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Risk factors for intensive care unit admission and mortality among adult meningitis patients

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Abstract

Objectives: To assess the risk factors for intensive care unit admission and inpatient all-cause mortality among adult meningitis patients.

Method: The retrospective study was conducted at the Aga Khan University Hospital, Karachi, and comprised data between July 2010 and June 2019 of patients of either gender aged ≥ 18 years diagnosed with bacterial, viral or tuberculous meningitis. Multivariable logistic regression analyses were used to explore independent predictors of inpatient mortality and intensive care unit admission. Data was analysed using SPSS 24.

Results: Of the 929 patients with suspected meningitis, 506(54.5%) had confirmatory diagnosis. Of them, 303(59.9%) were males. The overall median age of the sample was 47.0 years (interquartile range: 33.0 years). The most common aetiology was bacterial meningitis 324(64%), followed by viral meningitis 141(27.9%). Incidence of inpatient mortality was 53(10.5%), while 75(14.8%) patients required intensive care unit admission. Tuberculous aetiology, intensive care unit admission, concurrent

encephalitis, hydrocephalus, inpatient neurosurgery, and longer length of hospital stay were predictors of mortality ($p<0.05$). Non-indication of blood culture was found to be associated with reduced risk of mortality ($p<0.05$). For intensive care unit admission, diabetes mellitus, presentation with seizure, imaging suggestive of meningitis, and inpatient neurosurgery were associated with higher risk of admission, while hypertension, presentation with headache, viral aetiology and non-indication of blood culture reduced the risk ($p<0.05$).

Conclusion: Adult meningitis patients tend to have poor expected outcomes, and their management strategies should be planned accordingly.

Key Words: Meningitis, Mortality, Intensive care units, Critical care, Risk factors.

Introduction

Meningitis is a serious infection that results in inflammation of the meninges covering the brain and the spinal cord. With widespread vaccination against certain causative organisms, there has been a significant change in the epidemiology of meningitis, and the spectrum is shifting from paediatric to adult patients.¹⁻³ However, despite these advances, meningitis still accounts for significant mortality, and a high proportion of meningitis patients require intensive care unit (ICU) admission.⁴

Pakistan ranks 46th in the world in terms of meningitis-related mortality, with an age-adjusted mortality rate of 5.57 per 100,000 population.⁵ Being a resource-limited country, Pakistan has scarce ICU resources, with only 1.5 critical care beds available to cater to a population of 100,000.⁶ This situation necessitates efficient and evidence-based utilisation of these limited hospital resources along with an increased focus on national healthcare capacity-building activities.

Owing to limited resources, healthcare and intensive care in Pakistan and other low and middle-income countries (LMICs) are disproportionately impacted by ICU admissions due to meningitis. While several studies have been conducted globally to identify predictors of mortality and ICU admission, these studies are scarce in Pakistan and other LMICs.⁷⁻¹³ Evidence-based healthcare delivery warrants setting-specific research. The

current study was planned to identify predictors of inpatient mortality and ICU admission among meningitis patients within an LMIC context.

Patients and Methods

The retrospective study was conducted at the Aga Khan University Hospital (AKUH), Karachi, and comprised data between July 2010 and June 2019. The study was exempted by the institutional ethics review committee because only routinely available patient data was collected from the medical records without any direct interaction with patients. The AKUH is an academic tertiary care centre accredited with the Joint Commission International (JCI).¹⁴ It has an overall capacity of 700 hospital beds with 13 general care, 5 special care, and 9 intensive care beds dedicated for neurology. Clinical and diagnostic information is archived in an in-house computerised data system in a retrievable form.

The data retrieved related to patients of either gender aged ≥ 18 years diagnosed with meningitis. The data was classified into bacterial, viral and tuberculous meningitis groups.^{15,16}

In bacterial meningitis, diagnosis was established when patients had positive cerebrospinal fluid (CSF) culture or Gram's stain or alternatively had three of the following findings in their CSF: white blood cell (WBC) counts $\geq 1,000$ cells/mL; neutrophils $>80\%$ of the total WBCs; protein $>100\text{mg/dL}$; and glucose $\leq 40\text{mg/dL}$. And at least one of the typical symptoms of meningitis was present, like neck rigidity, fever, altered mental status, or severe headache.¹⁵

In viral meningitis, diagnosis was established when patients presented with clinical features of meningitis and had negative CSF culture or Gram's stains, negative CSF cryptococcal antigen test, and normal CSF findings, like normal glucose, normal or slightly elevated protein and lymphocytic predominance, along with the exclusion of nonviral causes of aseptic meningitis.¹⁶

In tuberculous meningitis, diagnosis was established when patients had clinical features of meningitis with negative CSF Gram stain and cultures for bacteria and negative CSF cryptococcal antigen test with either typical CSF findings, like pleocytosis with

lymphocytic predominance, elevated protein, and low glucose, or evidence of active tuberculosis (TB) at another body site.¹⁶

Data of patients with initial suspicion of meningitis without any confirmatory diagnoses, including those who did not undergo CSF analyses, was excluded.

