

Outcomes and Predictors of Severe Community-acquired Pneumonia Among Adults Admitted to the University of Gondar Comprehensive Specialized Hospital: A Prospective Follow-up Study

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Background: Severe community-acquired pneumonia is a common life-threatening infection with a high rate of unfavorable outcome. This study aimed to assess the outcomes and predictors of hospitalized severe community-acquired pneumonia patients at University of Gondar comprehensive specialized hospital.

Methods: A prospective follow-up study was conducted at University of Gondar comprehensive specialized hospital from May 1 to September 31, 2021. The data was collected by reviewing patients' charts and interviewing the patients themselves. Descriptive statistics, binary and multivariable logistic regression analysis were performed accordingly. Variables with p -value <0.2 on binary logistic regression were analyzed using multivariable logistic regression and variables with $p < 0.05$ were considered to have significant association.

Results: A total of 239 admitted patients with severe community-acquired pneumonia were enrolled in the study. An unfavorable outcome was observed in 105 (44%) patients; 24.27% was in-hospital all-cause mortality, 12.5% was nonresolution, 5.8% was complicated cases, and 1.26% were gone against medical care for poor prognosis. After analyzing multivariable logistic regression, confusion (OR= 4.84; 95%CI: 1.47–15.88), anemia (OR= 2.36; 95%CI: 1.01–5.52), leukopenia (OR=4.38; 95%CI: 1.26–15.25), leukocytosis (OR=3.15; 95%CI: 1.23–7.96), elevated creatinine (OR=5.67; 95%CI: 1.72–18.65), intubation (OR=7.27; 95%CI: 1.58–33.37) and antibiotic revision during treatment for a different reason (OR=0.02; 95%CI: 0.01–0.07) were variables significantly associated with unfavorable outcome.

Conclusion: Unfavorable outcome was high among hospitalized severe community acquired pneumonia patients, and confusion, elevated creatinine, anemia, leukopenia, leukocytosis, intubation during admission, and antibiotic revision during the course were independent predictors associated significantly with the unfavorable outcome. It is important to consider the development of a treatment protocol for the hospital and to further research incorporating the microbiologic profile of the patients.

Keywords: pneumonia, unfavorable outcome, community-acquired pneumonia, Ethiopia

Background

Pneumonia is one of the life-threatening infections of the lung parenchyma characterized by acute onset of symptoms like cough, pleuritic chest pain, fever, sputum production, and shortness of breath alone or in combination with variable degree of physical (crepitation, bronchial breath sound, effusion sign., etc), and radiologic findings (consolidation, infiltrations, effusion, etc).¹

Pneumonia can be classified in different ways: based on the origin of the site of patient, exposure to the infecting agent, it can be classified as community acquired or hospital acquired. The second way of classification is by using etiology and can be categorized as bacterial, viral, fungal, or parasitic. Using the anatomy of the affected lung parts, it is possible to classify as lobar, interstitial, or bronchial. Taking clinical presentation in to account, it can be also categorized as typical or atypical, mild (walking pneumonia), or severe. Community-acquired pneumonia (CAP) is a pneumonia with a source of infection in the community.^{2–6}

Community-acquired pneumonia severity ranges from mildly ambulating to severe necrotizing pneumonia with septic shock or requiring mechanical ventilation. The degree of severity affects the patients' outcome in the short- and long-term.⁷ There are many different well-defined predictor scores developed so far, including Infectious Disease Society Association/American Thoracic Society (IDSA/ATS) severity score, confusion, urea, respiratory rate, blood pressure and age >65 (CURB-65), pneumonia severity index (PSI) scores, etc, and these are helpful for proper management of a patient.^{2,8}

Community-acquired pneumonia is widespread infectious disease of the lung parenchyma caused by various etiologies like bacteria, viruses, fungi, and parasitic agents affecting the world population but proportionally it is rampant among low- and middle-income countries, mainly sub-Saharan Africa countries including Ethiopia.^{9–11}

In Africa, SCAP is related to in-hospital mortality of 6–15% from hospital-based reports^{11–13} of which more than four million pneumonia episodes and more than 200,000 deaths occur in sub-Saharan Africa. Secondary data analyzed in the US from 2014 to 2016 among 7449 patients admitted with a diagnosis of community-acquired pneumonia showed 77% of the patients improvement and nonresolving pneumonia was documented in 3% at the end of one week of therapy and 30-day mortality was 6%.¹⁴

The 2019 IDSA/ATS severity criteria define severe CAP by the presence of one of the two major criteria (septic shock requiring vasopressor support and requirement for mechanical ventilation) or presence of ≥ 3 minor criteria (respiratory rate ≥ 30 breaths/min, arterial oxygen tension / fractional inspired oxygen ratio ($\text{PaO}_2/\text{FiO}_2$) ≤ 250).

