Adult Bacterial Meningitis: Earlier Treatment and Improved Outcome following Guideline Revision Promoting Prompt Lumbar Puncture

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Abstract

Background: Acute bacterial meningitis (ABM) is a potentially fatal illness. In spite of modern therapy and intensive care, the death rate remains between ten percent and thirty percent, and the possibility of persistent neurological or auditory deficits is high.

Aim: To evaluate the outcome of lumbar puncture (LP) carried out rapidly or following neuroimaging in acute bacterial meningitis in adults

Patients and methods: This prospective investigation has been performed on 600 adult cases with acute bacterial meningitis (ABM) with age >16 years. The diagnoses of ABM have been dependent on cerebrospinal fluid analysis, clinical criteria, and blood micro154biological tests. This study was done at Al-Azhar University from May 2020 to Jan 2021.

Results: A statistically insignificant distinction has been observed among lumbar puncture without before CT and lumbar puncture following CT regarding age, sex, immunocompromised state, and reaction level scale (RLS) 2–3 mental status, while there was a statistically significant lower in LP after CT when compared to LP without prior CT regarding Neisseria meningitides, RLS 1 mental status, and time from admission to appropriate therapy and a significant increase regarding Streptococcus pneumoniae and RLS 4–8 mental status.

Conclusion: CT-conducted prior lumbar puncture slows and elevates the death possibility. In instances of mass lesions or impending herniation, a CT scan must be conducted. A prompt lumbar puncture is recommended, and altered mental status, seizures, and immunocompromised states shouldn't be considered for neuroimaging in cases with suspected ABM.

Key words: ABM, LP, neuroimaging

Introduction

Acute bacterial meningitis is a potentially fatal illness. In spite of modern therapy and intensive care, the death rate remains between ten percent and thirty percent, and the possibility of persistent neurological or auditory deficits is high. A favorable result depends on receiving appropriate treatment as soon as possible [(1)].

Lumbar puncture is essential for diagnosing acute bacterial meningitis; yet, a persistent debate surrounds the possible brain herniation risk caused by lumbar puncture [(2)].

Present international guidelines utilize the "red flags" of papilledema, focal neurological signs, moderate to severe mental status impairment, immunocompromised state, and newly developed seizures to determine cases at elevated possibility of cerebral mass lesions and elevated intracranial pressure, thereby indicating contraindications for immediate lumbar puncture. Cerebral computed tomography (CT) is advised before lumbar puncture in these cases [(3)].

Comparable guidelines have been implemented in Sweden in 2004. Nonetheless, similar to previous international reports, computed tomography has been conducted excessively, and compliance with the guidelines to initiate antibiotics prior to computed tomography in suspected acute bacterial meningitis was limited [(4)].

Multiple investigations emphasize the significance of early treatment. Additionally, new research suggests that conducting a computed tomography prior to a lumbar puncture frequently postpones the treatment process, and the diagnostic sequence of computed tomography–lumber puncture–antibiotics is prevalent, posing a risk factor for unfavorable outcomes [(5)].

The Swedish guidelines are the most liberal about rapid lumbar puncture, as impaired mental status and newly developed seizures have been excluded as criteria for computed tomography before lumbar puncture following the 2009 revision [(6)].

The ESCMID guidelines have been updated in 2016, lowering the consciousness level requiring a computed tomography before lumbar puncture from a Glasgow Coma Scale score (GCS) of less than twelve to less than ten [(7)].

The 2004 IDSA guidelines are the most conservative, advising the computed tomography prior to lumbar puncture if an aberrant mental status (GCS less than fifteen) is observed [(8)].

The primary objective of this investigation was to assess the outcomes of lumbar puncture conducted either rapidly or following neuroimaging in cases of ABM in adults.

Patients and methods

This prospective investigation has been performed on 600 adult cases with acute bacterial meningitis (ABM) with age >16 years. The diagnoses of ABM have been dependent on cerebrospinal fluid analysis, clinical criteria, and blood microbiological tests. This study was done at Al-Azhar University from May 2020 to Jan 2021.