Data was retrieved from the computerised data system and cross-checked with patient medical records using a pre-designed proforma. Information collected for each patient included age, gender, comorbidities, presenting signs and symptoms, concurrent encephalitis, brain imaging evidence suggesting meningitis, blood culture(s), CSF analyses and culture(s), antimicrobial susceptibility analyses, development of hydrocephalus, requirement of neurosurgical intervention, like ventriculoperitoneal shunt, external ventricular drain, or decompression, antimicrobial treatment, dexamethasone prescription, and length of stay. The primary outcomes were inpatient all-cause mortality and ICU admission.

Comorbidities included hypertension (HTN) (systolic blood pressure [SBP] ≥ 130 mmHg or diastolic blood pressure [DBP] ≥ 80 mmHg),¹⁷ diabetes mellitus (DM) (International Classification of Diseases-10 [ICD-10] codes E08 to E13), ischemic heart disease (IHD) (ICD-10 codes I20 to I25), chronic kidney disease (CKD) (glomerular filtration rate [GFR] < 60 mL/min/1.73m² for 3 or more months),¹⁸ malignancy, chronic liver disease having progressive deterioration of hepatic function for > 6 months,¹⁹ and existence of immunosuppression including human immunodeficiency virus (HIV) status, use of steroid therapies, chemotherapy, or other immunosuppressive drugs. Imaging techniques included magnetic resonance imaging (MRI) and computed topography (CT) scans.

Data was analysed using SPSS 24. Categorical variables were described using frequencies and percentages, and chi-square test was used to test the differences in their distributions in outcome groups. Fisher's exact test was used when assumptions for the chi-square test were not met. Shapiro-Wilk test for normality was conducted for continuous variables, which were found to have non-parametric distributions ($p < 0.001$).

Hence, median (interquartile range [IQR]) and Mann-Whitney U tests were used to report these variables and compare their differences in the outcome groups.

Multivariable binary logistic regression models were employed to establish the relationship between clinicodemographic covariates and outcomes. Clinically relevant covariates occurring prior to outcomes and with $p < 0.25$ on univariable logistic regression analyses were entered into the multivariable regression models. All statistical analyses were two-sided. Adjusted odds ratios (AOR), and 95% confidence intervals (CIs) were calculated. $P < 0.05$ was considered statistically significant.

Results

Of the 929 patients with suspected meningitis, 506(54.5%) had confirmatory diagnosis. Of them, 303(59.9%) were males. The overall median age of the sample was 47.0 years (IQR: 33.0 years). Comorbidities were found in 263 (52%) patients, with the commonest being HTN 194(38.3%) and DM 160(31.6%). Most patients presented to the hospital with fever 326(64.4%) and consciousness disturbance 233(46.0%).

Of the total, 324(64%) patients were diagnosed with bacterial, 141(27.9%) with viral and 41(8.1%) with tuberculous meningitis. Concurrent encephalitis was diagnosed based on clinical findings or imaging in 148(29.2%) patients, while CSF cultures were positive in 62(12.3%) patients. Of the 62 organisms isolated, streptococcus pneumoniae was the most common [32(51.6%)], followed by acinetobacter species and staphylococcus aureus [5(8.1% each)]. Other organisms included escherichia coli [3(4.8%)], streptococcus agalactiae [3(4.8%)], elizabethkingia meningoseptica [2(3.2%)], enterococcus species [2(3.2%)], group d streptococcus [2(3.2%)], klebsiella pneumoniae [2(3.2%)], unclassified streptococci [2(3.2%)], citrobacter freundii [1(1.6%)], haemophilus influenzae [1(1.6%)], listeria monocytogenes [1(1.6%)], and pseudomonas aeruginosa [1(1.6%)].

