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Clinical Manifestations and Risk Factors Analysis of Adverse Reactions in Syphilis Patients After Lumbar Puncture

Junjun Yu¹, Yanting Wang¹, Xiluo Xu¹, Fuquan Long^{1,*}, Lin Zhu^{1,*}¹Department of Sexually Transmitted Diseases, Shanghai Skin Disease Hospital, Tongji University School of Medicine, 200433 Shanghai, China*Correspondence: longfuquan@163.com (Fuquan Long); 17301809750@163.com (Lin Zhu)

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Abstract

Aims/Background: Cerebrospinal fluid (CSF) is a crucial type of biological specimen for neurosyphilis diagnosis. This study aims to comprehensively analyse the clinical manifestations and risk factors of adverse reactions in syphilis patients following lumbar puncture (LP). **Methods:** A total of 573 syphilis patients who underwent LP examinations between August 2023 and April 2024 at the Department of Sexually Transmitted Diseases, Shanghai Skin Disease Hospital, were selected. The clinical manifestations, onset timing, risk factors, and duration of relief from adverse reactions in these patients undergoing LP were statistically analysed. **Results:** Among 573 patients diagnosed with syphilis, 142 patients (24.8%) experienced adverse reactions following LP. Factors such as age, needle size, symptoms of paralysis, and the duration of postoperative bed rest were significantly associated with adverse reactions after LP ($p < 0.05$). Furthermore, age > 30 years, the use of a 20G needle, and paralysis symptoms were identified as independent protective factors ($p < 0.05$), whereas bed rest duration > 6 hours contributed to increased risk for adverse reactions (odds ratio [OR] = 3.544, $p = 0.010$). The average onset time for adverse reactions following LP was 14.34 ± 1.54 hours, while the average duration for resolution of these reactions was 5.52 ± 0.26 days postoperatively. **Conclusion:** The high incidence of adverse reactions following LP in patients with syphilis poses challenges to restoring quality of life among affected patients. A thorough assessment of risk factors for adverse reactions could inform the selection of appropriate measures to mitigate the occurrence of such reactions.

Keywords: syphilis; spinal puncture; postoperative complications; risk factors

1. Introduction

Syphilis is a chronic sexually transmitted disease caused by an infection with *Treponema pallidum*. Neurosyphilis is an irreversible disease caused by the invasion of *Treponema pallidum* into the central nervous system, leading to brain parenchyma destruction and central nervous system impairment [1,2]. Lumbar puncture (LP) remains the gold-standard diagnostic procedure for neurosyphilis. However, post-LP adverse reactions, particularly post-dural puncture headache (PDPH), remain a significant clinical challenge across various populations, with reported incidence rates ranging from 10% to 40% [3,4].

At present, the risk factors for post-LP adverse reactions remain undetermined in existing literature. Among the key determinants for the post-LP adverse reactions that have been investigated are needle size [5,6], patient positioning [7,8], body mass index (BMI) [5,9,10], and fluid replacement volume [11]. Notably, there is limited data specifically addressing syphilis patients, who may present unique characteristics due to potential central nervous system involvement. Given this knowledge gap, the current study aims to systematically evaluate the incidence, clinical manifestations, and risk factors of post-LP adverse reactions in syphilis patients.

2. Methods

2.1 Study Design

This retrospective cohort study analysed data from 573 syphilis patients undergoing diagnostic LP at the Department of Sexually Transmitted Diseases, Shanghai Skin Disease Hospital, between August 2023 and April 2024. Clinical basic data of patients were collected with Hospital Information System (HIS) and Nursing Information System (NIS), including gender, age, height, weight, bed number, hospital number, name, admission diagnosis, and BMI [12].

2.2 Inclusion and Exclusion Criteria

The inclusion criteria are as follows: (i) syphilis patients undergoing LP examination; (ii) patients or their family members who provided informed consent; (iii) patients who were conscious and capable of conducting normal communication and (iv) patients with no history of chronic headaches (to avoid confounding with pre-existing headache conditions). Exclusion criteria of this study include: (i) incomplete clinical data; (ii) malignant tumours; (iii) contraindications for LP and (iv) age < 18 years. This study has been approved by the Ethics Committee of Shanghai Skin Disease Hospital (approval number: 2024-37).



