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# Diagnosis and treatment of stroke associated pneumonia: Qualitative exploration of clinicians' practice

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| ARTICLE INFO | ABSTRACT |
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| | **Background:** Establishing and implementing a gold standard criteria for diagnosing and treating stroke-associated pneumonia (SAP) would have a significant positive impact on stroke outcomes and antibiotic stewardship. This study aimed to qualitatively explore current diagnostic and treatment practice for SAP among clinicians.<br><br>**Methods:** A qualitative study was employed to conduct semi-structured interviews at the tertiary-care Jordan University Hospital. A purposive sampling technique was employed to recruit the participants, including respiratory consultants (n=3) and residents (n=9) practicing in the internal medicine wards and intensive care unit, where stroke patients are treated. The interviews were audio-recorded, transcribed verbatim, translated, and analyzed thematically using framework analysis.<br><br>**Results:** Clinicians expressed their experiences, which were organized into two themes and eight emerged sub-themes: Terminology and diagnostic approach of SAP involved; no definite terminology, reliance on both clinical evidence and X-ray findings to decide, reliance on clinical evidence alone to suspect SAP and initiate empirical therapy, and SAP overdiagnosis. The treatment strategies include early treatment of SAP, treating SAP the same as CAP/HAP, predominant anaerobes coverage, and SAP overtreatment.<br><br>**Conclusion:** Our findings show a wide range of physician-based diagnostic and treatment approaches for SAP, with clinical criteria serving as the main driver for antibiotic initiation. Standard validated algorithmic-based criteria need to be established and implemented.<br><br>**Keywords:** stroke-associated pneumonia, diagnosis, treatment, clinicians' practice |

## INTRODUCTION

Stroke-associated pneumonia (SAP) is a serious and common complication that has a significant impact on stroke outcomes, being independently associated with increased mortality, and a higher risk of dependency at discharge [1-3]. SAP diagnosis and treatment are a clinical conundrum for many reasons: First, the clinical presentation may be nonspecific [4]; cough may be impaired due to neurological deficit [5]; fever and leukocytosis can occur in response to the acute phase of stroke without infectious etiologies [6]; and hypoxia may result from other comorbidities such as cardiac and respiraty diseases [7]. Second, the quality of the chest radiography may be affected by diaphragmatic impairment and reduced the ability to have a deep inspiration [8, 9]. Third, difficulties in acquiring sputum samples in non-ventilated stroke patients and the low diagnostic sensitivity of other available culture samples make identifying the microbiological

aetiology of SAP difficult and limit definite antibiotic therapy depending on microbial sensitivities [10].

A specific and feasible diagnostic approach is essential for decision-making in SAP management. There are currently no gold-standard criteria for diagnosing and treatment of SAP despite the availability of such criteria for community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP) [11, 12]. Given the challenges associated with the diagnosis and treatment of SAP, a multidisciplinary group called pneumonia in stroke consensus (PISCES) was created firstly to propose standardized terminology and diagnostic approaches [13]. They recommend a criterion-driven diagnosis based on many indicators defined by the Centers for Disease Control and Prevention (CDC) [14]. These criteria are based on clinical and laboratory evidence, as well as two or more serial chest X-rays showing new changes. Furthermore, a second PISCES group has convened to formulate antibiotic treatment recommendations for SAP [15].

Literature on clinicians' practices for diagnosing and treating SAP is scarce. One survey assessed decision-making in the diagnosis and treatment of SAP among 160 German clinicians using five different case vignettes developed based on CDC criteria [4, 14]. The study found that the diagnosis of SAP mostly depends on clinical parameters like stroke severity and fever, but the availability of chest X-rays, which is the central diagnostic component in the CDC criteria, is given only minor importance. The authors did not rule out the possibility that using simple clinical parameters to make a diagnosis could overestimate SAP; thus, antibiotics are often prescribed unnecessarily for stroke patients [4]. This overestimation has also been observed in a recent study, which found that physicians overestimated SAP diagnosis compared to algorithm-based diagnosis in which 16% of patients were diagnosed with SAP according to physician assessments while 11.3% were diagnosed using an algorithm. However, the study suggested that although an algorithmic-based diagnostic approach may improve SAP diagnosis, it needs to be informed by clinicians' judgement in order to allow for the weighting of criteria components and considering additional clinical data [16]. To date, there has been no qualitative study conducted on this topic. In this light, we aimed to qualitatively explore current diagnostic and treatment practices for SAP among clinicians in Jordan.

