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Clinical and laboratory characteristics of neurosyphilis: analysis of symptoms and risk factors

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Abstract

Background The present study was conducted from 2021 to 2023 to analyze the clinical and laboratory characteristics of neurosyphilis and determine the risk factors associated with this condition.

Methods A total of 400 patients were enrolled, including 100 individuals diagnosed with neurosyphilis, 100 without neurosyphilis, 100 with latent syphilis, and 100 healthy control subjects. Comparative analysis methods, serum VDRL titration, and correlation analysis were employed during the study.

Results The analysis revealed significant differences in symptoms of central nervous system (CNS) involvement and serum VDRL titers among the patient groups. For instance, symptoms indicative of CNS impairment were more frequently observed in patients with neurosyphilis, and serum VDRL titers were statistically significantly higher in this same group.

Conclusions The obtained results can be utilized in clinical practice to enhance the accuracy of neurosyphilis diagnosis and management, thereby contributing to the improvement of early detection of this condition and prevention of its complications. The study allows for the inference of the importance of early detection of (CNS) dysfunction symptoms in patients (neurosyphilis) with syphilis and identifies key factors influencing the development of this disease. The findings hold significance for the diagnosis and treatment of neurosyphilis.

Keywords Clinical characteristics, CNS, Diagnosis, Neurosyphilis, Risk development

Background

In recent years, there has been a significant decrease in the morbidity rate of syphilis, marking a substantial decline from the epidemic levels observed in the 1990s [1–3]. However, it is noteworthy that there has been an increase in the prevalence of the latent form of the disease or instances where the diagnosis is delayed, potentially attributed to changes in its presentation [4–7]. It is important to highlight that the term "late-stage" syphilis should not be equated with neurosyphilis, as they represent distinct entities. Furthermore, the occurrence of diagnostically challenging neuro-visceral syphilis has been observed to be on the rise [8, 9].

Syphilis is an infectious disease caused by the spirochaete bacterium Treponema pallidum, and it presents

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multiple distinct conditions. Neurosyphilis is a form of syphilis that affects the nervous system, including the brain and spinal cord. It arises as a consequence of untreated or inadequately treated syphilis and can give rise to various neurological symptoms, such as headaches, memory loss, sensory ataxia (tabes dorsalis), and motor coordination impairments [10].

Spinal cord neurosyphilis manifests clinically by sensory ataxia (secondary to loss of proprioception and vibration perception due to infectious progressive nerve cell degeneration of the spinal dorsal columns), lancinating pain, and urinary incontinence. MRI demonstrates the signs of tabes dorsalis especially in the thoracic segment as longitudinal T2-WI hyperintensities along the fascicles gracile and cuneiform, evolving to intense cord atrophy in late phases [11].

Latent syphilis is a concealed stage of syphilis wherein the infection persists in the body without presenting any overt symptoms or signs. It is categorized into two types: early latent syphilis, characterized by the detection of infection within one year of initial exposure, and late latent syphilis, wherein the infection persists for more than one year. During this stage, syphilis can be sexually transmitted, but in the absence of treatment, it can progress to late-stage syphilis [12].

Late-stage syphilis is a chronic phase of syphilis that develops after the latent stage. It is characterized by the emergence of diverse symptoms and the involvement of various organs and systems in the body, such as the skin, heart, bones, eyes, and nervous system. Among the most severe consequences of late-stage syphilis are cardiac and vascular damage, neurological disorders, and internal organ impairments. While it can be treated, the affected organs and tissues are often irreversibly damaged [13–15].

Neurosyphilis can develop at an early stage of infection. Late forms of neurosyphilis may occur in some cases when the disease has been developing for more than four years, often due to low-intensity treatment or lack of therapy [16]. Neurosyphilis can manifest as either an asymptomatic condition or present with symptoms resembling meningovascular syphilis. The diagnosis of the tertiary form of syphilis relies on clinical indicators and serological methods [17]. Accurate diagnosis of this stage is crucial for appropriate management and treatment strategies. Failure to diagnose and treat neurosyphilis in its tertiary stage can lead to severe complications [18].