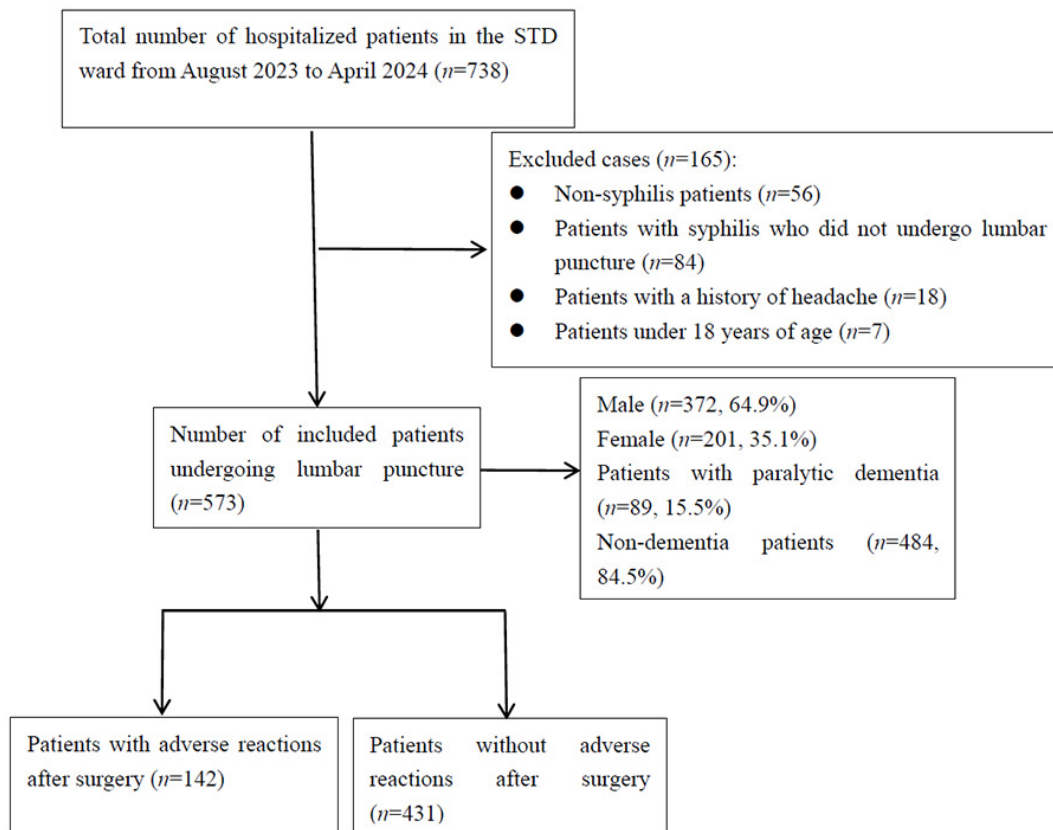


Fig. 1. Flowchart depicting selection and inclusion of syphilis patients undergoing lumbar puncture. STD, Sexually Transmitted Diseases.

Table 1. Clinical manifestations of syphilis patients undergoing lumbar puncture (n = 142).

Clinical manifestation	n	%
Headache/Dizziness	55	38.7
Isolated back pain	54	38.0
Nausea/Vomiting	4	2.8
Headache/Dizziness + Nausea/Vomiting	15	10.6
Headache/Dizziness + Back pain	13	9.2
Multisystem involvement*	1	0.7

Note: *Clinical manifestations with multisystem involvement include headache/dizziness, nausea/vomiting, and back pain.

2.3 Standardised LP Procedure

All procedures were performed by experienced clinicians following a standardised protocol: patients in the lateral decubitus position with flexed knees, and LP was performed at the L4–L5 interspace under strict aseptic technique using either 20G (0.9 mm) or 18G (1.2 mm) needles.

2.4 Outcome Measurement

Adverse reactions are defined as any new-onset symptoms within 96 hours post-LP, including headache, dizziness, nausea, vomiting, or back pain, as documented in medical records or reported during follow-up calls at 24 hours, 48 hours, and 7 days post-LP. Symptom severity was graded as mild (not interfering with daily activities), mod-

erate (limiting but not preventing activities), or severe (requiring bed rest).

2.5 Statistical Analysis

Continuous variables are presented as mean \pm standard deviation, whereas categorical variables are expressed as counts (percentages). Statistically significant variables ($p < 0.05$) in the univariate analysis (chi-square or Fisher's exact tests) were analysed in the multivariate binary logistic regression. Age and bed rest time were analysed as categorical variables with dummy coding. All analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA), with two-tailed $p < 0.05$ considered significant.

