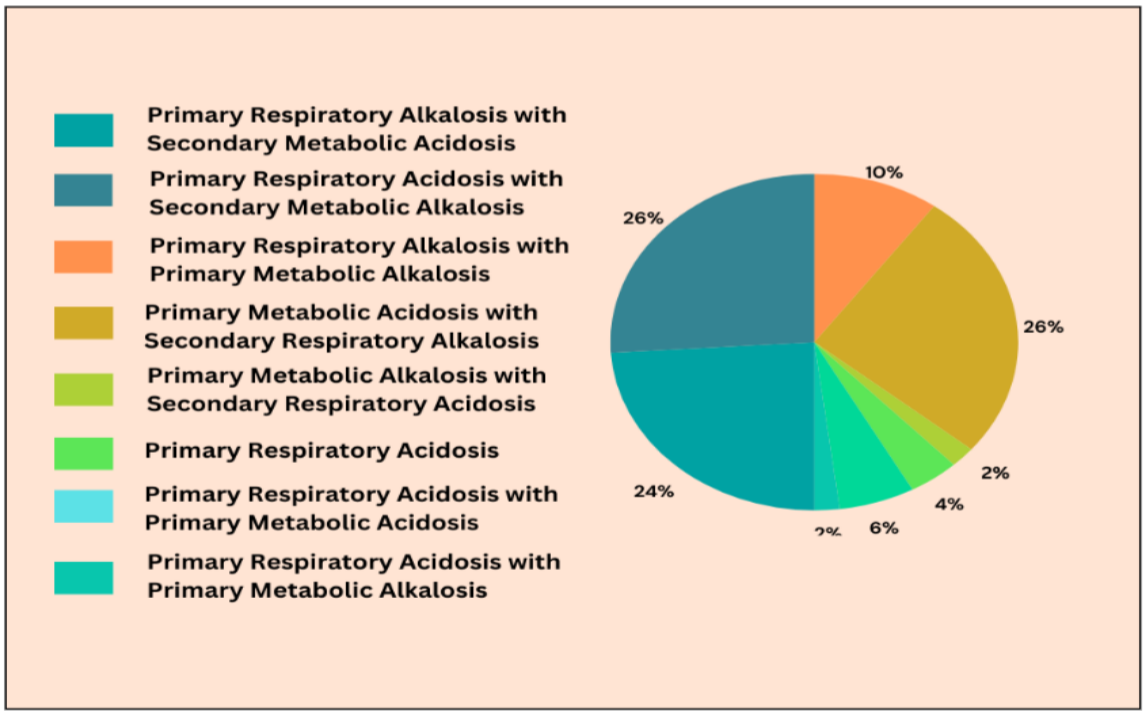

Figure 3: Pie chart of acid-base disorders among patients

The values of various ABG parameters on the day of admission were used to find an association with the type of sepsis - tropical sepsis and non-tropical sepsis.

A significant association was found among the age of patients, the level of HCO3-, the level of Cl-, and the partial pressure of Oxygen (PaO2) in arterial blood with the type of sepsis. The mean age of patients having tropical sepsis was 34.9±12.1 years which is significantly lower compared to the mean age of patients having non-tropical sepsis.

The level of HCO3- was found to be significantly higher among patients with tropical sepsis while in contrast, the level of Cl- and PaO2 is significantly lower among these patients compared to patients having non-tropical sepsis (Table 2).

Table 2: Differences between tropical and non-tropical sepsis

	Tropical/Non-tropical Sepsis	Number (N)	Mean ± SD	P-value
Age	Tropical	28	34.9±12.1	<0.001
	Non-tropical	72	58.4±14.8	
APACHE II	Tropical	28	14.8±10.3	0.804
	Non-tropical	72	14.1±7.3	
pH	Tropical	28	7.3±0.2	0.390
	Non-tropical	72	7.3±0.2	
PaO2	Tropical	28	98.6±6.3	0.829
	Non-tropical	72	101.6±5.2	
PaCO2	Tropical	28	56.8±30.6	0.001
	Non-tropical	72	29.3±20.7	
HCO3-	Tropical	28	25.4±3.5	0.003
	Non-tropical	72	16.6±10.2	
Na+	Tropical	28	130.1±19.8	0.596
	Non-tropical	72	133.1±19.8	
K+	Tropical	28	3.9±1.1	0.201
	Non-tropical	72	4.3±1.1	
Cl-	Tropical	28	96.1±4.9	0.006
	Non-tropical	72	105.1±11.4	
Anion Gap	Tropical	28	8.6±11.8	0.0456
	Non-tropical	72	11.3±11.2	

A significant association was found between the presence of MODS, a higher APACHE II score, and normal anion gap values on day 1 and the final outcome of the patients. Other parameters do not have a significant association with the outcome (Table 3).