Studies done globally showed that many sociodemographic, clinical related, laboratory related variables were significantly associated with unfavorable outcomes for SCAP. Among those variables age, sex, residence, educational level, occupation, marital status, smoking status, alcoholism, diabetics, HIV, cardiac diseases, nutritional status, elevated creatinine, chronic liver disease, stroke, residual physical disability, CURB65, pregnancy, tachypnea, blood pressure, tachycardia, temperature, and other variables were significantly associated with the unfavorable treatment outcomes of SCAP patients.^{2,8,15–23}

The hypothesis of this study was that there are different predicting factors to the unfavorable outcome of SCAP as it is still costing the lives of many despite advances are made in diagnostics and treatment in modern medicine and this problem is cumbersome in developing countries including Ethiopia.

The implementation of safe, effective, and affordable interventions toward these predictors may reduce the unfavorable outcomes of SCAP in the risky populations.²⁴ Therefore, knowing predictors of unfavorable outcome in SCAP has paramount benefit from individual patient level to country level in many aspects. In terms of patient care, it will guide physicians to have targeted evaluation and timely interventions.

However, little is known about the outcomes and associated factors of severe community-acquired pneumonia among adults in a developing country, specifically in Ethiopia. Therefore, this study aims to assess outcomes and predictors of severe community acquired pneumonia among adults admitted to the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, 2021.

Methods and Materials

Study Design, Setting, and Period

A hospital-based prospective follow-up study was conducted in the University of Gondar comprehensive specialized Hospital (UoGCSH) from May 1, 2021 to September 31, 2021. It is located at the middle of Gondar city in the northwestern part of the country. It is also one of the largest referral hospitals with easy access to about more than five million people and one of the oldest academic institutions in Ethiopia. Internal medicine department provides

services for both rural and urban populations and includes outpatient clinics, emergency service wards, and adult medical intensive care unit (ICU). The department has 25–30 senior internists, more than 55 residents, more than 15 general practitioner (GPs) and other health-care providers.

Population

All adults admitted with the diagnosis of severe community acquired pneumonia in University of Gondar comprehensive specialized hospital during the study period were included in this study. Patients who have risk of hospital-acquired pneumonia, aspiration pneumonia, and significant immunosuppression making them at risk of opportunistic infections were excluded from the study.

Sample Size and Sampling Procedure

Sample Size Determination and Sampling Procedure

The required sample size to conduct the study was estimated by a single population proportion formula. By considering 95% confidence level, 5% margin of error (d), and by taking 18% proportion (P) of unfavorable outcome of SCAP from previous study.²² By assuming the above assumptions, the required sample size (n) was calculated using the formula $n = \frac{(Z\alpha/2)^2 P(1-P)}{d^2} = \frac{(1.96)^2 (0.18 \times 0.82)}{(0.05)^2} = 226$. By adding a 5% of nonresponse rate, the final sample size was 239.

The required sample was taken by enumerating all patients during the study period (from May 1, 2021 to September 31, 2021) consecutively until the required sample size was secured.

Data Collection Methods and Instruments

The data sources for the study were patients' medical records, care givers or guardians and physicians. A structured and pretested questionnaire was used to collect the raw data. Trained interns, GPs and residents collected the data after training was provided on the objectives of the study and how to collect the data. Data collection involved both patient interview and chart review. Focused history was asked addressing sociodemographic characteristics, duration of symptoms, previous pneumonia diagnosis, and antibiotics used and for the presence of smoking, alcohol drinking, and other substance abuse. Focused physical examination (day one, findings of mental status, mid-upper arm circumference, and vital signs) was documented on the chart or performed. Laboratory findings of complete blood count, renal function test, serum electrolyte, and COVID-19 test, PICT, and chest radiography results were documented. Type of treatment and any antibiotic revision during treatment were also recorded.

Study Variables

The outcome variable of the study was the outcomes of SCAP. It was defined as favorable outcome or unfavorable outcome. Favorable outcome was defined as a patient who improved and discharged ultimately, and unfavorable outcome was defined as all-in-hospital death, complications, nonresolutions, and went against medical care. And the possible independent variables for this study were sociodemographic variables like (age, sex, residency, religion, education level, marital status, cigarette smoking), comorbidity, and clinical related variables.

Operational Definition of Some Variables

Desaturation – oxygen saturation <90% and tachypnea defined as >16 breaths/min; malnourished – MUAC <23 cm; bradycardia and tachycardia defined heart rate <60 and >90 bpm, respectively; hypertension defined as systolic BP ≥130 mmHg and/or diastolic BP ≥90 mmHg; hypotension defined as systolic BP <90 mmHg and/or diastolic BP <60 mmHg; fever and hypothermia defined as axillary temperature measurement of >37.2 and <35.5°C respectively; leukocytosis and leukopenia defined as ≥11,000 and <4000/μL, respectively; lymphocytosis and lymphopenia defined as >40% and <20%, respectively; thrombocytosis and thrombocytopenia defined >450,000 and <150,000/μL respectively; hypernatremia >145 and hyponatremia <135 mEq/L, hyperkalemia >5.5 mEq/L and hypokalemia <3.5 mEq/L.^{25–27}

Data Quality Management

The questionnaire was evaluated with the pretesting tool, training was given for data collectors, checking the completeness of filled questionnaires, daily supervision, and checkup was done as planned, and finally, double data entry was performed.