Table 2. Univariate analysis of factors associated with post-lumbar puncture adverse reactions (n = 573).

Variable	Category	Without adverse reactions (n = 431)	With adverse reactions (n = 142)	χ^2 statistic	p-value
Demographics					
Gender	Male	288 (66.8%)	84 (59.2%)	2.757	0.097
	Female	143 (33.2%)	58 (40.8%)		
Procedural factors					
Needle gauge	20G (0.9 mm)	274 (63.6%)	74 (52.1%)	5.882	0.015*
	18G (1.2 mm)	157 (36.4%)	68 (47.9%)		
First ambulation time	0–2 hours	8 (1.9%)	9 (6.4%)	33.842	<0.001*
	2–4 hours	22 (5.1%)	22 (15.5%)		
	4–6 hours	391 (90.7%)	101 (71.1%)		
	>6 hours	10 (2.3%)	10 (7.0%)		
Clinical factors					
Diagnosis at admission	Non-dementia**	349 (81.0%)	135 (95.1%)	16.176	<0.001*
	Dementia***	82 (19.0%)	7 (4.9%)		
Age group (years)	≤30	35 (8.1%)	23 (16.2%)	18.713	<0.001*
	31–59	166 (38.5%)	71 (50.0%)		
	≥60	230 (53.4%)	48 (33.8%)		
BMI category (kg/m ²)	Underweight (<18.5)	17 (3.9%)	9 (6.4%)	2.075	0.354
	Normal (18.5–23.9)	226 (52.5%)	78 (54.9%)		
	Overweight (≥24)	188 (43.6%)	55 (38.7%)		
Fluid intake					
24-hour volume (mL)	≤500	262 (60.8%)	78 (54.9%)	1.520	0.218
	>500	169 (39.2%)	64 (45.1%)		
Substance use					
Smoking status	Yes	90 (20.9%)	31 (21.8%)	0.058	0.810
	No	341 (79.1%)	111 (78.2%)		
Alcohol consumption	Yes	96 (22.3%)	37 (26.1%)	0.857	0.355
	No	335 (77.7%)	105 (73.9%)		
Education					
Highest level attained	Below college	229 (53.1%)	72 (50.7%)	0.253	0.615
	College or above	202 (46.9%)	70 (49.3%)		
Postoperative care					
Prolonged standing (>2 hours within 24 hours post-operation)	Yes	207 (48.0%)	75 (52.8%)	0.980	0.322
	No	224 (52.0%)	67 (47.2%)		

Note: *Statistically significant ($p < 0.05$); **Non-dementia refers to all syphilis patients who have undergone lumbar puncture but do not fulfill the diagnostic criteria for paralytic dementia; ***Dementia refers to all syphilis patients with symptoms of paralytic dementia. BMI, body mass index.

3. Results

3.1 Patient Characteristics and Adverse Reaction Incidence

Among 573 patients (372 males, 201 females; mean age 55.4 ± 15.8 years), 142 (24.8%) developed adverse reactions. The cohort included 89 patients (15.5%) with paralytic dementia and 484 (84.5%) without. The patient enrollment flow chart is shown in Fig. 1.

3.2 Clinical Manifestations

The most common adverse reactions were isolated headache/dizziness (38.7%) and isolated back pain (38.0%), nausea/vomiting (2.8%), headache/dizziness with nausea/vomiting (10.6%), headache/dizziness with back pain (9.2%), and multisystem involvement (0.7%) (Table 1).

3.3 Univariate Analysis of Adverse Reactions after Lumbar Puncture

The results of the univariate analysis of adverse reactions after LP in 573 syphilis patients showed that age, needle type, symptoms of paralytic dementia, and postoperative bed rest time were significant influencing factors for adverse reactions after the operation ($p < 0.05$) (Table 2). Gender and BMI did not have any significant impacts on the occurrence of adverse reactions after the operation ($p > 0.05$). 24-hour volume, smoking status, alcohol consumption, education, and prolonged standing (>2 hours within 24 hours post-operation) did not have any significant impacts on the occurrence of adverse reactions after the operation ($p > 0.05$).