## METHODS

### Research Design Setting and Data Collection

A qualitative study was conducted among clinicians at one academic tertiary hospital affiliated with the Jordan University Hospital located in the capital Amman, Jordan, with a capacity of 550 beds. A semi-structured interview took place via both zoom application and in-person between October and December 2021. A purposive sampling technique was employed to recruit the participants, including consultants and residents practicing in the internal medicine wards and intensive care unit, where stroke patients are treated. Purposive sampling refers to the deliberate selection of study participants to reflect various opinions and experiences that can provide relevant and different information to answer the study objectives [17, 18]. Initial outreach to potential candidates was done both by phone contact and in-person to explain the study's purpose. Five clinicians refused to participate in the study without mentioning any reason. Physicians who agreed to take part were interviewed by a trained female pharmacist (ZM) for 20 to 40 minutes. The same interviewer did all of the interviews to make sure they were conducted in a consistent manner. The interviewer had no prior relationship with any of the participants. The purpose of the study was explained by the interviewer to all clinicians before receiving the verbal consent, and they were informed that the interview would be recorded. Data collection ceased when no new themes emerged from the interviews, and the data became saturated. Theoretical saturation was reached through the 12 interviews.

### Interview Guide

The interview was based on a simple interview guide of open-ended discussion questions (**Appendix A**). They were established and developed by a researcher from the research team after reviewing literature and recent recommendations relevant to the diagnosis and treatment of SAP [13, 15]. As a validation process, four researchers then reviewed the interview guide for completeness and clarity, making changes as needed. Two interviews were piloted and assessed for clarity and appropriateness. Each interview included three sections; the first component was about general information of physicians such as gender, years of experience, and specialty. The second part included the diagnosis of SAP. The final section covered the current practice in therapeutic approaches of SAP.

### Data Analysis

All interviews with physicians were carried out in Arabic. They were audio-recorded under deidentified labels, transcribed verbatim, and translated to English. All the recorded interviews were transcribed by the researcher (MZ) and then translated to English immediately after each interview. The translation was in accordance with World Health Organization guidelines [19]. It was primarily based on the use of forward and back translation. Translated data were analyzed thematically using Framework analysis to understand clinicians' experiences and opinions [20]. This method includes six phases: familiarisation with the transcript, initial coding, searching for themes and subthemes across the data, reviewing the themes, defining and identifying the themes, and producing the report [20]. One of the authors coded the transcripts independently, while other researchers double-checked random subsets to ensure rigour. Following that, a discussion was held to assess agreement among the identified codes, reconcile disagreements based on majority vote, and organise the codes to create a final coding frame. To ease and arrange the analysis of textual transcripts, Microsoft Word Office was employed. To ensure the quality of reporting this study, the consolidated criteria for reporting qualitative studies was employed [20].

## RESULTS

### Participant Characteristics

The interviewed clinicians included pulmonology consultants (25%, 3/12) and internal medicine residents (75%, 9/12), with 33.3% being female. The participants had a range of experiences, from two to 17 years (**Table 1**).

The analysis of the interviews resulted in two themes and eight sub-themes, which are shown in the following section with representative quotations. **Table B1** in **Appendix B** has further illustrative quotes.

### Theme 1: Terminology and Diagnostic Approach of Stroke-Associated Pneumonia

#### Sub-theme 1: No definite terminology

Clinicians indicated that they are not aware of the term "stroke-associated pneumonia" but instead refer to it mostly as "primarily aspiration pneumonia" or "hospital-acquired pneumonia."

> "We label it as aspiration pneumonia most of the time; however, after 48 hours of hospitalization, we call it hospital-acquired pneumonia. We do not have in pneumonia such a thing as stroke associated

**Table 1.** Clinician characteristics (n=12)

| CN | Gender | Designation | Speciality | YP | NPPM |
|---|---|---|---|---|---|
| Cl 1 | Male | Resident | IM | 4 | 16 |
| Cl 2 | Male | Resident | IM | 3 | 16 |
| Cl 3 | Female | Resident | IM | 4 | 24 |
| Cl 4 | Female | Consultant | Pulmonologist | 9 | 8 |
| Cl 5 | Male | Resident | IM | 5 | 20 |
| Cl 6 | Male | Resident | IM | 4 | 20 |
| Cl 7 | Male | Consultant | Pulmonologist | 17 | 20 |
| Cl 8 | Male | Resident | IM | 3 | 16 |
| Cl 9 | Female | Resident | IM | 2 | 20 |
| Cl 10 | Male | Resident | IM | 5 | 16 |
| Cl 11 | Female | Resident | IM | 3 | 20 |
| Cl 12 | Male | Consultant | Pulmonologist | 10 | 16 |

Note. CN: Clinician's number; YP: Years in practice; NPPM: Number of patients per month; & IM: Internal medicine

pneumonia, meaning there is no definition. We do not have this term" (**Cl.4**).

"We talk in general, patients who have a stroke and got pneumonia, we call it aspiration pneumonia or hospital-acquired pneumonia" (**Cl.2**).

### Sub-theme 2: Reliance on both clinical evidence and chest X-ray findings to decide

Most residents and consultants agreed that clinical decision-making on SAP diagnosis requires both clinical indicators and alterations on a chest X-ray.

"In general, the diagnosis of such pneumonia is a new X-ray infiltrate associated with respiratory symptoms" (**Cl.2**).

"Usually, we diagnose pneumonia if there is fever, cough, sputum, WBCs increase, maybe unconsciousness, sometimes hypotension, and new infiltration in the chest X-ray" (**Cl.10**).