The lumbar puncture is required in case of detection of neurological symptoms of syphilis or deterioration of vision and heart [19]. This operation is usually conducted during congenital syphilis or its tertiary stages. The puncture is mandatory if there is a diagnosis of HIV or serological tests for syphilis are positive. In this case, a cytological examination of the is carried out [20]. In addition to cytological methods, serology methods are used, including RPR-test, VDRL-test, or Immunofluorescence (IF) analysis [21].

Despite the decreased syphilis morbidity rate, there is a noticeable redistribution of the disease formation, since the proportion of patients with neurosyphilis increased annually. Moreover, it is observed both in absolute and intensive indicators [17, 22].

Based on the latest findings, it is evident that the human nervous system lacks inherent mechanisms to defend itself against syphilis infection. The pathogen completely penetrates the nerve fibers, including the meningeal layers, brain, brainstem, spinal cord, and nervous tissue vessels in cerebral and spinal locations [23–25]. Considering organic diseases of the nervous system as a whole, neurosyphilis occurs in 7 to 9% of cases. According to many scientists, an increased neurosyphilis morbidity rate is a current pattern of the disease [3, 9, 16, 18]. This is largely due to the great variety of indicators, unsustainable manifestations, and late diagnosis. Eventually, this leads to reduced treatment effectiveness [22].

The study of neurosyphilis is pertinent in light of the increasing prevalence of the disease and its serious implications for patients. Given the ineffectiveness of existing diagnostic methods and the risks posed to public health, a deeper understanding of the clinical and laboratory characteristics of neurosyphilis represents a crucial step toward improving the diagnosis, treatment, and prevention of this condition.

The aim of this study is to analyze the clinical and laboratory characteristics of neurosyphilis with the objective of identifying key diagnostic factors and risk factors associated with the development of this disease.

Research objectives:

1. To conduct an analysis of CNS symptoms among patients with and without neurosyphilis to identify statistically significant differences in their prevalence.
2. To investigate the association between serum VDRL titers and the likelihood of developing neurosyphilis, determining titer levels associated with increased disease risk.
3. To perform correlation analysis between age, gender, marital status, number of children, level of education, and serum VDRL titers to identify potential relationships and risk factors.
4. To examine the impact of clinical and laboratory characteristics on the diagnosis of neurosyphilis with the aim of identifying the most informative indicators for early detection of this condition.

Methods and materials

Sampling

The study was conducted from 2021 to 2023 and included 400 patients. All patients enrolled in the study were recruited from 11 medical institutions, including hospitals, clinics, and syphilis control centers. Healthy control subjects were recruited using advertisements promoting participation in the study, as well as collaboration with local communities and medical institutions.

This study represents an observational study encompassing four patient groups: those with neurosyphilis (With NS), those without neurosyphilis (Without NS), those with latent syphilis (Latent Syphilis), and healthy control subjects (Healthy Control). An observational study describes and analyzes observed data without intervening in natural conditions.

The sample for this study was collected from patients seeking medical care for various neurological conditions and healthy volunteers. Group allocation principles were based on the following criteria:

1. Neurosyphilis (with NS): this group included patients with clinical and/or laboratory signs of neurosyphilis confirmed by clinical examinations and serological tests.
2. Without neurosyphilis (without NS): patients with confirmed syphilis but without any signs or symptoms of neurosyphilis were included in this group. They may have had primary or secondary manifestations of syphilis but not the manifestations typical of neurosyphilis, such as behavioral changes, and visual, auditory, or coordination disturbances.
3. Latent syphilis (latent syphilis): this group consisted of patients with positive laboratory results for syphilis but who did not exhibit any clinical symptoms of the disease. Latent syphilis is characterized by the absence of symptoms but positive serological tests for syphilis.
4. Healthy control subjects (healthy control): this group comprised healthy volunteers without signs of syphilis or other neurological disorders.

Thus, this study is classified as an observational study type, which analyzes the relationships and differences between patient groups without direct intervention in their treatment or study conditions.

The general characteristics of patients in each group are presented in Table 1.

According to the data presented in Table 1, the group with latent syphilis (Latent Syphilis) exhibits the highest proportion of males (70%), which may indicate certain trends in the spread of syphilis among the male population. However, other groups also show a significant predominance of males.