Data Processing and Analysis

Each completed data was checked for consistency before data entry. Then the data were coded and entered in to a computer by using EpiData version 4.6 and further clean-ups were made to check the accuracy and consistency. Then the data was exported to STATA version 16 for detail analysis. Bivariable analysis was carried out first to observe the crude association between independent and dependent variable. Multivariable logistic regression model was analyzed to identify covariates significantly associated with the outcome variables. All statistical inference were made at 5% level of significance. Both statistical and clinical significance of the variable were assessed. The independent variables with p -value <0.05 were considered statistically associated with the unfavorable outcomes of the patients. The model goodness of fitness was checked using Hosmer–Lemeshow. This result supports the model were well fitted to the data (p -value >0.05).

Ethical Considerations

After getting permission from the Internal medicine department, the study proposal was submitted to the Institutional Review Board (IRB) of the College of Medicine, University of Gondar. The study was done after approval was obtained from the board and hospital administration written informed consent was presented to the participants before the study was conducted.

Results

Sociodemographic and Behavioral Characteristics

A total of 239 patients hospitalized with SCAP were involved in the study, 129 (53.97%) were females. The median age was 52 years. The majority 167 (69.87%) were from urban areas, 119 (49.79%) had no formal education (Table 1).

Comorbidities

Among all enrolled participants, 66% had one or more comorbidities. Diabetes, hypertension, cardiac disease, and malnutrition were the most commonly identified (Table 2).

Clinical Related Factors

Among the 239 participants, 50 (20.92%) and 59 (24.69%) patients had pneumonia diagnosis and antibiotic exposure in the past three months, respectively. The median duration of symptoms was 6 days with the shortest and longest duration being 1 and 60 days, respectively.

Complete blood count, renal function test, and chest X-ray was done for all patients. Serum electrolyte (sodium and potassium) was done for 187 and 185 patients, respectively. COVID-19 test was done for 105 (43.93%) patients but only 42 (17.57%) were positive. Leukocytosis, leukopenia, anemia, thrombocytopenia were seen in 78 (32.99%), 43 (17.99%), 70 (29.29%), and 79 (33.05%) respectively. Among all, 33 (13.81%) and 182 (76.15%) patients had elevated creatinine and urea levels in order. Hypokalemia and hyponatremia were seen among 69 (37.3%) and 72 (38.5%) patients, respectively. On chest X-ray, 83 (34.73%) had pneumonia 76 (31.80%) had pneumonia with one or more of the following: effusion, obstructive airway disease, fibrosis and cardiomegaly; 64 (26.80) had multifocal or multilobe pneumonia and 16 (6.69%) had different reports including normal, obstructive airway disease, fibrosis or effusion alone. CURB65 score was done for all participants and 154 (64.44%) patients had ≤ 2 and 85 (35.56%) patients had ≥ 3 values. Regarding the antibiotic treatment, patients were given ceftriaxone combined with either vancomycin, azithromycin, or doxycycline for 102 (42.68%) patients, 71 (29.7%) patients and 31 (12.97%) patients, respectively and antibiotic revision was made in 55 (23%) of the cases during treatment (Table 3).

Table I Sociodemographic and Behavioral Characteristics of Patients Admitted to SCAP, UoGCSH, 2021 (n=239)

Variable	Category	Frequency	Percent (%)
Age	Median age of participants = 52 year, (Q1=36 and Q2=69)		
Sex	Male	110	46.03
	Female	129	53.97
Residence	Urban	167	69.87
	Rural	69	28.87
	Refugee camp	3	1.26
Marriage	Married	149	62.34
	Single	50	20.92
	Separated	19	7.95
	Widowed	21	8.79
Religion	Orthodox	195	81.59
	Muslim	36	15.06
	Other	8	3.36
Occupation	Civil servant	40	16.74
	Merchant	28	11.72
	Farmer	57	23.85
	Housewife	57	23.85
	Self-employed	18	7.53
	Student	14	5.86
	Other (soldier, daily labor)	25	10.46
Education	No formal education	119	49.79
	Primary level	44	18.41
	Secondary level	43	17.99
	College and above	33	13.81
Smoking	Smoker	15	6.28
	Nonsmoker	224	93.72
Alcoholism	Alcoholic	60	25.10
	Nonalcoholic	179	74.89
Kat chewing	Yes	14	5.86
	No	225	94.14

Table 2 Comorbidities of Patients Hospitalized for SCAP at UoGCSH from May to September 2021 (n=239)

Variable	Category	Frequency	Percent (%)
Diabetes mellitus	Yes	36	15.06
	No	203	84.94
Hypertension	Yes	52	21.76
	No	187	78.24
HIV	Positive	22	9.21
	Negative	217	90.79
Cancer	Yes	17	7.11
	No	122	92.89
Pregnancy	Yes	7	5.43
	No	122	94.57
Cardiac disease	Yes	50	20.92
	No	189	79.08
CKD	Yes	12	5.02
	No	227	94.98
CLD	Yes	7	2.93
	No	232	97.07
COPD	Yes	14	5.86
	No	225	94.14
ILD	Yes	9	3.77
	No	230	96.23
Asthma	Yes	32	13.39
	No	207	86.61
Stroke (old)	Yes	9	3.77
	No	230	96.23
Corticosteroid	Yes	16	6.69
	No	223	93.31
Nutritional status (MUAC based)	Normal	144	60.25
	Undernourished	95	39.75

Abbreviations: HIV, human immunodeficiency virus; CLD, chronic liver disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease.