### Sub-theme 3: Reliance on clinical evidence alone to suspect stroke-associated pneumonia and initiate empirical therapy

Although clinicians would consider clinical presentation and chest X-ray changes to diagnose SAP, some remarked that they can initiate empirical therapy relying on the clinical presentation alone without chest X-ray confirmation, particularly in the early evaluation of suspected pneumonia or if the patient was critically ill.

"Usually in the early stage of aspiration pneumonia, usually in the first 24 hours, X-ray is normal, so even to do an X-ray and its normal at the hypoxic patient and he is coughing, and he is respiratory compromised, then you would start antibiotics because it appears later on in the X-ray. So, in aspiration pneumonia, within the first 24 hours, an X-ray may not show anything, so we look for clinical evidence and oxygenation of the patient" (**Cl.4**).

"I initiate empirical therapy if the stroke patient was critically ill, for example, ICU patient, hypoxic had a choking episode, spiking fever, and the X-ray result was delayed, I would suspect pneumonia and start treatment" (**Cl.7**).

### Sub-theme 4: Stroke-associated pneumonia overdiagnosis

Most clinicians thought that they were overdiagnosing SAP because they typically rely on clinical symptoms than the chest X-ray finding (67%, n=8).

"I think we usually over-diagnose aspiration pneumonia post CVA because any stroke patient was choking, we assume that he developed aspiration pneumonia" (**Cl.7**).

"I think we over-diagnose it because we label someone with aspiration pneumonia if he is hypoxic post-stroke or he is febrile and related to pneumonia and especially in the ICU most of the times they have lower lobe pneumonia, and we do X-ray and we see the infiltration. Sometimes we do an ultrasound to detect the infiltration, or we do CT- scan. I think we over-diagnose because we rely on clinical symptoms more than X-ray findings" (**Cl.4**).

## Theme 2: Treatment Strategies for Stroke-Associated Pneumonia

### Sub-theme 1: Early treatment

Clinicians tend to initiate empirical treatment of SAP early to avoid poor prognosis of diseases. They may be scared of treating SAP too late if they rely on X-ray results because positive symptoms of pneumonia on chest X-ray are usually delayed in the course of diseases.

"We start treatment as early as possible because, particularly post-stroke pneumonia, it has a poor prognosis compared with the other types of pneumonia, and their outcomes are also poor compared to other pneumonia because you want to catch up with yourself" (**Cl.2**).

"As early as possible, if we are having signs and symptoms, we directly start empirical therapy" (**Cl.11**).

### Sub-theme 2: Treated as community-acquired pneumonia or hospital-acquired pneumonia

Clinicians typically treat SAP as CAP or HAP depending on the time of diagnosis, with a cut-off of 48-72 hours.

"If stroke patient admitted and developed pneumonia early, we give them respiratory fluoroquinolones as monotherapy; however, if the patients presented with pneumonia after 72 hours, in this case, we deal it as hospital-acquired pneumonia, and we think of broader spectrum such as piperacillin-tazobactam to cover anaerobes, and sometimes we add vancomycin" (**Cl.6**).

"Any patient who is admitted to the hospital and he developed evidence of pneumonia either blood test, clinically, or X-ray or oxygen, if this happens within 48 hours this is called community-acquired pneumonia regardless stroke" (**Cl.4**).

"In general, if the stroke patient was coming with pneumonia, or after a day or two he developed pneumonia, you would consider it CAP, So, you have choices levofloxacin IV, fluoroquinolones IV would do the job" (**Cl.2**).

### Sub-theme 3: Predominant anaerobes coverage

Of note is anaerobic empiric coverage was predominantly considered as a part of the treatment regimen of SAP. Some clinicians start with a broad-spectrum antibiotic like meropenem or penicillin/tazobactam. But, others prescribe metronidazole in addition to either the CAP or HAP regimen.

> "Usually, we start antibiotic that cover anaerobes, so we do not go with an antibiotic that covers community-acquired pneumonia such as cephalosporins and macrolides we go to the antibiotics that cover anaerobes such as piperacillin/tazobactam, imipenem, usually we start with these because we need anaerobic coverage if we confirm its aspiration pneumonia or even hospital-acquired pneumonia" **(Cl.4)**.

> "In aspiration pneumonia, we have to cover the anaerobes because part of the aspiration will come from the oral cavity. Really, I prescribe antibiotics covering anaerobes plus community-acquired pneumonia usually I give amoxicillin/clavulanic acid or piperacillin/tazobactam or ceftriaxone plus Flagyl®" **(Cl.7)**.

### Sub-theme 4: Stroke-associated pneumonia overtreatment

Most clinicians believed they tend to overtreat SAP in the hospital because initiating antibiotics for stroke patients could be linked to particular variables such as CRP concentration or WBC level without confirmed evidence of pneumonia.

> "We overtreat because from my practice I see patients who admitted with stroke, and they have elevated CRP they are on an empirical antibiotic without evidence of pneumonia some doctors do so" **(Cl.4)**.