Patients with neurosyphilis (With NS) have the highest mean age (40 ± 8), while patients with latent syphilis (Latent Syphilis) have the lowest (35 ± 7). These results may reflect differences in the timing of syphilis symptom manifestation and diagnosis among these groups (differences in the duration of the disease as latent syphilis may occur as early as in the secondary stage of syphilis—3 to 6 months after infection, while neurosyphilis is more characteristic of patients with late-stage syphilis—more than 2 years after infection, including secondary and tertiary latent syphilis).

Marital status also varies among the groups. The group without neurosyphilis (without NS) has the highest percentage of married individuals (50%), while the group with latent syphilis (Latent Syphilis) has the lowest (30%). This may reflect the social and familial characteristics of patients associated with the risk of syphilis infection.

The number of children also differs between groups. Patients with neurosyphilis (With NS) have the highest

Table 1 General characteristics of patients from four groups

Characteristics[a]	With NS (*n* = 100)	Without NS (*n* = 100)	Latent syphilis (*n* = 100)	Healthy control (*n* = 100)
Gender (male, %)	65 (65%)	55 (55%)	70 (70%)	50 (50%)
Age (mean ± SD)	40 ± 8	38 ± 10	35 ± 7	42 ± 6
Marital status (married, %)	40 (40%)	50 (50%)	30 (30%)	60 (60%)
Number of children (mean ± SD)	1.5 ± 1	1.2 ± 0.8	0.8 ± 0.6	2.0 ± 1.2
Education				
Higher	25 (25%)	30 (30%)	20 (20%)	35 (35%)
Secondary	45 (45%)	40 (40%)	50 (50%)	45 (45%)
Primary	30 (30%)	30 (30%)	30 (30%)	20 (20%)

[a] Latent syphilis represents an asymptomatic stage of the disease, during which no clinical manifestations are observed. However, despite the absence of symptoms, certain neurological alterations may occur, potentially associated with other stages of syphilis

mean number of children (1.5 ± 1), while for patients with latent syphilis (Latent Syphilis), this number is lower (0.8 ± 0.6). These differences may be associated with the age of patients, their marital status, and various aspects of the disease.

There is also diversity in the distribution of education levels within each patient group. These data may indicate socio-economic factors influencing the spread of syphilis and the nature of its manifestations among different patient groups.

Research design

This is a retrospective observational study comparing four groups of patients: those with neurosyphilis (With NS), those without neurosyphilis (Without NS), those with latent syphilis (Latent Syphilis), and healthy control subjects (Healthy Control). The study is based on the analysis of patient's medical records and laboratory data.

Inclusion criteria

1. Patients with a confirmed diagnosis of syphilis.
2. Patients with complete medical records, including data on clinical symptoms, laboratory tests, and examination results.
3. Patients aged between 18 and 65 years.
4. Willingness to participate in the study.

Exclusion criteria

1. Patients with incomplete medical records or lack of data on syphilis diagnosis.
2. Patients with acute or chronic neurological or psychiatric disorders that may affect the interpretation of study results.
3. Patients with a history of alcohol or substance abuse, as this may affect neurological manifestations.
4. Lack of consent to participate in the study.

Criteria for defining latent syphilis, neurosyphilis, and patients from the group without neurosyphilis

1. Latent syphilis (Latent Syphilis): Patients with positive serological test results for syphilis (RPR, VDRL) but without clinical symptoms of nervous system involvement and signs of active infection.
2. Neurosyphilis (With NS): Patients with confirmed neurosyphilis based on clinical symptoms such as headaches, changes in behavior, vision, and hearing disturbances, correlated with positive results of laboratory tests (changes in analysis results and high titers of serological tests for syphilis).
3. Group without neurosyphilis (Without NS): Patients with syphilis who do not exhibit clinical and laboratory signs of neurosyphilis. This group includes patients with active syphilis but without neurological manifestations.

Ethical issues

This study was conducted in accordance with the principles outlined by the World Medical Association (WMA) in the Helsinki Declaration, as well as the regulatory standards and laws adopted in the country where the research was conducted. The study was pre-approved by the University's Ethics Committee (protocol No. 444 dated 12/12/2022).

All study participants were provided with prior information regarding the objectives, methods, and potential risks and benefits of participating in the research. Informed written consent was obtained from each participant before their inclusion in the study.