3.4 Risk Factor Analysis

According to the multivariate analysis results (Table 3), the risk for adverse reactions was significantly lower in those within the age groups of 31–59 years (odds ratio [OR]: 0.351, 95% confidence interval [CI]: 0.184–0.669, $p = 0.001$) and ≥ 60 years (OR: 0.521, 95% CI: 0.334–0.812, $p = 0.004$), as well as patients with an admission diagnosis of paralytic dementia (OR: 0.212, 95% CI: 0.09–0.50, $p < 0.001$), as compared to their respective reference groups. The risk was significantly increased in patients using 18G needles (OR: 1.634, 95% CI: 1.084–2.461, $p = 0.019$) and those having >6 hours of bed rest (OR: 3.544, 95% CI: 1.360–9.239, $p = 0.010$).

3.5 Temporal Characteristics

Among the 142 syphilis patients who had received LP, the shortest time to onset of adverse reactions was 1 hour post-operation, while the longest was 96 hours post-operation, with an average onset time of 14.34 ± 1.54 hours. The duration of relief from adverse reactions ranged from 1 day to 16 days, with an average duration of 5.52 ± 0.26 days (Table 4).

4. Discussion

LP is an essential diagnostic tool for neurological diseases, with primary diagnostic indications including infectious diseases, inflammation, and related conditions affecting the central nervous system [13,14]. In our department, syphilis patients constitute 95% of the inpatients, and thus, LP stands as an essential approach to distinguishing patients with syphilis from those with neurosyphilis. PDPH is a widely recognised common complication after LP, with symptoms including neck stiffness, lower back soreness, nausea, vomiting, as well as ear and eye symptoms [15]. PDPH is a typical positional headache that worsens when the patient is upright and improves or resolves when lying flat, typically lasting for several days with severity ranging from mild to debilitating; in severe cases, medical intervention may be required [16–18]. Post-procedural lower back soreness and pain refer to pain around the puncture site in the spine [19]. According to several studies, the occurrence rates of PDPH range from 3% to 30% [11,20]. Meanwhile, our research findings indicate that 24.8% of syphilis patients experienced adverse reactions following an LP, with headache/dizziness being the most common adverse reaction, occurring in 59.2% of cases, followed by back pain noted in 47.9% of the cases.

Our research results indicated that the thickness of the puncture needle influences the occurrence of post-LP adverse reactions. Specifically, the use of an 18G puncture needle (1.2 mm) relative to a 20G needle (0.9 mm) increased the risk of post-procedural adverse reactions, consistent with the findings of Azzi *et al.* [3] and Destrebecq *et al.* [21], who recommended that smaller needles could significantly reduce the incidence of PDPH. This may be attributed to reduced dural trauma associated with a smaller skin puncture created by a finer needle [22–24], which can result in slower cerebrospinal fluid outflow during the procedure and a lower risk of post-procedural leakage at the puncture site. Therefore, smaller-gauge needles are recommended for use during the LP procedures in order to reduce the occurrence of adverse reactions in patients.

This study demonstrated that the likelihood of adverse reactions following LP decreased with advancing age. This finding contrasts with several previous reports indicating a lower rate of PDPH in patients with cognitive impairment and a higher incidence of post-procedural adverse reactions in younger populations—patterns that align with the observed rarity of such reactions in both infants and the elderly [25–27]. This trend may be attributed to the decline in cognitive impairment or the gradual onset of brain atrophy with advancing age. Additionally, it has been reported that older age acts as a protective factor against post-LP headaches [11,28,29].

Patients with paralytic dementia exhibit abnormal mental and behavioural symptoms, such as lack of concentration, forgetfulness, reduced judgment and memory, cognitive impairment, dementia, mood swings, depression,

Table 3. Multivariable binary logistic regression analysis of factors associated with post-lumbar puncture adverse reactions (n = 573).

Factor	β (SE)	Wald χ^2	p-value	Adjusted OR (95% CI)
Age group (years)		13.258	<0.001*	
≤30 (reference)	-	-	-	1.00
31–59	–1.048 (0.330)	10.088	0.001*	0.351 (0.184–0.669)
≥60	–0.653 (0.227)	8.294	0.004*	0.521 (0.334–0.812)
Diagnosis at admission				
Non-dementia (reference)	-	-	-	1.00
Dementia	–1.549 (0.437)	12.573	<0.001*	0.212 (0.090–0.500)
Needle gauge				
20G (reference)	-	-	-	1.00
18G	0.491 (0.209)	5.507	0.019*	1.634 (1.084–2.461)
First ambulation time (hours)		31.486	<0.001*	
0–2 (reference)	-	-	-	1.00
2–4	–0.587 (0.722)	0.662	0.416	0.556 (0.135–2.287)
4–6	–0.173 (0.574)	0.090	0.764	0.841 (0.273–2.593)
>6	1.265 (0.489)	6.701	0.010*	3.544 (1.360–9.239)

Note: *Statistically significant ($p < 0.05$). OR, odds ratio; CI, confidence interval; SE, standard error.