> "Basically, to diagnose pneumonia, you have to see infiltration on the X-ray, but what happens is we diagnose it as aspiration pneumonia and start empirical antibiotics, and sometimes we forget to order an X-ray later on to confirm, or sometimes we could not find evidence of pneumonia on the X-ray" **(Cl.7)**.

## DISCUSSION

Variations in the approach to diagnosing and managing SAP are well-recognized in stroke research and clinical practice, which may affect clinical decision-making in the appropriate use of antibiotics [4, 21]. To our knowledge, this study is the first that directly interviewed clinicians about their experiences with the diagnostic criteria and the treatment approach of SAP in Jordan.

We found that aspiration pneumonia and HAP were the predominant labels used by clinicians for pneumonia complicating stroke. This is not consistent with the recommendations by the PISCES group in which the SAP was the preferred diagnostic terminology covering the spectrum of lower respiratory tract infections associated with stroke within the first week, with early SAP (<72 h of stroke onset) and late SAP (72 h-seven days of stroke onset). However, pneumonia that occurs after one week should be labelled as HAP [13]. Clinicians believe that having a patient admitted with a stroke and pneumonia simultaneously is unusual because most stroke patients may get pneumonia later. Moreover, those patients are predisposed to aspiration due to non-intact gag reflex. Traditionally, such pneumonia is thought to be secondary to only pulmonary aspiration [22, 23]; however, another mechanism has been suggested to the SAP pathogenesis, such as stroke-induced immunosuppression, which might pave the way for new diagnostic and treatment approaches to combat SAP by altering the immune system [24].

In our study, most residents and consultants indicated that both clinical presentation and chest X-ray changes are needed to decide on SAP diagnosis. This is consistent with the CDC criteria for 'clinically defined pneumonia', which involves a combination of clinical, laboratory, and chest radiographic evidence [14]. However, some clinicians commented on the lower sensitivity of chest X-ray to the early changes. They stated that they would start empirical therapy relying on only clinical and/or laboratory evidence (i.e., fever, leucocytosis, or CRP increase), omitting chest X-ray data. This practice is also consistent with a German study that assessed the diagnostic approach of SAP based on five case vignettes and a standardized questionnaire and found that clinicians were highly influenced by the presence of clinical indicators such as fever, CRP concentration, and the severity of the stroke, with chest X-rays being given only negligible value in the diagnosis [4]. These findings may reflect the unreliability of chest X-ray in SAP diagnosis, as seen in bedridden patients and the early evaluation of pneumonia [8]. Chest infiltrates may also occur from other causes such as atelectasis, heart failure, or pulmonary embolism, all of these factors are also increased in stroke patients. Nonetheless, in recent studies, it has been suggested that the higher sensitivity and specificity given by pulmonary ultrasound or computed tomographic (CT) imaging can significantly improve the diagnosis of SAP. Still, there is a need to evaluate the utility, timing, and cost-effectiveness of lung CT in SAP diagnosis [25-27].

Furthermore, the physicians in this study acknowledged that there is a risk of overdiagnosis and overtreatment of SAP because some clinical signs other than chest X-ray results are used. This result was in line with a previous study that compared the physicians' diagnosis with algorithmic, adjudicated diagnostic criteria for SAP and found that clinicians tend to over-diagnose SAP compared to algorithm-based approaches [16]. Overdiagnosis and overtreatment of SAP inevitably lead to serious repercussions such as excessive and unnecessary antibiotics usage in stroke patients, which often considered the main driver for bacterial resistance and also associated with and increase the economic burden on the patients [28, 29]. Clinicians are guided to treat SAP as early as possible. They might be afraid of treating SAP too late if they rely on X-ray results because positive signs of pneumonia on chest X-ray are usually delayed in the course of the disease. Although most stroke guidelines recommend early empiric treatment of infections, there is a discrepancy with guidelines for pneumonia treatment, which mandate pathological chest X-ray evidence for diagnosis [30, 31]. This was found in two recent clinical trials in which the proportion of patients getting treatment antibiotics for SAP was three times higher than the number of patients having SAP [32, 33]. Despite many patients who were misdiagnosed as SAP may actually have sepsis elsewhere, excessive use of antibiotics for patients who had a stroke not only increases the risk of bacterial resistance or Clostridium difficile infections but also the likelihood of poor 90-day outcomes and prolonged hospitalization [28, 32].