Incidence of inpatient mortality was 53(10.5%). Older patients had higher inpatient mortality than younger ones ($p=0.017$) (Table 1). In terms of comorbidities, patients with DM, IHD, CKD and chronic liver disease were more likely to belong to the

mortality group compared to those without these comorbidities ($p<0.05$). Mortality rates were also higher in patients with encephalitis, hydrocephalus, those requiring inpatient neurosurgical intervention, and patients with prolonged length of stay ($p<0.05$).

The most common treatment regimen comprised ceftriaxone, vancomycin and acyclovir 340(67.2%). Dexamethasone was given to 415(82%) patients. Compared to non-mortality group, patients with mortality received antimicrobials for shorter durations ($p<0.001$) and were more commonly treated with meropenem ($p<0.001$), colistin ($p<0.001$) and fluoroquinolones ($p<0.001$). Antimicrobial resistance to ampicillin and ceftriaxone was more common in the mortality group ($p<0.05$).

Risk factors of inpatient mortality included tuberculous aetiology, ICU admission, concurrent diagnosis of encephalitis, hydrocephalus, inpatient neurosurgery, and longer length of hospital stay, while non-indication of blood culture was associated with reduced risk of mortality (Table 2).

A total of 75(14.8%) patients required ICU admission. Compared to the non-ICU group, patients with seizures were significantly more in the ICU group ($p<0.001$), while those of patients presenting with headache and neck stiffness were significantly lower in the ICU group ($p<0.05$). Hydrocephalus, inpatient neurosurgery, longer length of stay and inpatient mortality were also more common in the ICU group ($p<0.05$).

The ICU group received antimicrobials for longer durations ($p<0.001$) and were more commonly treated with vancomycin ($p=0.011$), meropenem ($p<0.001$), colistin ($p<0.001$), rifampin ($p=0.003$), fluoroquinolones ($p<0.001$), ampicillin ($p=0.020$) and fluconazole ($p<0.001$). Antimicrobial resistance to meropenem was more common in the ICU group ($p=0.026$).

Risk factors for ICU admission included DM, presentation with seizure, imaging suggestive of meningitis, and inpatient neurosurgery, while HTN, presentation with headache, viral aetiology, and non-indication of blood culture were associated with reduced risk of requiring ICU admission (Table 3).

Discussion

Meningitis in adult patients is associated with significant mortality and morbidity. In this study, the incidence of inpatient mortality was observed to be 10.5% which was lower compared to similar studies conducted globally.^{4,8-10,20} However, most of these studies were published in the 1990s and 2000s. The burden of mortality among meningitis patients has been alleviated, considering improvements in management and standards of healthcare delivery in the past years.¹² Additionally, the current study only assessed mortality during the index admission. Mortality rates among adult meningitis patients could be even higher in Pakistan when accounted for post-discharge mortality. In this study, most of the patients were prescribed antimicrobials, including patients with viral meningitis. This might be attributed to diagnostic delays and empirical treatment with ceftriaxone and vancomycin until aetiology has been determined. Patients with mortality tended to receive antimicrobials for shorter durations compared to the non-mortality cohort. This was because antimicrobials were stopped at the time of death for the mortality group, but continued for the non-mortality group beyond discharge to complete regular courses. In addition, patients with mortality tended to receive meropenem, colistin and fluoroquinolones more often. At AKUH, meropenem and fluoroquinolones are indicated in patients who have received suboptimal doses of cephalosporins at referring healthcare facilities, considering the high resistance to cephalosporines in Pakistan. Moreover, colistin is only indicated in resistant cases with poor response to primary antimicrobials. Such cases are expected to have poorer prognoses, and that could explain the association observed in the current study. On multivariable logistic regression, concurrent diagnosis of encephalitis (3.047 [1.074-8.644]), hydrocephalus (5.841 [1.055 -32.350]), and longer length of hospital stay (1.836 [1.494-2.257]) were found to be predictors of inpatient mortality. Several studies have reported the association of longer length of stay and mortality for different diseases,^{21,22} but the current study is unique when it comes to adult meningitis patients. Hydrocephalus is a dangerous complication that often requires surgical intervention. The current findings in this regard are in accordance with other studies.²³⁻²⁵

202 Additionally, tuberculous aetiology, ICU admission and inpatient neurosurgery were
203 found to be risk factors of mortality. Other studies have also reported a higher incidence
204 of mortality in cases of tuberculous meningitis compared to non-tuberculous aetiologies.
205 Neurosurgical interventions are sometimes indicated for the management of
206 complications in meningitis patients, such as hydrocephalus. Such interventions can
207 potentially increase the risk of hospital-acquired infections, contributing to mortality
208 and morbidity in such patients.²⁶