Outcomes of Severe Community Acquired Pneumonia

Composite unfavorable outcomes of patients hospitalized with SCAP in this study were 105 (44%; 95%CI: 37.59–50.27) (Figure 1).

Unfavorable Outcomes by Sociodemographic and Behavioral Characteristics of the Patients

The proportion of patient's age above 65 years with unfavorable outcome were 35 (14.6%). Males had 22.6% and females had 21.6% unfavorable outcome. Among all, 76 (31.8%), 59 (24.7%), and 56 (23.4%) patients with unfavorable outcome were from urban areas, were unemployed and had no formal education, respectively (Table 4).

Table 3 Clinical Features of Patients Hospitalized for SCAP at UoGCSH from May to September 2021 (n=239)

Variable	Category	Frequency	Percent (%)
History and physical examination			
Pneumonia diagnosis in last 3 months	Yes	50	20.92
	No	189	79.08
Antibiotic use in the past 3 months	Yes	59	24.69
	No	180	75.31
Level of consciousness	Conscious	189	79.08
	Confused ^a	50	20.9
Pulse rate	Normal	30	12.55
	Tachycardia	209	87.45
Systolic BP	Normal	129	53.97
	Hypertension	50	20.92
	Hypotension	60	25.10
Diastolic BP	Normal	196	82.01
	Hypertension	28	11.72
	Hypotension	15	6.28
Temperature	Normal	104	43.51
	Fever	108	45.19
	Hypothermia	27	11.30
Respiratory rate	20–30	101	42.26
	30 ^a	138	57.74
Oxygen saturation (%)	<70	52	21.76
	70–90	187	78.24
White blood cell count	Normal	118	49.37
	Leukopenia	43	17.99
	Leukocytosis	78	32.64
Hemoglobin	Normal ^a	143	59.83
	Anemia	96	40.17
Platelet	Normal ^a	160	66.95
	Thrombocytopenia	79	33.05
Creatinine	Normal	206	86.19
	Elevated	33	13.81
Blood urea level	Normal	57	23.85
	Elevated	182	76.15

(Continued)

Table 3 (Continued).

Variable	Category	Frequency	Percent (%)
Sodium	Normal	100	53.48
	Hyponatremia	72	38.50
	Hypernatremia	15	8.02
Potassium	Normal	114	61.62
	Hypokalemia	69	37.30
	Hyperkalemia	2	1.08
Chest X-ray	Pneumonia	83	34.73
	Pneumonia ^a	76	31.80
	Multifocal pneumonia	64	26.78
	Others ^b	16	6.69
COVID-19 test	Positive	42	17.57
	Negative	73	30.54
	Not tested	124	51.88
Intubated	Yes	29	12.13
	No	210	87.87
Septic shock management	Yes	27	11.30
	No	212	88.70
Antibiotic type given	Ceftriaxone + vancomycin ^a	122	51.05
	Ceftriaxone + doxycycline	31	12.97
	Ceftriaxone + azithromycin	71	29.71
	Others ^c	15	2.93
Antibiotic changed (revised)	Yes	55	23.01
	No	184	76.99
CURB 65 score	≤2	154	64.44
	≥3	85	35.56

Notes: ^aEffusion, OAD, fibrosis, cardiomegaly – either coexist; ^bnormal, effusion, ARDS, fibrotic change – only one present; ^cceftriaxone + doxycycline, vancomycin or ceftriaxone + ciprofloxacin.

Abbreviation: BP, Blood Pressure.

Unfavorable Outcome by Comorbidity

The proportion of patients having DM comorbidity with unfavorable outcome was 19 (7.95%), patients having hypertension comorbidity had 10.46% and HIV comorbidity had 10.58% unfavorable outcome (Table 5).

History and Physical Examination Findings as Predictors

Unfavorable outcome was identified in 24 (10%) of patients who reported pneumonia diagnosis and 30 (12.6%) of patients who used antibiotics in the past three months. Similarly, unfavorable outcome was also identified in 40 (16.7%), 47 (19.7%), 18 (7.5%), 20 (8.4%), 75 (31.4%), 95 (39.7%) patients who altered mental status, fever, hypothermia, oxygen saturation less than 70%, respiratory rate greater than 30 and tachycardic patients respectively. Among all