When we discussed the treatment approaches, we found that all clinicians tend to treat SAP either as for CAP or HAP based on the time of diagnosis with cut off 24-72 hr, but the anaerobic coverage was predominantly considered in the treatment regimens. Some clinicians initiate with broad-spectrum antibiotics such as meropenem or penicillin/tazobactam as empirical therapy for SAP; however, others prescribe metronidazole in addition to either CAP or HAP regimen. This is not consistent with PISCES recommendations for antibiotic treatment of SAP, which concluded that treatment for early SAP should cover CAP microorganisms, and for late SAP should cover CAP microorganisms + coliforms /pseudomonas spp; however, treatment of non SAP (pneumonia that develops after seven days of stroke onset) should follow HAP guidelines [15]. The widespread use of antibiotics with anaerobic coverage in our study could be because clinicians suspect aspiration in stroke patients and prescribe anti-anaerobes based on previous recommendations. However, although anaerobic organisms were isolated at significant rates in earlier studies of patients with aspiration pneumonia, more recent studies, have not found that anaerobes play a major role in its aetiology. Therefore, adding anaerobic coverage might cause harm without adding benefit [34, 35]. Recently, the American Thoracic Society and Infectious Diseases Society of America guidelines are against the use of empiric anaerobic coverage for aspiration pneumonia unless lung abscess or empyema is suspected [12]. Additionally, recommendations from the PISCES group suggest not routinely adding anaerobic coverage for SAP patients with suspected aspiration or dysphagia [15].

As a general limitation of the qualitative research, these findings may not be generalized to non-tertiary care hospitals as the practice may differ. While the study was limited to a specific hospital in Jordan, the tertiary care hospital setting is consistent throughout the country. It hence may be transferred to other tertiary care hospitals. Though the sample size was small, it was guided by data saturation and the non-emergence of new themes.

## CONCLUSIONS

This study gains valuable insight into clinicians' experiences with the diagnostic criteria and the treatment approach to SAP in Jordan. Although clinical evidence and X-ray findings were needed for deciding on SAP diagnosis, empirical therapy would be started without X-ray confirmation. Clinicians tend to treat SAP either as for CAP or HAP based on the time of diagnosis; however, anaerobic coverage was predominantly considered in the treatment regimens. Our research reveals a wide range of clinicians-based diagnostic and treatment approaches for SAP. Standard, validated algorithmic-based criteria are needed to be implemented because they could significantly impact antibiotic stewardship, decrease antibiotic and healthcare costs, and antibacterial resistance.

## REFERENCES

1. Wilson RD. Mortality and cost of pneumonia after stroke for different risk groups. J Stroke Cerebrovasc Dis. 2012;21(1):61-7. https://doi.org/10.1016/j.jstrokecerebrovasdis.2010.05.002 PMid:22225864 PMCid:PMC3255072

2. Kumar S, Selim MH, Caplan LR. Medical complications after stroke. Lancet Neurol. 2010;9(1):105-18. https://doi.org/10.1016/S1474-4422(09)70266-2 PMid:20083041

3. Kalra L, Hodsoll J, Irshad S, Smithard D, Manawadu D. Association between nasogastric tubes, pneumonia, and clinical outcomes in acute stroke patients. Neurology. 2016;87(13):1352-9. https://doi.org/10.1212/WNL.0000000000003151 PMid:27566745 PMCid:PMC5047037

4. Harms H, Hoffmann S, Malzahn U, Ohlraun S, Heuschmann P, Meisel A. Decision-making in the diagnosis and treatment of stroke-associated pneumonia. J Neurol Neurosurg Psychiatry. 2012;83(12):1225-30. https://doi.org/10.1136/jnnp-2012-302194 PMid:23024353

5. Ward K, Seymour J, Steier J, et al. Acute ischaemic hemispheric stroke is associated with impairment of reflex in addition to voluntary cough. Eur Respir J. 2010;36(6):1383-90. https://doi.org/10.1183/09031936.00010510 PMid:20413536

6. Emsley HCA, Smith CJ, Gavin CM, et al. An early and sustained peripheral inflammatory response in acute ischaemic stroke: relationships with infection and atherosclerosis. J Neuroimmunol. 2003;139(1-2):93-101. https://doi.org/10.1016/S0165-5728(03)00134-6 PMid:12799026

7. Ferdinand P, Roffe C. Hypoxia after stroke: A review of experimental and clinical evidence. Exp Transl Stroke Med. 2016;8:9. https://doi.org/10.1186/s13231-016-0023-0 PMid:27980710 PMCid:PMC5143450

8. Esayag Y, Nikitin I, Bar-Ziv J, et al. Diagnostic value of chest radiographs in bedridden patients suspected of having pneumonia. Am J Med. 2010;123(1):88.e1-5. https://doi.org/10.1016/j.amjmed.2009.09.012 PMid:20102999

9. Cohen E, Mier A, Heywood P, Murphy K, Boultbee J, Guz A. Diaphragmatic movement in hemiplegic patients measured by ultrasonography. Thorax. 1994;49(9):890-5. https://doi.org/10.1136/thx.49.9.890 PMid:7940429 PMCid:PMC475186

10. Kishore AK, Vail A, Jeans AR, et al. Microbiological etiologies of pneumonia complicating stroke: A systematic review. Stroke. 2018;49(7):1602-9. https://doi.org/10.1161/STROKEAHA.117.020250 PMid:29915122

11. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61-111.

12. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200(7):e45-67. https://doi.org/10.1164/rccm.201908-1581ST PMid: 31573350 PMCid:PMC6812437

13. Smith CJ, Kishore AK, Vail A, et al. Diagnosis of stroke-associated pneumonia: Recommendations from the pneumonia in stroke consensus group. Stroke. 2015;46(8):2335-40. https://doi.org/10.1161/STROKEAHA.115.009617 PMid:26111886

14. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36(5):309-32. https://doi.org/10.1016/j.ajic.2008.03.002 PMid:18538699

15. Kishore AK, Jeans AR, Garau J, et al. Antibiotic treatment for pneumonia complicating stroke: Recommendations from the pneumonia in stroke consensus (PISCES) group. Eur Stroke J. 2019;4(4):318-28. https://doi.org/10.1177/2396987319851335 PMid:31903430 PMCid:PMC6921946

16. Kalra L, Hodsoll J, Irshad S, Smithard D, Manawadu D. Comparison of the diagnostic utility of physician-diagnosed with algorithm-defined stroke-associated pneumonia. J Neurol Neurosurg Psychiatry. 2016;87(11):1163-8. https://doi.org/10.1136/jnnp-2016-313508 PMid:27432801

17. Smith F. Health services research methods in pharmacy: Qualitative interviews. Int J Pharm Pract. 1998;6(2):97-108. https://doi.org/10.1111/j.2042-7174.1998.tb00923.x

18. Kuper A, Reeves S, Levinson W. An introduction to reading and appraising qualitative research. BMJ. 2008;337:a288. https://doi.org/10.1136/bmj.a288 PMid:18687727

19. WHO. Process of translation and adaptation of instruments. World Health Organization. 2009. Available at: http://www.who.int/substance_abuse/research_tools/translation/en/ (Accessed: 23 November 2022).

20. Ritchie J, Lewis J, Nicholls CM, Ormston R. Qualitative research practice: A guide for social science students and researchers. Thousand Oaks, CA: SAGE; 2013.

21. Kishore AK, Vail A, Chamorro A, et al. How is pneumonia diagnosed in clinical stroke research? A systematic review and meta-analysis. Stroke. 2015;46(5):1202-9. https://doi.org/10.1161/STROKEAHA.114.007843 PMid:25858238

22. Huang JY, Zhang DY, Yao Y, Xia QX, Fan QQ. Training in swallowing prevents aspiration pneumonia in stroke patients with dysphagia. J Int Med Res. 2006;34(3):303-6. https://doi.org/10.1177/147323000603400310 PMid:16866025

23. Hannawi Y, Hannawi B, Rao CPV, Suarez JI, Bershad EM. Stroke-associated pneumonia: major advances and obstacles. Cerebrovasc Dis. 2013;35(5):430-43. https://doi.org/10.1159/000350199 PMid:23735757

24. Liu D-D, Chu S-F, Chen C, Yang P-F, Chen N-H, He X. Research progress in stroke-induced immunodepression syndrome (SIDS) and stroke-associated pneumonia (SAP). Neurochem Int. 2018;114:42-54. https://doi.org/10.1016/j.neuint.2018.01.002 PMid:29317279

25. Busti C, Agnelli G, Duranti M, Orlandi C, Marcucci M, Paciaroni M. Lung ultrasound in the diagnosis of stroke-associated pneumonia. Intern Emerg Med. 2014;9(2):173-8. https://doi.org/10.1007/s11739-012-0832-7 PMid:22847729

26. Garin N, Marti C, Carballo S, et al. Rational use of CT-scan for the diagnosis of pneumonia: Comparative accuracy of different strategies. J Clin Med. 2019;8(4):514. https://doi.org/10.3390/jcm8040514 PMid:30991716 PMCid:PMC6518125

27. Kishore AK, Devaraj A, Vail A, et al. Use of pulmonary computed tomography for evaluating suspected stroke-associated pneumonia. J Stroke Cerebrovasc Dis. 2021;30(6):105757. https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105757 PMid:33873077

28. Srinivasan A. Engaging hospitalists in antimicrobial stewardship: the CDC perspective. J Hosp Med. 2011;6(Suppl 1):S31-3. https://doi.org/10.1002/jhm.863 PMid:21225948

29. Cordoba G, Llor C. Overdiagnosis paradigm: not suitable for decreasing the overuse of antibiotics. BMJ Evid Based Med. 2019;24(5):174-6. https://doi.org/10.1136/bmjebm-2018-111146 PMid:30745411 PMCid:PMC6837244

30. NICE Guidelines. Pneumonia: Diagnosis and management of community- and hospital-acquired pneumonia in adults. NICE. 2014. Available at: http://www.nice.org.uk/%0Aguidance/cg191/chapter/1-Recommendations#community-acquired-pneumonia (Accessed: 23 November 2022).