209 Being an LMIC, Pakistan has limited hospital resources. There are only 1.5 critical care
210 beds per 100,000 population. This number is significantly lower than high-income
211 countries (HICs), like Taiwan, Singapore and Japan (28.5, 11.4, and 7.3 respectively),
212 but it is comparable to other LMICs, such as India, Bangladesh and Sri Lanka (2.3, 0.7,
213 and 2.3 respectively).⁶ In these resource-limited settings, it is imperative to identify
214 predictors of ICU admission to inform the evidence-based allocation of ICU beds and
215 hospital resources.

216 In this cohort of adult meningitis patients, the incidence of ICU admission was 14.8%.
217 This is significantly lower than existing literature, which places incidence of ICU
218 admission between 34.2% and 79%.^{9,13,27} This could be attributed to Pakistan being an
219 LMIC with limited healthcare resources, allowing only the most high-risk patients. At
220 AKUH, ICU admission is only indicated for patients with Glasgow Coma Scale (GCS)
221 score <8, hypoxic state, and/or status epilepticus.

222 On adjusted analyses, risk of ICU admission was independently associated with DM,
223 HTN, presentation with seizure(s) or headache, imaging suggestive of meningitis, viral
224 aetiology, and inpatient neurosurgery. Presentation with seizures has been previously
225 associated with increased mortality and severe neurological deficits.^{9,11} Aronin et al.
226 also recommended that meningitis patients presenting with seizures should be managed
227 and observed in ICUs to improve prognosis.¹¹ Other risk factors of ICU admission
228 identified in the current study have not been reported in literature and necessitate further
229 research.

On adjusted analysis, non-indication of blood culture was found to be associated with reduced mortality and need for ICU admission. Blood cultures are usually indicated in meningitis patients when lumbar punctures cannot be performed or when CSF analyses are insignificant. In such cases, blood cultures can assist in identifying causative organisms and provide antimicrobial susceptibility analyses.¹² Better prognoses in cases without indication of blood culture could be attributed to early diagnoses via CSF analyses, eliminating the need for blood cultures while allowing timely and evidence-based management of patients.

Physicians managing meningitis patients in Pakistan should anticipate poorer prognoses with the highlighted risk factors. Early anticipation followed by optimisation of care could potentially improve outcomes among meningitis patients nationally.

The current study has some limitations. It was performed retrospectively, and post-discharge outcomes were not evaluated. More evidence is needed to determine prognostic factors in patients with adult meningitis, especially in an LMIC setting.

Conclusion

Healthcare personnel providing care to adult meningitis patients should expect poor outcomes with the highlighted risk factors and plan their management strategies accordingly. With prior anticipation, they can strive for providing early and prompt care to high-risk patients. This can potentially lead to improvements in resource utilisation, especially in resource-limited settings, while also improving outcomes in meningitis patients.

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Table 1: Clinical characteristics of adult meningitis patients, compared across outcome groups (n=506).