Inclusion criteria: Cases of both sexes with adult bacterial meningitis (ABM) and age >16 years

Methods:

All patients were subjected to medical history, physical examinations to identify any indications of infection, and laboratory analyses. ABM has been classified as community-acquired if cases hadn't been hospitalized or hadn't received central nervous system surgery within the preceding thirty-day period.

Age, sex, etiology, mental status upon admission, corticosteroid therapy, antibiotic type, timing of therapy relative to lumbar puncture, duration from admission to therapy initiation, and neurological sequelae during monitoring have been documented. The mental state upon

admission has been documented using Reaction Level Scale (RLS) (9), Glasgow Coma Scale (GCS), or both. In cases where the Glasgow Coma Scale has been recorded but the RLS wasn't, the GCS has been transformed into the Reaction Level Scale for standardized comparison [(9)]. Appropriate antibiotic therapy has been characterized as the administration of IV β-lactam antibiotics to which the isolated bacteria were susceptible, delivered in dosages appropriate for meningitis. In cases with unclear cause, the combination of third-generation cephalosporin and ampicillin or single therapy with meropenem has been regarded as adequate. Appropriate corticosteroid therapy has been defined as intravenous betamethasone eight milligrams administered every six hours, which started within one hour of antibiotic initiation. An immunocompromised state, newly developed seizures, neurological impairments, characteristic symptoms (headache, fever, and stiffness of neck), septic shock, 1^{ry} infection source, and intensive care have been documented.

Table 1 demonstrates the recommendations from the current Swedish, European Society for Clinical Microbiology and Infectious Diseases (ESCMID), and Infectious Diseases Society of America (IDSA) guidelines. ESCMID recommended conducting a computed tomography scan before a lumbar puncture in cases with altered mental status (RLS more than three). An abnormal level of consciousness, where IDSA guidelines advise a computed tomography scan prior to lumbar puncture, is characterized by an RLS of more than one, which corresponds to a GCS of less than fifteen **(2)**. The European Society for Clinical Microbiology and Infectious Diseases and IDSA recommend CT-preceded lumbar puncture in cases of severe immunocompromised state, characterized by HIV infection, transplant recipients, or intensive immunosuppressive therapy for cancer or autoimmune disorders.

Sample size calculation

This investigation is dependent on research conducted by **Glimåker, M., Sjölin, J.,** [(10)]**.** Epi Info STATCALC has been utilized to determine the sample size, taking into account the subsequent assumptions: -ninety-five percent two-sided confidence level, with an eighty percent power. Alpha error of five percent. Prevalence of adherence to ESCMID guidelines was fifty-three percent. The final maximum sample size derived from the Epi-Info output was 532. Consequently, the sample size has been raised to six hundred cases to account for potential dropout cases throughout monitoring. Sample size: number = [DEFF*Np(1-p)] / [(d2/Z21-α/2*(N-1) + p*(1-p)].

Statistical analysis: Information was input into the computer and analyzed utilizing IBM SPSS software version 20.0. (Armonk, NY: IBM Corp). Qualitative data have been represented utilizing numerical values and percentages. The Kolmogorov-Smirnov test has been utilized to assess the normality of the distribution. Quantitative data have been characterized by range (minimum and maximum), standard deviation, mean, median, and interquartile range (IQR). The significance of the outcomes acquired has been assessed at the five percent level. The tests utilized were: Chi-square test for categorical variables to compare multiple groups. Utilize Fisher's Exact test or Monte Carlo correction for chi-square analysis when over twenty percent of the cells exhibit an anticipated count of less than five. Student's t-test for normally distributed quantitative variables to compare both investigated groups. Paired t-test for normally distributed quantitative variables to compare both time durations. Mann-Whitney test for non-normally distributed quantitative data to compare both investigated groups. Wilcoxon signed-rank test for non-normally distributed quantitative data to compare both time durations.