31. National Collaborating Centre for Chronic Conditions (UK). Stroke: National clinical guideline for diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). London: Royal College of Physicians (UK); 2008. PMID:21698846

32. Kalra L, Irshad S, Hodsoll J, et al. Prophylactic antibiotics after acute stroke for reducing pneumonia in patients with dysphagia (STROKE-INF): A prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial. Lancet. 2015;386(10006):1835-44. https://doi.org/10.1016/S0140-6736(15)00126-9 PMid:26343840

33. Westendorp WF, Vermeij J-D, Zock E, et al. The preventive antibiotics in stroke study (PASS): A pragmatic randomised open-label masked endpoint clinical trial. Lancet. 2015;385(9977):1519-26. https://doi.org/10.1016/S0140-6736(14)62456-9 PMid:25612858

34. Marik PE, Careau P. The role of anaerobes in patients with ventilator-associated pneumonia and aspiration pneumonia: A prospective study. Chest. 1999;115(1):178-83. https://doi.org/10.1378/chest.115.1.178 PMid:9925081

35. El-Solh AA, Pietrantoni C, Bhat A, et al. Microbiology of severe aspiration pneumonia in institutionalized elderly. Am J Respir Crit Care Med. 2003;167(12):1650-4. https://doi.org/10.1164/rccm.200212-1543OC PMid: 12689848

## APPENDIX A: QUESTIONS GUIDE

### General

- Speciality: _____
- Years in practice: _____
- Gender: _____
- What do you call the pneumonia that may occur after stroke admission?
- Does this term could be changed by the time of pneumonia after hospitalization? If so, how?

### Diagnosis of Stroke-Associated Pneumonia

1. What are diagnostic indicators to determine whether the patient has SAP?
2. Does X-ray changes necessary to confirm and start therapy? Why?
3. Do you think we are over-diagnosing or under diagnosing SAP? Why?
4. What are the challenges to SAP diagnosis? How are these challenges handled in practice?
5. Do you feel comfortable dealing with SAP diagnosis? Why or why not?
6. Are you familiar with the so-called CDC criteria for **diagnosis of SAP**? If yes, what is your personal evaluation of their clinical relevance? High, moderate, low irrelevant.
7. Are you familiar with the recommendations from pneumonia in stroke consensus (PISCES) group for **diagnosis/treatment** of SAP? If yes, what is your personal evaluation of their clinical relevance? High, moderate, low irrelevant.

### Treatment and Therapeutic Procedure

1. How do you initiate empirical therapy? Can you give me an algorithm? Class, mono, combinations, rout of administration?
2. Does the choice of empirical therapy could be influenced by the time of SAP after hospitalization? If so, how?
3. Do you think we over-treat or under-treat for SAP? Why?
4. Do you feel comfortable dealing with SAP treatment? Why or why not?
5. What are the barriers/challenges to SAP treatment?