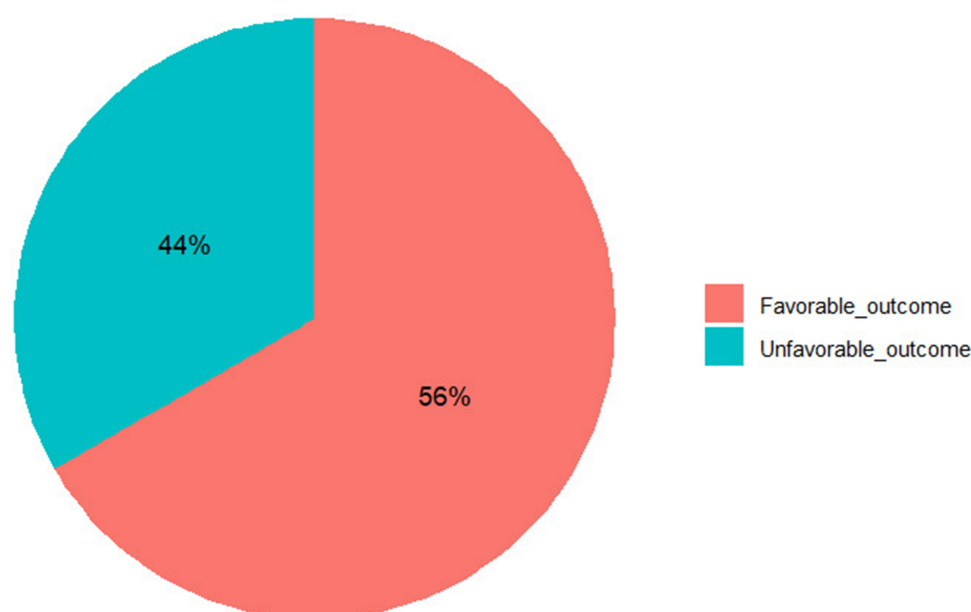


Figure 1 Outcomes of hospitalized patients with SCAP at UoGCSH from May to September 2021 (n=239).

participants, 11 (4.6%) and 12 (5%) patients with diastolic and systolic hypotension also had an unfavorable outcome (Table 6).

Laboratory Findings of the Patients

Unfavorable outcome was observed in 59 (24.68%) anemic, 43 (17.99%) thrombocytopenic, and 24 (10.04%) leukopenic patients, respectively. Unfavorable outcome was seen in 9 (3.77%) patients with elevated creatinine. Patients with elevated urea had a favorable outcome in 95 (39.75%) of cases. Similarly, 40 (21.39%), 34 (18.34%), and 67 (28.03%) with hyponatremia, hypokalemia, and COVID-19 positivity in the listed order had unfavorable outcomes (Table 7).

Patient Management Related Characteristics of the Patients

Among patients with CURB-65 score of ≥ 3 , 53 (22.18%) had unfavorable outcomes. Similarly, unfavorable outcomes occurred in 48 (20%) of patients after antibiotic revision. A total of 29 (12.13%) patients were intubated during admission and an unfavorable outcome was noted in 20 (8.37%) of them. Antibiotic revision was made for 55 patients of which 48 (20%) were having an unfavorable outcome. A total of 27 patients were treated with vasopressors for septic shock during admission of which 20 (74%) had an unfavorable outcome (Table 8).

Predictors of Unfavorable Outcome in Hospitalized Patients with SCAP

Among variables patient's occupation, asthma, respiratory rate, oxygen saturation, level of consciousness, CURB65, hemoglobin, platelet count, white blood cell count, creatinine, urea, antibiotic revision and intubation status were having an association with the unfavorable outcome. After analyzing multivariable binary logistic regression, the level of consciousness, hemoglobin, white blood cells, creatinine, intubation status, and antibiotic revision were significantly associated with the occurrence of unfavorable outcomes.

The odds of unfavorable outcome were five, two, four, three, six, and seven times higher among patients who had confusion, anemia, leukopenia, leukocytosis, elevated creatinine, and those who required intubation compared to conscious, normal hemoglobin, WBC, creatinine and those who were not intubated, respectively. The odds value of unfavorable outcome was reduced by 98% antibiotics revision compared to those for who no antibiotic revision was made (Table 9).

Table 4 Sociodemographic and Behavioral Characteristics as a Predictor of Unfavorable Outcome Among Hospitalized SCAP Patients at UoGCSH, May to September 2021 (n=239)

Variable	Category	Outcome			
		Favorable	Percent (%)	Unfavorable	Percent (%)
Age	18–40	42	17.6	38	15.9
	41–64	46	19.24	32	13.4
	≥65	46	19.24	35	14.6
Sex	Male	56	23.4	54	22.6
	Female	78	32.6	51	21.6
Residence	Urban	94	39.3	76	31.8
	Rural	40	16.7	29	12.1
Marriage	Married	89	37.3	60	25.1
	Single	25	10.5	25	10.5
	Other	20	8.4	20	8.4
Occupation	Employed	37	15.5	21	8.8
	Unemployed	65	27.2	59	24.7
	Farmer	32	13.4	25	10.5
Education level	No formal education	46	26.4	56	23.4
	Primary level	25	10.5	19	7.9
	Secondary level and above	63	19.4	30	12.6
Smoking	Smoker	6	2.5	9	3.8
	Non smoker	127	53.1	96	40.2
Alcoholism	Alcoholic	28	11.7	32	13.4
	Non alcoholic	106	44.4	73	30.5
Kat chewing	Yes	6	2.5	8	3.3
	No	125	52.3	96	40.2

Table 5 Comorbidities as Predictor of Unfavorable Outcome Among Hospitalized SCAP Patients at UoGCSH, May to September 2021 (n=239)

Variable	Category	Favorable Outcome		Unfavorable Outcome	
		Frequency	Percent	Frequency	Percent
Diabetes mellitus	Yes	17	7.11	19	7.95
	No	117	48.95	86	35.98
Hypertension	Yes	27	11.29	25	10.46
	No	74	30.96	59	24.68
HIV	Positive	11	10.58	11	10.58
	Negative	48	46.15	34	32.69
Cancer	Yes	8	3.35	9	3.77
	No	126	52.71	96	40.17
Pregnancy	Yes	4	3.10	3	2.32
	No	76	58.91	46	35.66

(Continued)

Table 5 (Continued).