Result

Table 1: Recommendations for neuroimaging of the brain prior to LP based on various guidelines in 600 cases with ABM

	Swedish Guidelines		**ESCMID Guidelines**		**IDSA Guidelines**	
Impaired mental status	Cerebral herniation	7(1.2 percent)	GCS less than ten (RLS more than three)	91(15.2 percent)	GCS less than fifteen (RLS more than one)	350(58.3 percent)
Neurologic deficit (suspected mass lesion)	Arm or leg drift More than four days of neurological symptoms or Acute bacterial meningitis-atypical symptoms	33(5.5 percent) NA	Leg or arm drift	33(5.5 percent)	Leg or arm drift Abnormal ocular motility, visual field, dilated pupil	33(5.5 percent) 6(1 percent)
Newly developed seizures	Not recommended		Within one week of presentation	43(7.2 percent)	Within 1 week of presentation	43(7.2 percent)
Severe immuno-compromised state	Not recommended		Transplant recipients, human immunodeficiency virus infection, or severe immunos	65(10.8 percent)	Transplant recipients, human immunodeficiency virus infection, or severe immunosuppressive therapy	65(10.8 percent)

			uppressive treatment			
History of central nervous system disease	Not recommended		Not recommended		Stroke, mass lesion, focal infection	NA
Papilledema	Not recommended		Not recommended		Increased intracranial pressure	NA

Table (2): Distribution of case characteristics in the investigated group.

	investigated cases (N=600)	
	Mean	**±SD**
Age	50.98	19.1
	N	**%**
Sex		
Male	307	51.2
Female	293	48.8
Immunocompromised state		
Moderate	167	27.8
Sever	64	10.7
Etiology		
Streptococcus pneumoniae	309	51.5
Neisseria meningitides	64	10.7
Other bacteria	171	28.5
Unknown	56	9.3
Mental status		
RLS 1	231	38.5

RLS 2–3	274	45.7
RLS 4–8	95	15.8

SD: Standard Deviation

According to table 1, the mean age of cases was 50.98±19.1 years. As regards sex, there were 51.2% of cases that were men, while 48.8% of them were women. As regards immunocompromised state, 27.8% of cases had moderate immunocompromised state, while 10.7% of them had severe immunocompromised state. As regards etiology, the most prevalent etiology of bacterial meningitis was Streptococcus pneumoniae. As regards mental status, RLS 1 was present in 38.5% of cases, RLS 2–3 was present in 45.7% of cases, while RLS 4–8 was present in 15.8% of cases.