# APPENDIX B

**Table B1.** Main themes and sub-themes from the interviews and examples of representative quotations

| Theme | Sub-theme | Representative quotations |
|---|---|---|
| Terminology & diagnostic approach of SAP | No definite terminology | *"This type we call it aspiration pneumonia, this that occur after CVA, because the patient could not swallow, or the patient was not evaluated well by the doctor if he can swallow or not, so they may be choked and cause aspiration so this type we call it aspiration pneumonia" (Cl.7).*<br>*"In stroke patients, we call it hospital-acquired pneumonia after the patient is hospitalized and it occurred within 48hours, but if there are episodes of aspiration you can't call it hospital-acquired because you have an event of aspiration whether it happened in the first day or after a week and we witnessed aspiration so its aspiration at the end" (Cl.10).*<br>*"… so mostly pneumonia in stroke patients is aspiration pneumonia. Unless the patient was on a ventilator, they may develop ventilator-associated pneumonia" (Cl.3).* |
| | Reliance on both clinical evidence & chest X-ray findings to decide | *"In general, the diagnosis of such pneumonia is a new X-ray infiltrate associated with respiratory symptoms" (Cl.2).*<br>*"Usually, we diagnose pneumonia if there is Fever, cough, sputum, WBC increase, maybe unconsciousness, sometimes hypotension, and new infiltration in the chest X-ray" (Cl.10).*<br>*"… you have the whole clinical scenario, history, physical examination, parameters like vital signs, images chest X-ray for example, lab tests inflammatory markers, elevated CRP, elevated WBCs" (Cl.12).* |
| | Reliance on clinical evidence alone to suspect SAP & initiate empirical therapy | *"Usually in the early stage of aspiration pneumonia, pneumonia that may occur for a stroke patient with a low level of consciousness, usually in the first 24 hours, X-ray is normal So, even to do an X-ray and its normal at the hypoxic patient and he is coughing, and he is respiratory compromised, then you would start antibiotics because it appears later on in the X-ray. So, in aspiration pneumonia, the first 24 hours, an X-ray may does not show anything, so we look for clinical evidence and oxygenation of the patient" (Cl.4).*<br>*"For me, honestly, if there was no X-ray, and the clinical presentation of the patient was very suggestive that they are aspirated, and with clinical examination, we found something in the chest, and the patient became febrile, producing sputum, I may deal with him as a case of aspiration pneumonia, and start therapy" (Cl.3).*<br>*"I initiate empirical therapy if the patient was critically ill, for example, ICU stroke patient, hypoxic had a choking episode, spiking fever, and the X-ray result was delayed, I would suspect pneumonia and start treatment" (Cl.7).* |
| | SAP overdiagnosis | *"I think we usually over-diagnose aspiration pneumonia post CVA because any stroke patient was choking, we assume that he developed aspiration pneumonia. Basically, to diagnose pneumonia you have to see infiltration on the X-ray, but what happens is we diagnose it as aspiration pneumonia and start empirical antibiotics, and sometimes we forget to order an X-ray later on to confirm, or sometimes we couldn't find evidence of pneumonia on the X-ray" (Cl.7).*<br>*"I think we over-diagnose maybe, as we said some stroke patients may stay for long in the hospital and develop hospital-acquired pneumonia and the patient is not aspirated. They have not aspirated from the stroke itself it's due to a hospital stay that pneumonia happened, but we usually attribute pneumonia that occurs during a stroke to an aspiration that's what I usually see" (Cl.3).*<br>*"I think we over because we label someone with aspiration pneumonia if he is hypoxic post-stroke or he is febrile and related to pneumonia and especially in the ICU most of the times they have lower lobe pneumonia, and we do X-ray and we see the infiltration. Sometimes we do an ultrasound to detect the infiltration, or we do CT- scan. I think we over-diagnose because we rely on clinical symptoms more than X-ray findings" (Cl.4).* |
| Treatment strategies for SAP | Early treatment | *"We start treatment as early as possible because, particularly post-stroke pneumonia, it has a poor prognosis compared with the other types of pneumonia, and their outcomes are also poor compared to other pneumonia because you want to catch up with yourself" (Cl.5).*<br>*"As early as possible, if we are having signs and symptoms, we directly start empirical therapy" (Cl.11).*<br>*"… immediately, as soon as possible, I think there is evidence that if the patients admitted with pneumonia and you delayed the treatment for more than six hours this increases mortality, so within four to six hours after diagnosis the patient should receive the antibiotic" (Cl.1).* |
| | Treated as CAP/HAP | *"If stroke patient admitted and developed pneumonia early, we give them respiratory fluoroquinolones as monotherapy, however, if the patients presented with pneumonia after 72 hours, in this case, we deal it as hospital-acquired pneumonia and we think of broader spectrum such as piperacillin-tazobactam to cover anaerobes and sometimes we add vancomycin" (Cl.6).*<br>*"… so, after 72 hours if the patient developed pneumonia, I call it hospital-acquired pneumonia, so in this case, you have to give broader spectrum antibiotics and cover anaerobes and may add vancomycin if needed" (Cl.7).*<br>*"Any patient who is admitted to the hospital and he developed evidence of pneumonia either blood test, clinically, or X-ray or oxygen, if this happens within 48 hours this is called community-acquired pneumonia regardless stroke" (Cl.4).*<br>*"In general, if the stroke patient was coming with pneumonia, or after a day or two he developed pneumonia, you would consider it CAP, So, you have choices levofloxacin IV, fluoroquinolones IV would do the job" (Cl.2).* |

**Table B1 (Continued).** Main themes and sub-themes from the interviews and examples of representative quotations

| Theme | Sub-theme | Representative quotations |
|---|---|---|
| | Predominant anaerobes coverage | *"Usually, we start antibiotic that cover anaerobes, so we don't go with an antibiotic that covers community-acquired pneumonia such as cephalosporins and macrolides we go to the antibiotics that cover anaerobes such as piperacillin/tazobactam, imipenem, usually we start with these because we need anaerobic coverage if we confirm its aspiration pneumonia or even hospital-acquired pneumonia" (Cl.4).*<br>*"… in stroke patients, we should cover anaerobes even its community-acquired we don't use empirical for community-acquired we add anaerobic coverage" (Cl.12).*<br>*"In aspiration pneumonia, we have to cover the anaerobes because part of the aspiration will come from the oral cavity. Really, I prescribe antibiotics covering anaerobes plus community-acquired pneumonia usually I give amoxicillin/clavulanic acid or piperacillin/tazobactam or ceftriaxone plus Flagyl®" (Cl.7).* |
| Treatment strategies for SAP | SAP overtreatment | *"We overtreat because from my practice I see patients who admitted with stroke, and they have elevated CRP they are on an empirical antibiotic without evidence of pneumonia some doctors do so" (Cl.4).*<br>*"… so, I think we overtreat because sometimes we start empirical antibiotic if just elevated CRP or elevated WBC without localizing the infection" (Cl.9).*<br>*"I think we may over-treat a little a lot of doctors who give a mix of antibiotics from the beginning. you can sometimes use one antibiotic and wait for the response, but some doctors use a lot of antibiotics with a weird regimen to hit hard from the beginning" (Cl.3).*<br>*"I think we over treat, sometimes if you have a regular a neuro rotation and you have a lot of patients plus shifts so sometimes you just leave the patients on IV antibiotics" (Cl.2).*<br>*"Basically, to diagnose pneumonia you have to see infiltration on the X-ray, but what happens is we diagnose it as aspiration pneumonia and start empirical antibiotics, and sometimes we forget to order an X-ray later on to confirm, or sometimes we couldn't find evidence of pneumonia on the X-ray" (Cl.7).* |