Variable	Category	Favorable Outcome		Unfavorable Outcome	
		Frequency	Percent	Frequency	Percent
Cardiac disease	Yes	26	10.88	24	10.04
	No	108	45.19	81	33.89
CKD	Yes	5	2.09	7	2.93
	No	129	53.97	98	41
CLD	Yes	2	0.87	5	2.09
	No	132	55.23	100	41.84
COPD	Yes	8	3.35	6	2.51
	No	126	52.71	99	41.42
ILD	Yes	6	2.51	3	1.25
	No	128	53.6	102	42.68
Asthma	Yes	24	10.04	8	3.35
	No	110	46.03	97	40.59
Stroke (old)	Yes	1	0.42	8	3.35
	No	133	55.64	97	40.59
Nutritional status	Normal	85	35.56	59	24.69
	Undernourished	49	20.5	46	19.24

Abbreviations: HIV, human immunodeficiency virus; CLD, chronic liver disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease.

Table 6 History and Physical Exam Findings Related to Unfavorable Outcome Among Hospitalized SCAP Patients at UoGCSH, May to September 2021 (n=239)

Variable	Category	Favorable Outcome		Unfavorable Outcome	
		Frequency	Percent	Frequency	Percent
Symptom duration	Median = 6 (IQR =7) days				
Pneumonia diagnosis in last 3 months	Yes	26	10.88	24	10
	No	108	45.19	81	33.9
Antibiotic use in the past 3 months	Yes	29	12.13	30	12.6
	No	105	43.93	75	31.4
Level of consciousness	Conscious	124	51.88	65	27.2
	Confused ^a	10	4.16	40	16.7
Pulse rate	Normal	20	8.37	10	4.2
	Tachycardia	114	47.69	95	39.7
Systolic BP	Normal	103	43.09	70	29.3
	Hypotension	4	1.67	12	5.0
	Hypertension	27	11.29	23	9.62
Diastolic BP	Normal	117	48.95	79	33.1
	Hypotension	4	1.67	11	4.6
	Hypertension	13	5.44	15	6.3

(Continued)

Table 6 (Continued).

Variable	Category	Favorable Outcome		Unfavorable Outcome	
		Frequency	Percent	Frequency	Percent
Temperature	Normal	64	26.78	40	16.7
	Hypothermia	9	3.77	18	7.5
	Fever	61	25.52	47	19.7
Respiratory rate	20–30	71	29.70	30	12.6
	30+	63	26.36	75	31.4
Oxygen saturation (%)	<70	114	47.69	20	8.4
	70–90	73	30.54	32	13.4

Note: ^aPatients who had poor mental status/condition from confusion up to lethargy, stuporous and coma.

Abbreviation: BP, Blood Pressure.

Table 7 Investigation Findings as Predictors of Unfavorable Outcome Among Hospitalized SCAP Patients at UoGCSH, May to September 2021 (n=239)

Variable	Category	Favorable Outcome		Unfavorable Outcome	
		Frequency	Percent	Frequency	Percent
White blood cell	Normal	76	31.80	42	17.57
	Leukopenia	19	7.95	24	10.04
	Leukocytosis	39	16.32	39	16.32
Hemoglobin	Normal and polycythemia	97	40.59	46	19.24
	Anemia	37	15.48	59	24.68
Platelet	Normal ^a	98	41	62	25.94
	Thrombocytopenia	36	15.06	43	17.99
Creatinine	Normal	125	52.30	81	33.89
	Elevated	9	3.77	24	10.04
Blood urea level	Normal	39	16.32	18	7.53
	Elevated	95	39.75	87	36.40
Sodium	Normal	66	35.29	34	18.18
	Hyponatremia	32	17.11	40	21.39
	Hypernatremia	5	1.60	10	2.67
Potassium	Normal	66	35.68	48	25.95
	Hypokalemia	35	18.92	34	18.34
	Hyperkalemia	1	0.54	1	0.54
Chest X-ray	Pneumonia	51	21.34	32	13.39
	Pneumonia ^b	43	17.99	43	17.99
	Multifocal pneumonia	37	15.48	27	11.30
	Others ^c	3	1.26	3	1.26
COVID-19 test	Positive	19	7.94	23	9.62
	Negative	45	18.83	28	11.72
	Not tested	70	29.28	54	22.59

Notes: ^aPatients who had normal and increased platelet count. ^bPatients who had radiologic diagnosis of pneumonia plus other radiologic findings (effusion, fibrosis, cardiomegaly and obstructive airway disease). ^cIncludes patients who had normal, effusion only, obstructive airway disease only, fibrotic change only, or combination of these lists as CXR finding.