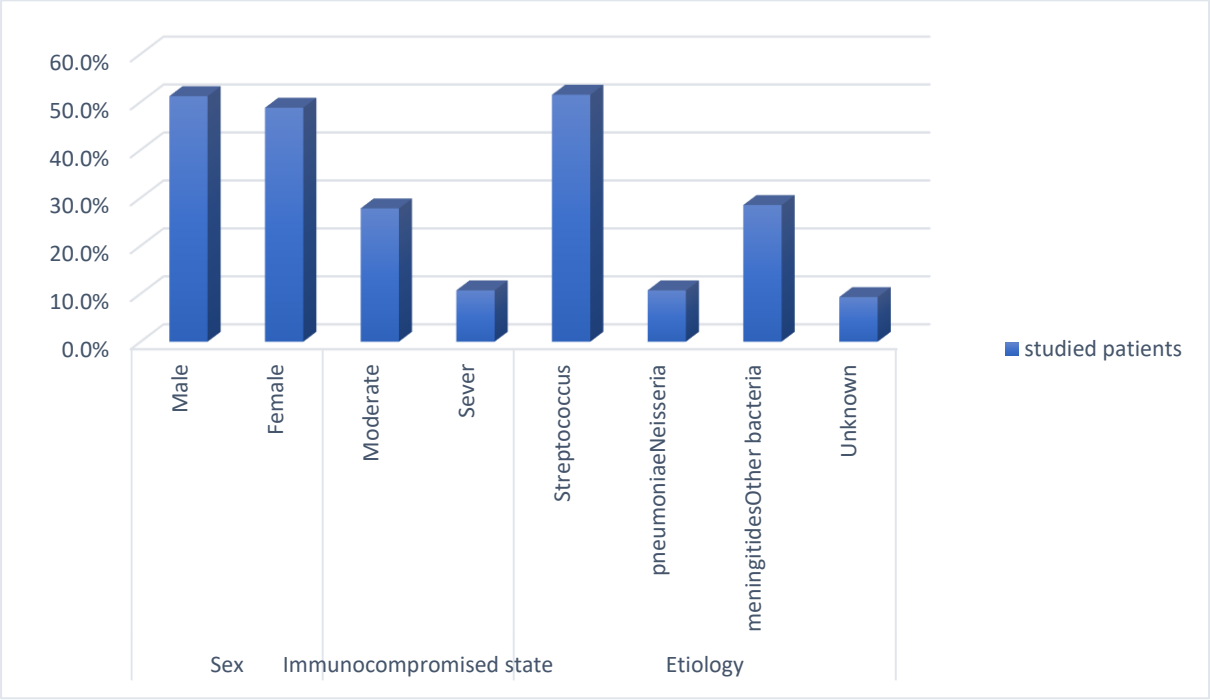

Figure (1): Distribution of case characteristics in the investigated group.

Table (3): Distribution of antibiotic treatment and time to adequate treatment in the investigated group.

	investigated cases (N=600)	
	N	**%**
Antibiotic treatment		
Cefotaxime + Ampicillin	312	39

Cefotaxime	138	17.3	
Meropenem	282	35.3	
Other antibiotics	68	8.5	
Time from admission to appropriate antibiotic and corticosteroid therapy			from admission to appropriate antibiotic and corticosteroid therapy
<1 h	144	24	
<2 h	216	36	

As regards antibiotic treatment, the majority of cases received cefotaxime + ampicillin (39%), followed by meropenem (35.3%). There were 24% of cases that took <1 h from admission to appropriate antibiotic and corticosteroid therapy, while 36% of them took <2 h from admission to appropriate antibiotic and corticosteroid therapy (Table 2).

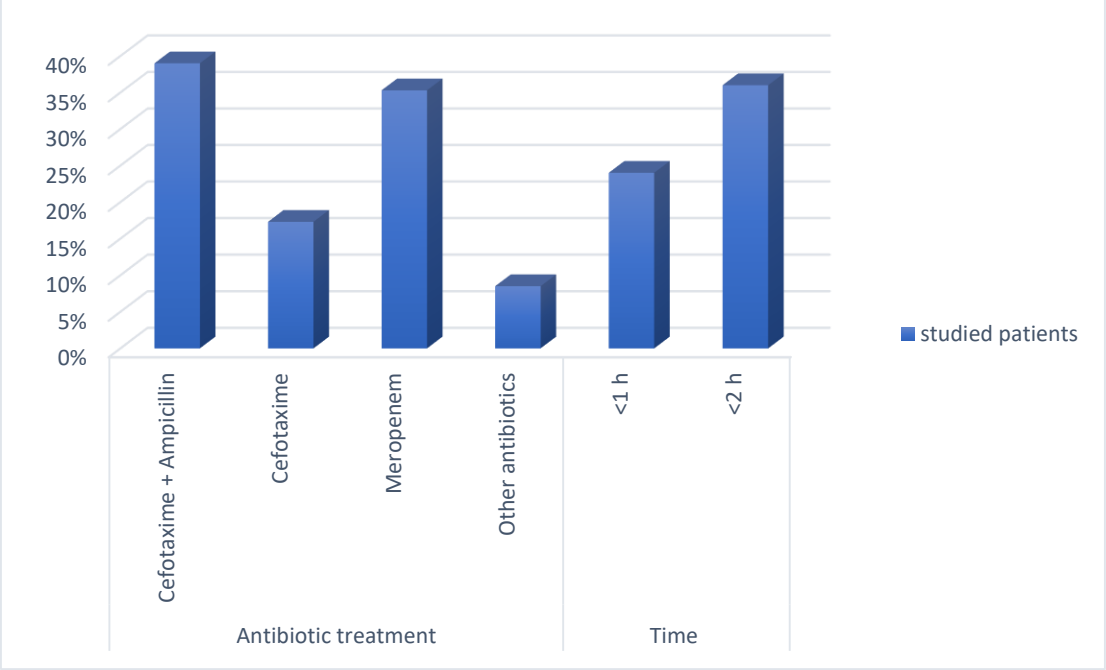

Figure (2): Distribution of antibiotic treatment and time from admission to appropriate antibiotic and corticosteroid therapy in the investigated group.