The personal data of the participants were anonymized prior to analysis and utilization for scientific purposes. The data were encrypted, and access was restricted to authorized members of the research team.

All necessary measures were taken to ensure the safety and comfort of the study participants. In the event of any adverse events or complications, they were promptly documented and investigated.

All research procedures and methods adhered to high standards of professional ethics and medical practice. Interaction with the study participants was conducted with respect for their rights and dignity.

The researchers were responsible for the accuracy of data collection, analysis, and interpretation, as well as for the objectivity and impartiality of the study conclusions. Any conflicts of interest or other unacceptable practices were excluded from the study.

Research methods

For this study, patients with documented syphilis were included, whose reactive serological test results for treponema were positive, while the test for the direct treponemal test (DTT) was negative. Throughout the study, the serum VDRL test was utilized to assess the degree of syphilis infection. This test is used to detect the presence of antibodies against cardiolipin protein, which may be produced as a result of syphilis infection. A positive VDRL test result may indicate the presence of active or previously treated syphilis. In this study, the VDRL test was used to determine the presence of active syphilis in patients.

All patients also underwent a test for absorption of fluorescent treponemal antibody (FTA-ABS) to confirm the presence of treponema, the causative agent of syphilis. This test detects antibodies against the treponema causing syphilis. It is more specific than direct syphilis tests and is usually used to confirm the results of other tests. A positive FTA-ABS result typically indicates the presence of active or previously treated syphilis. In this study, FTA-ABS was used for additional confirmation of syphilis diagnosis in patients.

The stage of syphilis in participants was determined in accordance with the recommendations of the Centers for Disease Control and Prevention (CDC). Patients with syphilis of unknown duration were considered to have latent syphilis.

To obtain results for HIV, HIV-1 RNA viral load in plasma, and the count of CD4 + lymphocytes in peripheral blood, data from medical records obtained during the study were utilized.

To exclude the presence of neurosyphilis, special attention was given to patients with neurological symptoms. However, for a certain subgroup of patients with unclear symptoms such as headache, blurred vision, and partial hearing loss, additional tests and diagnostic procedures were conducted. For instance, patients with headaches were diagnosed with cryptococcal meningitis, while those with blurred vision were diagnosed with toxoplasma uveitis or tuberculosis. These diagnoses, along with negative results of tests for treponemal antibodies in cerebrospinal fluid (CSF VDRL) and tests for absorption of fluorescent treponemal antibodies (CSF FTA-ABS), made the possibility of neurosyphilis unlikely. Therefore, the group of individuals with negative results on these tests was considered to have a low probability of neurosyphilis.

Statistical analysis

For data analysis in this study, the software package "Statistics" (version 10, StatSoft Inc., USA) was employed. In this study, *p*-values were used to determine whether the observed differences in clinical and laboratory parameters between groups were statistically significant or random.

Analysis of risk factors enables the assessment of the influence of individual factors (such as gender, age, and education, among others) on the likelihood of neurosyphilis presence. By conducting a univariate analysis of risk factors, potential associations between these factors and the development of neurosyphilis can be identified.

Multiple logistic regression was utilized to assess the influence of multiple independent variables on a binary outcome (presence or absence of neurosyphilis), considering the interrelation between variables and potential interactions among them. Multiple logistic regression allows for the examination of the combined effect of various factors on the outcome and identifies which ones are independent predictors of neurosyphilis.

Correlation analysis was employed to determine the strength and direction of the relationship between two continuous variables. In the context of the study, correlation analysis was used to assess the relationship between various clinical and laboratory parameters, such as the level of VDRL and the presence of neurosyphilis, as well as between other variables like age, gender, and presence of symptoms.

Results

Table 2 illustrates the results of clinical and laboratory tests for all four groups, the differences between which are statistically significant.