Table 8 Treatment Related Characteristics of Unfavorable Outcome Among Hospitalized SCAP Patients at UoGCSH, May to September 2021 (n=239)

Variable	Category	Favorable Outcome		Unfavorable Outcome	
		Frequency	Percent	Frequency	Percent
CURB 65 score	≤2	102	42.68	52	21.76
	≥3	32	13.38	53	22.18
Antibiotic type given	Ceftriaxone + azithromycin	52	21.75	19	7.95
	Ceftriaxone + doxycycline	20	8.37	11	4.60
	Ceftriaxone + vancomycin	35	14.64	67	28.03
	Others ^a	7	2.93	8	3.35
Antibiotic changed (revised)	Yes	7	2.93	48	20.00
	No	127	53.14	58	24.23
Intubated	Yes	9	3.77	20	8.37
	No	130	54.39	80	33.47
Septic shock management	Yes	7	2.93	20	8.37
	No	130	54.39	82	34.31
Length of hospital stay	1–7 days	36	15.06	31	12.97
	>7 days	98	41.00	74	30.96

Note: ^aCeftriaxone + ciprofloxacin/cefepime/Augmentin/amoxicillin.

Table 9 Bivariable and Multivariable Logistic Regression Analysis of SCAP Patients Hospitalized at UoGCSH, 2021 (n=239).

Variable	Category	Favorable Outcome	Unfavorable Outcome	COR (95%CI)	AOR (95%CI)
Occupation	Employed	37	21	1	1
	Farmer	32	25	1.35 (0.58–3.15)	1.72 (0.5–5.94)
	Unemployed	65	59	1.20 (0.58–2.52)	2.83 (0.99–8.12)*
Asthma	Asthmatic	24	8	1	1
	Not asthmatic	110	97	3.76 (1.10–12.83)	0.72 (0.20–2.60)
Respiratory rate	20–30	71	30	1	1
	30+	63	75	3.21 (1.65–6.24)	1.22 (0.52–2.82)
Oxygen saturation	71–90	114	73	1	1
	≤70	20	32	3.88 (2.02–7.47)	0.89 (0.33–2.39)
Mental status	Conscious	124	65	1	1
	Confused ^a	10	40	14.63 (7.03–30.44)	4.84 (1.47–15.88)***
CURB65	0–2	102	52	1	1
	≥3	32	53	5.63 (3.01–10.54)	1.28 (0.50–3.24)

(Continued)

Table 9 (Continued).

Variable	Category	Favorable Outcome	Unfavorable Outcome	COR (95%CI)	AOR (95%CI)
Hemoglobin	Normal and polycythemia	97	46	1	1
	Anemia	37	59	3.76 (2.04–6.93)	2.36 (1.01–5.52)**
Platelet	Normal ^b	98	62	1	1
	Thrombocytopenia	36	43	2.80 (1.53–5.105)	0.41 (0.15–1.12)*
White blood cell count	Normal	76	42	1	1
	Leukopenia	19	24	4.40 (2.06–9.44)	4.38 (1.26–15.25)**
	Leukocytosis	39	39	1.49 (0.74–2.99)	3.15 (1.23–7.96)**
Creatinine	Normal	125	81	1	1
	Elevated	9	24	5.30 (2.45–11.43)	5.67 (1.72–18.65)***
Urea	Normal	39	18	1	1
	Elevated	95	87	2.13 (0.98–4.66)	0.92 (0.34–2.48)
Antibiotic revision	Changed	7	48	1	1
	No revision	127	57	0.50 (0.26–0.96)	0.02 (0.01–0.07)***
Intubation	Not intubated	130	80	1	1
	Intubated	6	23	5.34 (2.38–12.02)	7.27 (1.58–33.37)**

Notes: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$; model fitness with Hosmer–Lemeshow test, $p = 0.2563$. ^aPatients who had poor mental status/condition from confusion up to lethargy, stuporous and coma. ^bPatients who had normal and increased platelet count.

Discussion

The present study showed increased rates of unfavorable patient outcomes following admission due to SCAP with over all composite unfavorable outcome of 44% of which all-cause-in-hospital mortality accounted for 24.27%, nonresolution cases were 12.55% and complication in the course of treatment was 5.86%.

The result of in-hospital mortality from this study was higher than the findings from the studies conducted in USA, Spain, Netherlands.^{14,20,28} This difference was most likely ascribed to the level of better care provided in these high-income countries with better health-care infrastructure which includes early case detection, early treatment initiation, advanced supportive treatment options; early care-seeking behavior by patients may also contribute. This finding, however, was consistent with studies done in Spain, Portuguese, and Egypt.^{29–31} The finding in this study was higher than from the finding from the study conducted previously in Ethiopia²² and the possible explanation is that this study included critical patients admitted to ICU admissions in addition to ward admitted patients, who have better outcome comparatively.

For a similar explanation mentioned above, this study showed increased rates of nonresolution cases compared to the study done in the USA¹⁴ which was consistent with findings from the study done in China from secondary data.²⁰

The complications in the course of treatment in this study were fewer than in the study done in Ethiopia previously;²² the likely reason is that the patients in this study included critical cases requiring ICU admission who are at risk of higher in-hospital mortality once they develop the complications compared to patients who were not critically sick, admitted in the ward from the previous study.