Table (4): Distribution of main results and main confounders associated with various sequences of LP and CT of the brain in the investigated group.

	Lumber puncture Without Prior computed tomography N=268	Lumber puncture following computed tomography N=332	P-value
Age	50.54±18.5	51.21±18.1	0.68
Sex			
Male	127 (47.4%)	180 (54.2%)	0.09
Female	141(52.6%)	152 (45.8%)	
Immunocompromised state			
Moderate	78 (29.1%)	89 (26.8%)	0.53
Sever	25 (9.3%)	39 (11.7%)	0.34
Etiology			
Streptococcus pneumoniae	120 (44.8%)	189 (56.9%)	**0.003**
Neisseria meningitides	43 (16%)	21 (6.3%)	**0.0001**
Other bacteria	77 (28.7%)	94 (28.3%)	0.91
Unknown	28 (10.4%)	28 (8.4%)	0.39
Mental status			
RLS 1	118 (44%)	107 (32.2%)	**0.002**
RLS 2–3	120 (44.8%)	157 (47.3%)	0.54
RLS 4–8	30 (11.2%)	68 (20.5%)	**0.002**
Time from admission to appropriate antibiotic and corticosteroid therapy			
<1 h	77 (28.7%)	61 (18.4%)	**0.003**
<2 h	109 (40.7%)	99 (29.8%)	**0.005**

P value more than 0.05: Not significant; P value less than 0.05 is statistically significant; P value more than 0.001 is highly significant. SD: standard deviation.

According to table 3, a statistically insignificant distinction has been observed among lumbar puncture without prior computed tomography and lumbar puncture following computed tomography regarding age, sex, immunocompromised state, and RLS 2–3 mental status, while there was a statistically significant lower in LP after CT when compared to LP. Without prior CT regarding Neisseria meningitides, RLS 1 mental status and time from admission to appropriate therapy and significant increase regarding Streptococcus pneumoniae and RLS 4–8 mental status.