Table 3: Association of age, MODS, causative organism, APACHE II score, and ABG parameters with the final outcome

Parameter	**Outcome**		
Age (years)	**Discharge**	**Death**	**P-value**
18-30	12	4	0.315
31-40	16	2	
41-50	8	2	
51-60	18	0	
>60	22	16	
MODS	**Discharge**	**Death**	**P-value**
Present	10	16	<0.0001
Absent	66	8	
Organism Causing Sepsis	**Discharge**	**Death**	**P-value**
Gram-Negative	32	10	0.789
Gram-Positive	16	10	
Parasite	16	4	
Virus	8	0	
Fungus	4	0	
APACHE 2 Score	**Discharge**	**Death**	**P-value**
<10	34	4	0.0001
10-19	38	6	
>19	4	14	
pH (day1)	**Discharge**	**Death**	**P-value**
<7.4	40	20	0.058
≥7.4	36	4	
Na+ (mEq/L) (day 1)	**Discharge**	**Death**	**P-value**
Low (135)	30	10	0.205
Normal (135-145)	36	6	
High (>145)	10	8	
K+ (mEq/L) (day 1)	**Discharge**	**Death**	**P-value**
Low (<3.5)	16	2	0.512
Normal (3.5-5)	44	18	
High (>5)	16	4	
PCO2 (mmHg) (day 1)	**Discharge**	**Death**	**P-value**
<35	48	8	0.117
35-45	16	6	
>45	12	10	
HCO3- (mEq/L) (day 1)	**Discharge**	**Death**	**P-value**
≤22	48	14	0.764
>22	28	10	
Anion Gap (mEq/L) (day 1)	**Discharge**	**Death**	**P-value**
Normal (<16)	46	22	0.0438
High (>16)	30	2	

Discussion

ABGA is a crucial investigation in sepsis patients to monitor for acid-base imbalances and dyselectrolytemia. Patients suffering from sepsis may often have altered acid-base balance conditions, such as respiratory acidosis and metabolic alkalosis most commonly, which may be a contributor to the high mortality seen in such patients. In the present study, the mortality rate amongst septic patients was 24% which is half of that observed by Desai et al (48%), and also lesser than another study by Silva et al (34%) [11,12]. The relatively low mortality in our study may be a testament to the ideal diagnostic procedures and treatment followed in our setup.

The mortality and morbidity in patients with sepsis and severe sepsis are largely attributed to the occurrence of MODS in which there is a failure of multiple organ systems [13]. This is in concordance with our study which shows that 16 out of the 24

deaths were seen in MODS patients. In our study, 26% of patients developed MODS which is higher than the study by Esper et al, in which only 15% of patients with sepsis had a dysfunction of more than one organ system [14]. Microbiological investigation revealed that the majority of sepsis patients (74%) were infected by non-tropical organisms (63.6% by gram-negative microbes, 30.3% by gram-positive microbes, and 6.06% by fungi). Tropical infections accounted for only 26% of patients, which is similar to another observational study in India [15].

However, in contrast to that study which recorded Acinetobacter as the most common pathogen, Klebsiella was found to be the culprit in the most number of patients in our study. This data must be analyzed with caution as it varies greatly with geography. Indian data suggests a higher incidence of gram-negative infections causing sepsis, with Klebsiella, Acinetobacter, and Escherichia coli being the most common pathogens. A small, but significant number of infections are also contributed by Plasmodium species, Dengue virus, and Arboviruses, owing to the country's tropical location [15,16]. On the other hand, data from sepsis patients in Europe indicate a higher load of gram-positive Staphylococcus aureus infections in addition to Klebsiella and Pseudomonas [17]. Tropical sepsis deserves a separate focus as it is different from non-tropical sepsis in relation to pCO2, bicarbonate level, and anion gap. Hypoventilation may play a role in the abnormally high pCO2 levels recorded in tropical sepsis. It also seems to affect the younger age groups compared to non-tropical sepsis. APACHE II score is used in the assessment of patients and the disease severity, and a higher score is associated with an increasing risk of death. The mean APACHE II score in our study (14.5 ± 8.1) was lower as compared to other studies, which directly correlates to the relatively lesser mortality seen [9,12,18].

The mean pH upon admission of sepsis patients in our study was 7.3±0.3, which is similar to a study by Kreu et al [8]. Unlike our study, Suri et al observed hypernatremia and hyperkalemia in most of their patients with sepsis [19]. The administration of sodium bicarbonate to correct metabolic acidosis can explain the high prevalence of hypernatremia in septic patients.

On day 1, more patients had a normal anion gap metabolic acidosis, but from day 2 onwards, nearly half of the patients had a high anion gap metabolic acidosis, which may be a result of lactic acidosis. Kiran et al observed that 69% of patients with metabolic acidosis had a high anion gap [18]. Our study observed that the most common acid-base disorders in ICU patients with sepsis were primary respiratory alkalosis with secondary metabolic acidosis and primary metabolic acidosis with secondary respiratory alkalosis, which is similar to the other studies [4,5,20,21]. On analyzing the final outcome of patients, an increased risk of mortality was noted with MODS and an APACHE II score >19, which is in concordance with other studies [13,22].

However, the results derived must be validated further by multi-center large population studies, owing to a relatively smaller sample size of 100 patients in the present study. Also, these results are largely from a rural tertiary care center, and geographical variations may exist even inside India. The APACHE II scoring system has been used in this study, which may have a slightly lower discriminative power as compared to the APACHE III scoring system; however, it must be noted that there is no general consensus regarding this.

Conclusions

Sepsis is a very common and fatal condition encountered in the ICU, but our study recorded a relatively low mortality rate of 24%. The most common causative agent in this study was Klebsiella, a gram-negative organism, as opposed to the dominance of gram-positive microbes in European sepsis studies. This microbiological result and the presence of tropical infections causing sepsis are unique to India due to its geographical location and seasons. Tropical sepsis affects younger patients and often leads to a much higher pCO2. Mixed acid-base disorders are more common in sepsis patients, with primary respiratory alkalosis with secondary metabolic acidosis, and primary metabolic acidosis with secondary respiratory alkalosis being the most common disorders. The development of MODS and an increasing APACHE II score are significantly associated with a higher rate of mortality.

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