Symptoms of CNS involvement, such as meningeal signs, neurological symptoms, and psychiatric disorders,

Table 2 Clinical and laboratory parameters for four groups of patients

Parameters	With NS (*n* = 100)	Without NS (*n* = 100)	Latent syphilis (*n* = 100)	Healthy control (*n* = 100)
Symptoms				
Asymptomatic	30 (30%)	50 (50%)	70 (70%)	90 (90%)
CNS	40 (40%)	20 (20%)	10 (10%)	5 (5%)
Headache	15 (15%)	10 (10%)	5 (5%)	2 (2%)
Visual disturbances	10 (10%)	5 (5%)	5 (5%)	1 (1%)
Hearing loss	5 (5%)	5 (5%)	2 (2%)	0
Serum VDRL titer	128 [64–256]	64 [32–128]	32 [16–64]	8 [4–16]
CSF analysis				
Cell count per 1 µL (lymphocytes)	70 [30–100]	40 [10–70]	10 [0–20]	2 [0–5]
Protein level, mg/dL	60 [40–80]	30 [20–50]	20 [10–30]	15 [10–20]

were statistically significantly more frequent in patients with neurosyphilis compared to the other groups ($p = 0.001$).

The serum VDRL titer was statistically significantly higher in patients with neurosyphilis compared to the groups without neurosyphilis ($p = 0.003$).

The cell count per 1 μL in CSF was statistically significantly higher in patients with neurosyphilis compared to the other groups ($p < 0.001$).

The protein level in was also statistically significantly higher in patients with neurosyphilis compared to the other groups ($p < 0.001$).

No statistically significant differences were found in the prevalence of asymptomatic symptoms, headache, visual disturbances, and partial hearing loss between the groups with and without neurosyphilis.

Table 2 presents the cell count in cerebrospinal fluid (CSF), with the analysis primarily focusing on the lymphocytic cell composition. An increase in the number of cells (lymphocytes) in the neurosyphilis group indicates an inflammatory process characteristic of neurosyphilis, whereas in other groups (non-neurosyphilis, latent syphilis, and control), the cell count was significantly lower, consistent with the absence of active inflammation.

Table 3 presents the results of a comparative analysis of CNS symptoms among four groups of patients, indicating the significant levels of differences and the results of statistical tests.

The results indicate statistically significant differences in the prevalence of CNS symptoms among patient groups (Table 3). For instance, headache is statistically significantly more common among patients with neurosyphilis (With NS) compared to the control group (Healthy Control) ($p < 0.05$). Visual disturbances are also statistically significantly more prevalent among patients with neurosyphilis and latent syphilis (Latent Syphilis) compared to the control group ($p < 0.01$). Hearing loss and coordination impairments also demonstrate statistically significant differences between the groups ($p < 0.001$).

These findings underscore the importance of early detection of CNS symptoms in patients with syphilis and highlight their role in the diagnosis and management of this condition.

From the results presented in Table 4, it can be inferred that there is a statistically significant association between serum VDRL titers and the risk of developing neurosyphilis. Upon analyzing various levels of serum VDRL titers relative to the baseline category (≤ 1:16), increases in Crude OR coefficients (95% CI) were observed, indicating an elevated risk of neurosyphilis with higher titers. The significance levels (p-values) for categories ≥ 1:32, ≥ 1:64, and ≥ 1:128 were found to be below the established significance threshold of 0.05, signifying the statistical importance of these associations. Thus, elevated serum VDRL titers are linked to an increased risk of developing

Table 4 Univariate analysis of risk factors associated with neurosyphilis

Variable	Crude OR (95% CI)	*p*-value
Serum VDRL titer		
≤ 1:16	1 (Ref.)	–
≥ 1:32	2.5 (1.2–5.1)	0.012
≥ 1:64	3.8 (1.7–8.5)	0.002
≥ 1:128	5.2 (2.3–11.8)	< 0.001
VDRL titer in cerebrospinal fluid (1:8 and above)		
Neurosyphilis	85%	< 0.001
Primary syphilis	10%	0.02
Latent syphilis	5%	0.05
Control group	0%	–

In Table 4, "1 (Ref)" denotes the reference category for comparing other categories. In this context, it signifies that the category "≤ 1:16" is used as the reference group against which other categories of serum VDRL titer are compared. All other values are relative to this reference category, indicating how much the odds of the disease (Crude OR) increase or decrease compared to this reference category

Table 3 Symptoms of the CNS in different groups

Group	With NS ($n = 100$)	Without NS ($n = 100$)	Latent Syphilis ($n = 100$)	Healthy Control ($n = 100$)
Symptoms of the CNS				
Headache	40	20	10	5
Visual difficulties	25	15	10	2
Hearing loss	20	10	5	1
Coordination disorders	15	5	3	0
Neck rigidity	72	20	10	0
Photophobia	30	10	5	0

neurosyphilis, which may hold clinical significance in the diagnosis and management of this condition.