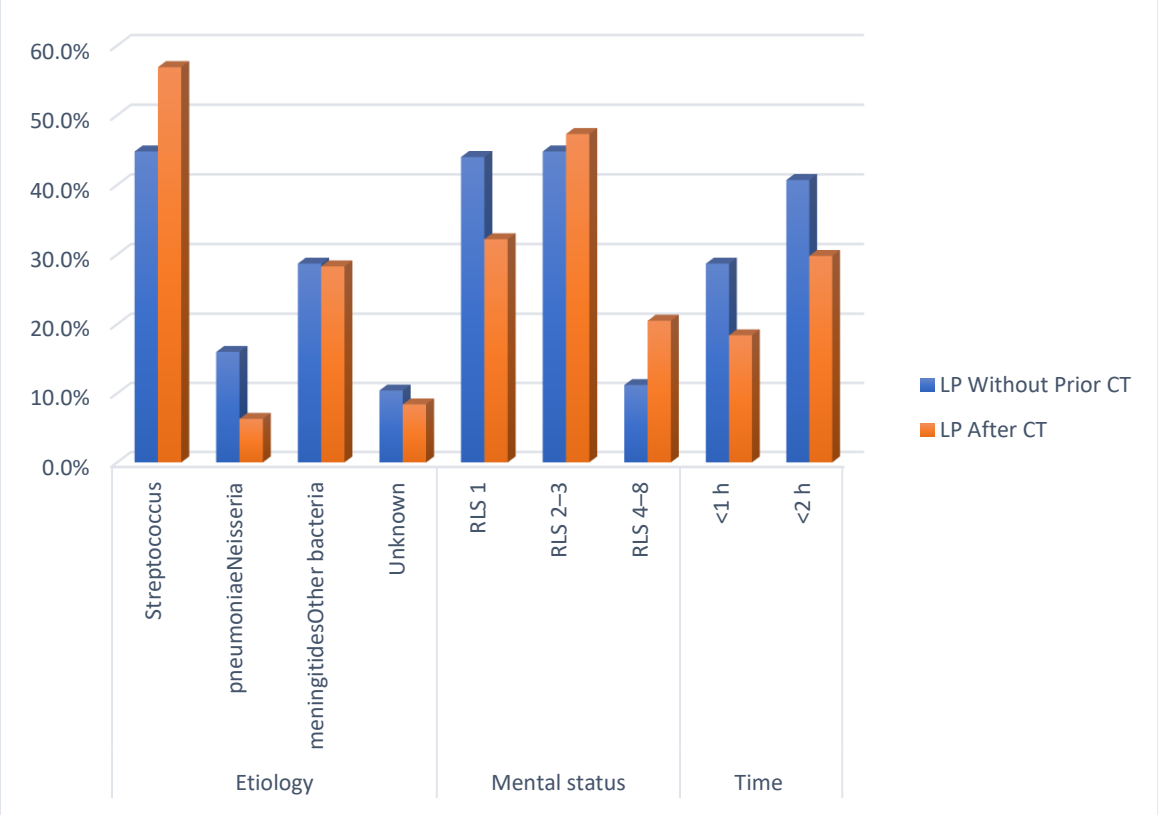

Figure (4): Distribution of main results and main confounders associated with various sequences of LP and CT of the brain in the investigated group.

Discussion

The current investigation revealed that the mean age of cases was 50.98±19.1 years, 51.2% of cases were males, and 48.8% of them were females. As regards the immunocompromised state, 27.8% of cases had moderate immunocompromised state, while 10.7% of them had severe immunocompromised state.

As regards etiology, the most prevalent etiology of bacterial meningitis was Streptococcus pneumoniae. As regards mental status, RLS 1 was present in 38.5% of cases, RLS 2–3 was present in 45.7% of cases, while RLS 4–8 was present in 15.8% of cases.

Our results were consistent with those of **Glimåker et al. (10),** who assessed the impact on mortality and favorable outcomes of compliance with the Swedish, European Society for Clinical Microbiology and Infectious Diseases, and IDSA guidelines concerning the indications for neuroimaging before lumbar puncture. Moreover, they assessed the impact of conducting rapid versus CT-preceded lumbar punctures. They reported that the age of their investigated cases varied from 17 to 95 years; 51.16% of cases were men, and 48.84% were women. As regards the immunocompromised state, 27.6% of cases had moderate immunocompromised state and 10.7% had severe immunocompromised state. As regards etiology, the most prevalent etiology of bacterial meningitis was Streptococcus pneumoniae 420 (51.5%).

As regards antibiotic treatment, our findings reported that the majority of cases received cefotaxime + ampicillin (39%) followed by meropenem (35.3%). Twenty-four percent of cases

took <1 h from admission to appropriate antibiotic and corticosteroid therapy, while 36% of them took <2 h from admission to appropriate antibiotic and corticosteroid therapy.

Significantly earlier therapy with antibiotics and corticosteroids has been facilitated by the rapidly carried out lumbar puncture, aligning with previous research outcomes [1, 11, 12]. The reduction in death and enhancement of good results observed from the quick administration of lumbar puncture were likely related to this distinction in timely management. All guidelines highlight the significance of early antibiotic therapy, strongly recommending that if lumbar puncture is postponed (for example, because of neuroimaging), empiric antibiotics should be initiated promptly based on clinical suspicion, regardless of whether a diagnosis has been confirmed. Consistent with previous results, antibiotics have been initiated prior to neuroimaging in only 50% of cases when lumbar puncture has been performed following the computed tomography scan. [13].