Table 4. Temporal characteristics of post-lumbar puncture adverse reactions (n = 142).

Parameter	Minimum	Maximum	Mean ± SD
Time to adverse reaction onset (hours)	1	96	14.34 ± 1.54
Duration of adverse reaction relief (days)	1	16	5.52 ± 0.26

Note: SD, standard deviation.

personality changes, delusions, mania, or psychosis [2,30]. The results of this study indicate that symptoms of paralytic dementia act as a protective factor against adverse reactions after LP. El-Mallakh *et al.* [31] reported that post-LP headaches are less frequent and severe in patients with schizophrenia compared to normal individuals, due to the reduced pain perception in mentally ill patients (i.e., higher pain threshold) [32] and decreased ability to verbally express pain (i.e., reduced tendency to complain) [33]. This aligns with our research findings, although the exact mechanisms remain unclear.

In the current clinical practice, patients are typically advised to lie flat without a pillow for 4–6 hours after LP for the reason of reducing the risk of adverse reactions. However, our study found that bed rest exceeding 6 hours was associated with an increased incidence of postoperative adverse reactions.

The adverse reaction may arise from prolonged immobilisation, coupled with anxiety toward postoperative complications, which eventually causes sleep disruptions. Extended bed rest can also lead to muscle tension, hindering relaxation and resulting in lower back pain and soreness. Furthermore, patients who remain supine without pillows for more than 6 hours typically exhibit decreased water intake compared to their more active counterparts, and the production rate of cerebrospinal fluid is also diminished. In contrast to other studies, our findings suggest that post-LP bed rest, regardless of the duration, does not

contribute to lowered incidence of PDPH [34,35]. Specifically, our results contradict the findings of Zhang [36], which indicate that haematology patients who took rest for ≤2 hours after LP are more likely to experience post-procedural headaches, which can be caused by the higher volume of cerebrospinal fluid collected during diagnostic LP in syphilis patients.

There are several limitations in this study. Firstly, this was a single-center study with a small sample size; therefore, additional multi-center studies with larger cohorts are needed in the future. In addition, several critical variables, such as syphilis stage, patient complications, disease course, and type of treatment, were not considered in our analysis, and it is currently unknown if the collection speed of cerebrospinal fluid during LP would affect the incidence of postoperative complications. Therefore, an in-depth study of the above-mentioned factors is warranted in the future.

5. Conclusion

Our study provides several novel insights into post-LP adverse reactions, which impact approximately one-quarter (24.8%) of syphilis patients. These reactions primarily manifest as headache/dizziness (59.2%) or back pain (47.9%), possibly indicating unique pathophysiological changes in the meninges of syphilis patients. The use of small-gauge needles (20G), age >30 years, paralytic de-

mentia, and a bed rest period <6 hours are protective factors in the context of adverse reactions affecting syphilis patients after receiving LP. These findings highlight the need for personalised post-LP management in specific patient populations. Healthcare providers should apply evidence-based practices while remaining vigilant for individual patient variations.

Key Points

- The incidence of adverse reactions after lumbar puncture in patients with syphilis was as high as 24.8%, with headache/dizziness (59.2%) and back pain (47.9%) being the most common adverse reactions.
- Key factors that contribute to reduced incidence of these adverse reactions include the use of small-gauge needles (20G), age >30 years, paralytic dementia, and a bed rest period <6 hours.
- The risk factors identified in this study form the clinical basis for assessing patients who may be susceptible to adverse reactions and implementing measures to minimise their occurrence, thereby enhancing clinical practice.

Availability of Data and Materials

The datasets generated during and/or analysed during the current study are available from the corresponding authors upon reasonable request.

Author Contributions

Conceptualization: JY, LZ, YW, FL; Methodology: LZ, FL; Formal analysis and investigation: JY, YW, XX; Writing—original draft preparation: JY, LZ, YW, FL; Writing—review and editing: LZ. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study adhered to the Declaration of Helsinki and received approval from the Ethics Committee of Shanghai Skin Disease Hospital (approval number: 2024-37). Written informed consent was obtained from all participants, and all data used for research analyses were anonymised.

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Conflict of Interest

The authors declare no conflict of interest.

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