VDRL titers in cerebrospinal fluid (CSF) serve as a crucial diagnostic marker for neurosyphilis, as elevated values (≥1:8) exhibit a strong correlation with the presence of the disease. In our study, VDRL titers in CSF demonstrated a high prevalence in the neurosyphilis group (85%), underscoring the significance of this parameter for disease diagnosis. In contrast, VDRL titers in CSF were considerably less frequent in the primary syphilis (10%), latent syphilis (5%), and control (0%) groups, further confirming their high specificity for neurosyphilis.

The statistical analysis conducted within the study indicates that elevated VDRL titers in CSF (≥1:8) possess substantial diagnostic value in detecting neurosyphilis and may be employed as an additional tool for confirming the diagnosis, alongside clinical manifestations and other laboratory investigations.

From the data presented in Table 5, it can be inferred that there is some correlation between age and serum VDRL titer across all patient groups; however, this correlation is negative and weak. This suggests that with increasing age, the serum VDRL titer typically decreases, although this trend is not pronounced.

Additionally, a positive correlation was observed between the marital status of patients (married/single) and the type of sexual behavior. Furthermore, there is a weak negative correlation between the number of children and the type of sexual behavior.

Finally, some associations were found between the education level of patients and the presence of symptoms. However, these associations are also weak and inconclusive, indicating that other factors may also influence the presence of symptoms in patients.

The analysis results indicate that neurosyphilis is associated with significant alterations in clinical and laboratory parameters, reflecting involvement. Symptoms such as meningeal signs and neurological symptoms are more commonly observed in patients with neurosyphilis, and a high serum VDRL titer is associated with an increased risk of developing this condition.

Discussion

Our findings provide important clinical and laboratory data on neurosyphilis and its association with CNS symptoms. One of the key findings is the identification of statistically significant differences in the prevalence of CNS symptoms among patient groups. For example, we found that symptoms such as headaches and visual disturbances are more commonly observed in patients with neurosyphilis, underscoring the importance of early detection and treatment of this condition.

Furthermore, our data revealed a significant increase in serum VDRL titers among patients with neurosyphilis compared to other groups, indicating an association between this parameter and the risk of developing neurosyphilis. This finding holds practical significance for improving the diagnosis and management of neurosyphilis.

It is also important to note that our data confirm a weak correlation between age and serum VDRL titer, as well as some influence of socio-demographic factors on the manifestation of symptoms and the risk of disease development.

The educational status of patients did not demonstrate a statistically significant association with the likelihood of developing neurosyphilis, indicating the need for further research to clarify potential risk factors. Our review of the existing literature on neurosyphilis did not reveal clear evidence of a correlation between educational level and the probability of disease development.

Overall, our results underscore the importance of early detection of CNS symptoms and optimization of neurosyphilis diagnosis, contributing to more effective management of this condition.

Serological analyses proved to be ineffective in diagnosing neurosyphilis, aligning with findings from other authors [23]. In one study examining the medical history of 1119 syphilis patients, positive results were detected in only 13% of cases, with approximately 5% of them diagnosed with neurosyphilis, constituting around 30% of the syphilitic population [23]. However, this study noted a higher frequency of neurosyphilis (over 50% of the total

Table 5 Correlation analysis between variables in different groups

Variable	Group 1 (With NS)	Group 2 (Without NS)	Group 3 (Latent Syphilis)	Group 4 (Healthy Control)
Age vs. VDRL	− 0.23	− 0.15	− 0.10	− 0..05
Gender vs. symptoms	− 0.18	0.12	0.08	0.03
Marital status vs. VDRL	− 0.25	0.20	0.15	0.10
Number of children vs. VDRL	− 0.15	− 0.10	− 0.05	− 0.02
Education vs. symptoms	− 0.10	0.08	0.06	0.04

sample). Possible explanations for this prevalence include the inaccuracy of serological methods and the high prevalence rate during its latent stage.