Our findings aligned with those of **Glimåker et al.** [10]**,** who showed that antibiotics have been initiated prior to the computed tomography in 170 cases (forty-seven percent). For fast lumbar puncture, antibiotics and corticosteroids have been given within an hour and two hours of admission in 80 of 277 (29%) and 113 of 277 (41%) of cases, respectively. This was not the case for cases with CT-preceded LP, which happened in only 18% of cases (P =.002) and 30% of cases (P =.005).

Our results demonstrated that a statistically insignificant distinction has been observed among LP without prior CT and LP after CT regarding age, sex, immunocompromised state, and RLS 2–3 mental status. On the other hand, Neisseria meningitides, RLS 1 mental status, and time from admission to appropriate therapy were significantly lower in LP After CT when compared to LP Without Prior CT, and Streptococcus pneumoniae and RLS 4–8 mental status were significantly increased in LP After CT compared to LP Without Prior CT.

Similarly, our results were consistent with **Glimåker et al.** [10]**,** who showed that a statistically insignificant distinction has been observed among LP without prior CT and LP after CT regarding sex, immunocompromised state, and RLS 2–3 mental status. While Neisseria meningitides, RLS 1 mental status and time from admission to appropriate therapy were significantly lower in LP After CT when compared to LP Without Prior CT, and Streptococcus pneumoniae and RLS 4–8 mental status were significantly increased in LP After CT compared to LP Without Prior CT.

In 2015, **Glimåker et al.** [14] assessed the impact of the 2009 revision on the duration until appropriate antibiotic therapy and the resulting outcomes. The efficacy of computed tomography before lumbar puncture has been assessed. From 2008 to 2012, cerebral computed tomography has been conducted in eighty-three percent of the cases. Computed tomography has been performed prior to lumbar puncture in over fifty percent of instances, and antibiotic therapy wasn't initiated prior in thirty-nine percent of cases. Similar to recent research by **Hasbun et al.** [12] **and Auburtin et al.** [15]**,** the sequence of neuroimaging before lumbar puncture resulted in a delay of 1.6 hours in appropriate antibiotic therapy and heightened the possibility of mortality or complications.

Lumbar puncture without before computed tomography scan has been conducted in forty-six percent of cases, a higher frequency than observed in the Netherlands (twenty-six percent) and Canada (twenty-nine percent) [11, 13]. Prompt lumbar puncture led to a considerable reduction in death and enhanced long-term favorable results, irrespective of guideline recommendations for computed tomography prior to the procedure. These results contrast with a recent Dutch investigation indicating that computed tomography prior to lumbar puncture didn't correlate with an elevated incidence of poor outcomes at discharge (mortality wasn't evaluated) [13].

Our data demonstrate that lumbar puncture is safe in acute bacterial meningitis cases with impaired mental status or coma, consistent with previous reports [16,17]. Moreover, the significance of prompt lumbar puncture escalates in critically ill acute bacterial meningitis cases, wherein a computed tomography scan is frequently advised prior to the procedure [18].

Conclusion

Our results showed that Neisseria meningitides, RLS 1 mental status, and time from admission to adequate treatment were significantly lower in LP After CT when compared to LP Without Prior CT, and Streptococcus pneumoniae and RLS 4–8 mental status were significantly increased in LP After CT compared to LP Without Prior CT. We determined that conducting a computed tomography scan prior to a lumbar puncture result in considerable delays and is a risk factor for elevated death and unfavorable outcomes, regardless of mental status. In cases where clinical outcomes suggest a mass lesion or impending herniation, an initial cerebral computed tomography must be conducted. Alternatively, guidelines might promote rapid lumbar puncture liberally, and altered mental status, newly developed seizures, and an immunocompromised condition shouldn't be regarded as criteria for neuroimaging before LP in suspected cases of ABM.

References

1. Domingo P, Pomar V, Benito N, Coll P. The changing pattern of bacterial meningitis in adult cases at a large tertiary university hospital in Barcelona, Spain (1982–2010). Journal of Infection. 2013 Feb 1;66(2):147-54.

2. Glimåker M, Johansson B, Bell M, Ericsson M, Bläckberg J, Brink M, Lindquist L, Sjölin J. Early lumbar puncture in adult bacterial meningitis—rationale for revised guidelines. Scandinavian journal of infectious diseases. 2013 Sep 1;45(9):657-63.