In this study, presence of unfavorable outcome was significantly associated with the presence of confusion during admission. Patients with confusion were having the unfavorable outcome five times more than conscious patients during

admission. This result is consistent with the finding of the study done in Barcelona, Spain.¹⁵ This might be explained by patients who had confusion at admission being likely to have severe hypoxia, hypo perfusion, acidosis, inflammation, and other end organ damage with metabolic complications that results in altered level of mental status.

The presence of anemia at admission had significantly increased the occurrence of unfavorable outcomes. Patients who had anemia, hemoglobin level <12 mg/dL for both sexes during admission were 2.36 times more at risk of having unfavorable outcomes compared to those with normal and above hemoglobin levels. This finding was consistent with studies done in the US, Switzerland, Pakistan, and Singapore.^{16,19,28,32} The presence of anemia compromise the already sick patient who is hypoxic, hypo perfused, and severely inflamed.

The presence of leukocytosis at admission had a significant association with unfavorable outcomes. Patients who had leukocytosis >11,000 during admission were 3.15 times more at risk of having unfavorable outcomes compared to those with normal white blood cells. This finding was in agreement with studies done in China and Singapore.^{20,32,33} Leukocytosis is the body's immune response, predominantly the polymorph nuclear type, as a means to control the infection. However, the presence of an extremely high white cells may tell the underlying leukemia or leukemoid reaction.

The presence of leukopenia at admission had a significant association with unfavorable outcomes. Patients who had leukocytosis <4000 during admission were 4.38 times more at risk of having unfavorable outcomes as compared to those with normal white blood cells. This finding was in line with the finding in the study done in Singapore.³² The presence of leukopenia tells the presence of intense inflammation suppressing leukocyte production in the bone marrow or increasing their destruction. It may also occur with the effect of the underlying comorbidity or cause of pneumonia, like some viruses can cause leukopenia.

Patients with SCAP who had elevated creatinine >1.3 mg/dL during admission had an increased risk of unfavorable outcome 5.3 times compared to SCAP patients who had a serum creatinine level <1.3 mg/dL. Different studies done in Ethiopia and Spain^{22,31} showed consistent evidence. This might explain the presence of bacteremia (sepsis).

In this study, the presence of unfavorable outcomes was significantly associated with invasive mechanical ventilation. Patients who were managed invasively with mechanical ventilation were 7.27 times at risk of having the unfavorable outcome compared to those who were not intubated. This result was in agreement with the prospective observational study done in Barcelona and other studies also show similar evidence.^{15,30,34} This may be due to the complication of mechanical ventilation including barotrauma, pneumothorax, ventilator-associated pneumonia, etc. Conversely, patients who are treated with invasive mechanical ventilation likely do have severe infection and end organ damage.

The odds of unfavorable outcome were reduced by 98% in those for whom antibiotic revision was made compared to those for whom change was not done. This finding suggests that initial empiric antibiotic choice may be discordant. The result is consistent with the study done in Portuguese, Ethiopia, Spain, and China.^{15,20,22,30} Subsequent escalation or de-escalation of antibiotics may require covering different etiologies and resistant organisms, if possible, guided by culture.

Strength and Limitations of the Study

This study was conducted using a prospective study design, which clarifies the temporal sequence of the outcome. This outcome is possible because researchers can observe definitive behaviors or characteristics. However, this study had limitations, including the lack of a microbiologic profile of the patients due to resource constraints, the failure to address specific causes of death and complications, and the fact that some variables, such as CXR reading, were inconsistent due to varying levels of training.

Conclusion

Hospitalized patients with SCAP had high in-hospital mortality and clinical nonresolution cases. Confusion, high creatinine, anemia, leukopenia, leukocytosis, intubation during admission and antibiotic revision during the course were independent predictors that were significantly associated with the unfavorable outcome. It is better the clinicians prepare SCAP treatment protocol considering the unfavorable outcome.

Abbreviations

AIDS, acquired immunodeficiency syndrome; AOR, adjusted odds ratio; ATS, American Thoracic Society; ART, anti-retroviral therapy; CAP, community-acquired pneumonia; CBC, complete blood count; CI, confidence interval; CURB 65, confusion, urea, respiratory rate, blood pressure and age >65; COPD, chronic obstructive pulmonary disease; CLD, chronic liver disease; CKD, chronic kidney disease; ED, emergency department; EMCC, emergency medicine and critical care; FIO₂, fraction of inspired oxygen; GCS, Glasgow coma scale; GP, general practitioner; UOGCSH, University of Gondar Comprehensive Specialized Hospital; HIV, human immunodeficiency virus; ICU, intensive care unit; IDSA, Infectious Disease Society Association; ILD, interstitial lung disease; IQR, interquartile range; MUAC, mid-upper arm circumference; *p*, probability-value; PCCM, pulmonologist and critical care management; PSI, pneumonia severity index; PaO₂, partial arterial oxygen; RCT, randomized control trial; US, United States; WBC, white blood count.

Data Sharing Statement

The datasets supporting the conclusions of this article are available upon request to the primary/corresponding author.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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