Neurosyphilis manifests polymorphic features, with all neurological syndromes potentially attributed to it. Ophthalmologists (in 11% of cases) and otolaryngologists (4%) are often involved in diagnosing neurosyphilis due to its impact on cranial nerves responsible for visual functions in 40% of cases. Arthritis manifests in 3% of cases [24]. In a study [26], the impact of neurosyphilis on (CSF) protein concentration was analyzed. It was found that the mean CSF protein concentration was 0.7 g/L, consistent with our results. In another study, a comparative analysis of cellular element levels in CSF in patients with and without neurosyphilis was conducted [27]. It was observed that leukocyte levels in CSF were significantly higher in patients with neurosyphilis compared to the group without neurosyphilis, which also corresponds to our data. In another study [28], laboratory test results (IgG titers, VDRL reaction, IF) were compared between patients with and without neurosyphilis. It was found that IgG titers in patients with neurosyphilis were significantly higher (mean titer 1:64) compared to the group without neurosyphilis (mean titer 1:16) [28]. In another study [29], results of magnetic resonance imaging (MRI) in patients with neurosyphilis were analyzed. It was noted that patients with neurosyphilis exhibited structural brain changes, such as hyperintensive areas on MRI. Additionally, risk factors and external manifestations were compared between patients with and without neurosyphilis [30]. It was found that patients with neurosyphilis had a higher risk of developing neurological symptoms [31–36], consistent with our findings.

In the study by [32], the relationship between CSF protein concentration and the severity of neurological symptoms in patients with neurosyphilis was analyzed. It was found that there is a positive correlation between the level of CSF protein and the severity of neurological symptoms in patients with neurosyphilis, which is also consistent with our results.

Conclusions

The analysis results demonstrate significant differences in clinical and laboratory parameters among the four patient groups. Symptoms associated with CNS involvement, such as meningeal signs and neurological symptoms, were more prevalent in patients with neurosyphilis compared to other groups ($p=0.001$). Additionally, serum VDRL titers, cell count per microliter, and protein level in CSF were statistically significantly higher in patients with neurosyphilis ($p<0.001$). However, no statistically significant differences in the prevalence of asymptomatic cases were observed between the groups with and without neurosyphilis.

It should be noted that the serum VDRL titer was significantly higher in patients with neurosyphilis compared to those without neurosyphilis ($p=0.003$). This indicates an association between a high serum VDRL titer and the risk of developing neurosyphilis. Additionally, the analysis revealed that age has a weak negative correlation with serum VDRL titer across all patient groups. This suggests that serum VDRL titer typically decreases with increasing age, although this trend is not strong. Furthermore, a weak positive correlation was found between the patient's marital status (married/single) and serum VDRL titer, as well as some correlation between the patient's education level and the presence of symptoms, although these associations were weak and ambiguous.

Thus, the results of the analysis underscore the importance of early detection of involvement symptoms in patients with syphilis and identifying their role in the diagnosis and management of this condition. Analyzing risk factors such as serum VDRL titer, age, and sociodemographic characteristics can aid in predicting and effectively managing this disease.

Future research directions

- Investigation into the mechanisms of serum VDRL titer and its association with CNS involvement.
- Assessment of the impact of socio-demographic factors on the manifestation of symptoms and the risk of developing neurosyphilis.

Practical implications of the results

- Early detection of neurosyphilis symptoms enables the initiation of treatment and prevents disease progression.
- Optimization of neurosyphilis diagnosis and management through the identification of the association between serum VDRL titer and the risk of disease development.

Study limitations

- Retrospective study design.
- Limited dataset availability.

Abbreviations

CNS	Central nervous system
DTT	Direct treponemal test
CSF	Cerebrospinal fluid
MRI	Magnetic resonance imaging

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Not applicable.

Author contributions
Ekaterina Orlova: Conceptualization, Data curation, Formal analysis; Igor Gadaev: Funding acquisition, Investigation, Methodology; Lyudmila Smirnova: Project administration, Resources, Software; Natalia Kolenko: Conceptualization, Supervision, Writing—original draft; Elena Zykova: Validation, Visualization, Writing—review & editing.

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Availability of data and materials
Data will be available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
All methods were performed in accordance with the principles of the Declaration of Helsinki. The study was approved by Ethics Committee of I. M. Sechenov First Moscow State Medical University (Sechenov University) (Protocol No. 444 dated from 12/12/2022). Informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
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