Variables N (%) or median (interquartile range)	Mortality		p-value	ICU admission		p-value
	Yes N = 53 (100%)	No N = 453 (100%)		Yes N = 75 (100%)	No N = 431 (100%)	
Male sex	31 (58.5%)	272 (60.0%)	0.827	43 (57.3%)	260 (60.3%)	0.626
Age (years)	55.0 (36.5)	45.0 (33.0)	0.017	43.0 (31.0)	47.0 (33.0)	0.556
Hypertension	26 (49.1%)	168 (37.1%)	0.090	23 (30.7%)	171 (39.7%)	0.139
Diabetes mellitus	27 (50.9%)	133 (29.4%)	0.001	30 (40.0%)	130 (30.2%)	0.091
Ischemic heart disease	14 (26.4%)	50 (11.0%)	0.001	11 (14.7%)	53 (12.3%)	0.569
Chronic kidney disease	8 (15.1%)	19 (4.2%)	0.004	4 (5.3%)	23 (5.3%)	1.000
Malignancy	3 (5.7%)	13 (2.9%)	0.229	2 (2.7%)	14 (3.2%)	1.000
Chronic liver disease	5 (9.4%)	11 (2.4%)	0.019	4 (5.3%)	12 (2.8%)	0.275
PS: Fever	25 (47.2%)	301 (66.4%)	0.006	45 (60.0%)	281 (65.2%)	0.386
PS: Disturbed consciousness	23 (43.4%)	210 (46.4%)	0.682	38 (50.7%)	195 (45.2%)	0.385
PS: Headache	8 (15.1%)	183 (40.4%)	<0.001	12 (16.0%)	179 (41.5%)	<0.001
PS: Seizure	12 (22.6%)	89 (19.6%)	0.606	29 (38.7%)	72 (16.7%)	<0.001
PS: Altered sensorium	10 (18.9%)	105 (23.2%)	0.479	15 (20.0%)	100 (23.2%)	0.541
PS: Neck stiffness	1 (1.9%)	42 (9.3%)	0.071	1 (1.3%)	42 (9.7%)	0.016
PS: Unconsciousness	3 (5.7%)	7 (1.5%)	0.077	1 (1.3%)	9 (2.1%)	1.000
Meningitis category						
Bacterial	39 (73.6%)	285 (62.9%)	0.079	56 (74.7%)	268 (62.2%)	0.080
Viral	8 (15.1%)	133 (29.4%)		13 (17.3%)	128 (29.7%)	
Tuberculous	6 (11.3%)	35 (7.7%)		6 (8.0%)	35 (8.1%)	
Encephalitis	24 (45.3%)	124 (27.4%)	0.007	27 (36.0%)	121 (28.1%)	0.164
Imaging of meningitis						
Yes	22 (41.5%)	305 (67.3%)	0.125	34 (45.3%)	117 (27.1%)	0.004
No	30 (56.6%)	129 (28.5%)		40 (53.3%)	295 (68.4%)	
Unavailable	1 (1.9%)	19 (4.2%)		1 (1.3%)	19 (4.4%)	
Blood culture						
Positive	12 (22.6%)	50 (11.0%)	<0.001	10 (13.3%)	52 (12.1%)	<0.001
Negative	40 (75.5%)	294 (64.9%)		64 (85.3%)	270 (62.6%)	
Not indicated	1 (1.9%)	109 (24.1%)		1 (1.3%)	109 (25.3%)	
Hydrocephalus	14 (26.4%)	21 (4.6%)	<0.001	12 (16.0%)	23 (5.3%)	0.001
Inpatient neurosurgery	7 (13.2%)	12 (2.6%)	0.002	9 (12.0%)	10 (2.3%)	0.001
Length of stay (days)	6.0 (6.5)	4.0 (5.5)	0.002	10.0 (11.0)	4.0 (5.0)	<0.001

ICU: Intensive care unit, PS: Presenting sign.

Table 2: Unadjusted and adjusted models of predictors for inpatient mortality (n=506).

Variables	Unadjusted odds ratio [95% CI]	p-value	Adjusted odds ratio [95% CI]	p-value
Male Sex	0.938 [0.526-1.671]	0.827	-	-
Age (years)	1.019 [1.003-1.035]	0.018	1.021 [0.984-1.060]	0.272
Hypertension	1.634 [0.923-2.892]	0.092	1.429 [0.348-5.859]	0.620
Diabetes mellitus	2.499 [1.406-4.441]	0.002	0.986 [0.250-3.886]	0.984
Ischemic heart disease	2.893 [1.469-5.698]	0.002	2.242 [0.628-8.010]	0.214
Chronic kidney disease	4.061 [1.682-9.802]	0.002	2.361 [0.449-12.420]	0.311
Malignancy	2.031 [0.560-7.370]	0.281	-	-
Chronic liver disease	4.186 [1.396-12.553]	0.011	2.622 [0.287-23.949]	0.393
Immunosuppression	0.463 [0.051-4.223]	0.495	-	-