3. Chaudhuri A, Martin PM, Kennedy PG, Andrew Seaton R, Portegies P, Bojar M, Steiner I, EFNS Task Force. EFNS guideline on the management of community-acquired bacterial meningitis: report of an EFNS Task Force on acute bacterial meningitis in older children and adults. European journal of neurology. 2008 Jul;15(7):649-59.

4. Mölstad S, Löfmark S, Carlin K, Erntell M, Aspevall O, Blad L, Hanberger H, Hedin K, Hellman J, Norman C, Skoog G. Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance. Bulletin of the World Health Organization. 2017 Nov 11;95(11):764.

5. Michael B, Menezes BF, Cunniffe J, Miller A, Kneen R, Francis G, Beeching NJ, Solomon T. Effect of delayed lumbar punctures on the diagnosis of acute bacterial meningitis in adults. Emergency medicine journal. 2010 Jun 1;27(6):433-8.

6. Segal S. Cranial CT before lumbar puncture in suspected meningitis. The New England journal of medicine. 2002 Apr 1;346(16):1248-51.

7. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, Leib SL, Mourvillier B, Ostergaard C, Pagliano P, Pfister HW. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clinical microbiology and infection. 2016 May 1;22:S37-62.

8. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, Whitley RJ. Practice guidelines for the management of bacterial meningitis. Clinical infectious diseases. 2004 Nov 1;39(9):1267-84.

9. Starmark JE, Stålhammar D, Holmgren E. The reaction level scale (RLS 85) manual and guidelines. Acta neurochirurgica. 1988 Mar;91:12-20.

10. Glimåker M, Sjölin J, Åkesson S, Naucler P. Lumbar puncture performed promptly or after neuroimaging in acute bacterial meningitis in adults: a prospective national cohort study evaluating different guidelines. Clinical infectious diseases. 2018 Jan 18;66(3):321-8.

11. Proulx N, Frechette D, Toye B, Chan J, Kravcik S. Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. Qjm. 2005 Apr 1;98(4):291-8.

12. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed tomography of the head before lumbar puncture in adults with suspected meningitis. New England Journal of Medicine. 2001 Dec 13;345(24):1727-33.

13. Costerus JM, Brouwer MC, Bijlsma MW, Tanck MW, van der Ende A, van de Beek D. Impact of an evidence-based guideline on the management of community-acquired bacterial meningitis: a prospective cohort study. Clinical microbiology and infection. 2016 Nov 1;22(11):928-33.

14. Glimåker M, Johansson B, Grindborg Ö, Bottai M, Lindquist L, Sjölin J. Adult bacterial meningitis: earlier treatment and improved outcome following guideline revision promoting prompt lumbar puncture. Clinical Infectious Diseases. 2015 Apr 15;60(8):1162-9.

15. Auburtin M, Wolff M, Charpentier J, Varon E, Le Tulzo Y, Girault C, Mohammedi I, Renard B, Mourvillier B, Bruneel F, Ricard JD. Detrimental role of delayed antibiotic administration and penicillin-nonsusceptible strains in adult intensive care unit cases with pneumococcal meningitis: the PNEUMOREA prospective multicenter study. Critical care medicine. 2006 Nov 1;34(11):2758-65.

16. Van de Beek D, De Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. New England Journal of Medicine. 2004 Oct 28;351(18):1849-59.

17. Glimåker M, Johansson B, Halldorsdottir H, Wanecek M, Elmi-Terander A, Ghatan PH, Lindquist L, Bellander BM. Neuro-intensive treatment targeting intracranial hypertension improves outcome in severe bacterial meningitis: an intervention-control study. PloS one. 2014 Mar 25;9(3):e91976.

18. Salazar L, Hasbun R. Cranial imaging before lumbar puncture in adults with community-acquired meningitis: clinical utility and adherence to the Infectious Diseases Society of America guidelines. Clinical infectious diseases. 2017 Jun 15;64(12):1657-62.