PS: Fever	0.451 [0.254-0.800]	0.006	0.647 [0.230-1.821]	0.409
PS: Disturbed consciousness	0.887 [0.500-1.575]	0.682	-	-
PS: Headache	0.262 [0.121-0.569]	0.001	0.496 [0.120-2.046]	0.332
PS: Seizure	1.197 [0.604-2.372]	0.606	-	-
PS: Altered sensorium	0.771 [0.374-1.586]	0.480	-	-
PS: Neck stiffness	0.188 [0.025-1.396]	0.102	0.167 [0.006-4.363]	0.282
PS: Unconsciousness	3.823 [0.958-15.252]	0.058	1.056 [0.067-16.522]	0.969
Category of meningitis				
Bacterial	Reference		Reference	
Viral	0.440 [0.200-0.967]	0.041	0.497 [0.120-2.055]	0.334
Tuberculous	1.253 [0.495-3.170]	0.634	16.584 [2.388-115.162]	0.005
ICU admission	9.675 [5.214-17.951]	<0.001	17.694 [4.777-65.547]	<0.001
Encephalitis	2.196 [1.231-3.918]	0.008	3.047 [1.074-8.644]	0.036
Imaging suggestive of meningitis				
Yes	1.734 [0.964-3.120]	0.066	0.611 [0.174-2.141]	0.442
No	Reference		Reference	
Unavailable	0.535 [0.069-4.138]	0.549	1.614 [0.144-18.045]	0.698
Blood culture				
Negative	Reference		Reference	
Positive	1.764 [0.866-3.593]	0.118	0.991 [0.182-5.390]	0.992
Not indicated	0.067 [0.009-0.496]	0.008	0.048 [0.003-0.759]	0.031
Positive CSF culture	3.295 [1.322-8.208]	0.010	5.427 [0.578-50.939]	0.139
Hydrocephalus	7.385 [3.483-15.656]	<0.001	5.841 [1.055-32.350]	0.043
Inpatient neurosurgery	5.592 [2.098-14.906]	0.001	15.374 [1.050-225.116]	0.046
Length of stay (days)	1.038 [1.009-1.068]	0.009	1.836 [1.494-2.257]	<0.001

PS: Presenting sign, ICU: Intensive care unit, CI: Confidence interval

Table 3: Unadjusted and adjusted models of predictors for intensive care unit (ICU) admission (n=506).

Variables	Unadjusted odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
Male sex	0.884 [0.538-1.452]	0.626	-	-
Age (years)	0.994 [0.981-1.008]	0.402	-	-
Hypertension	0.673 [0.397-1.140]	0.140	0.450 [0.224-0.904]	0.025
Diabetes mellitus	1.544 [0.931-2.559]	0.092	2.284 [1.134-4.599]	0.021
Ischemic heart disease	1.226 [0.608-2.472]	0.569	-	-
Chronic kidney disease	0.999 [0.336-2.976]	0.999	-	-
Malignancy	0.816 [0.182-3.666]	0.791	-	-
Chronic liver disease	1.967 [0.617-6.270]	0.253	-	-
Immunosuppression	1.151 [0.133-9.995]	0.898	-	-
PS: Fever	0.801 [0.484-1.324]	0.386	-	-
PS: Disturbed consciousness	1.243 [0.761-2.031]	0.385	-	-
PS: Headache	0.268 [0.140-0.512]	<0.001	0.285 [0.134-0.604]	0.001
PS: Seizure	3.143 [1.852-5.336]	<0.001	3.456 [1.837-6.503]	<0.001
PS: Altered sensorium	0.828 [0.450-1.521]	0.542	-	-
PS: Neck stiffness	0.125 [0.017-0.924]	0.042	0.165 [0.020-1.347]	0.093
PS: Unconsciousness	0.634 [0.079-5.075]	0.667	-	-
Category of meningitis				

Bacterial	Reference		Reference	
Viral	0.486 [0.257-0.921]	0.027	0.350 [0.149-0.823]	0.016
Tuberculous	0.820 [0.329-2.044]	0.671	0.432 [0.145-1.290]	0.133
Encephalitis	1.441 [0.860-2.415]	0.165	1.696 [0.863-3.336]	0.126
Imaging suggestive of meningitis				
Yes	2.143 [1.294-3.551]	0.003	3.151 [1.670-5.945]	<0.001
No	Reference		Reference	
Unavailable	0.388 [0.051-2.979]	0.363	0.612 [0.074-5.035]	0.648
Blood culture				
Negative	Reference		Reference	
Positive	0.811 [0.391-1.683]	0.574	0.614 [0.269-1.404]	0.258
Not indicated	0.039 [0.005-0.282]	0.001	0.046 [0.006-0.344]	0.003
Positive CSF culture				
Positive	1.698 [0.662-4.357]	0.271	-	-
Hydrocephalus	3.379 [1.601-7.129]	0.001	1.117 [0.441-2.829]	0.816
Inpatient neurosurgery	5.741 [2.249-14.655]	<0.001	6.041 [1.829-19.952]	0.003

PS: Presenting sign, CI: Confidence interval.