

ORIGINAL

## Neurological complications in patients with Human Immunodeficiency Virus infection at the Japanese Hospital in Santa Cruz, Bolivia

### Complicaciones neurológicas en pacientes con infección por Virus de Inmunodeficiencia Humana en el Hospital Japonés de Santa Cruz, Bolivia

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#### ABSTRACT

**Introduction:** neurological involvement is common among patients with Human Immunodeficiency Virus (HIV) infection. Between 40 and 60 % will develop symptomatic neurological complications with high morbidity and mortality at some point.

**Objective:** to analyze the clinical-epidemiological characteristics of patients with HIV infection who develop neurological complications at the Japanese Hospital of Santa Cruz de la Sierra in the period between March 2019 and February 2022.

**Method:** observational, descriptive, prospective, cross-sectional study. Universe and Sample: Patients admitted through the Emergency Service of the Japanese Hospital with a confirmed diagnosis of Human Immunodeficiency Virus Disease during the period between March 2019 and February 2022.

**Results and discussion:** a total of 42 patients were evaluated, the majority of whom were men and had a younger average age. For both sexes, the majority of patients reported having a source of employment. Regarding sexual orientation, almost all women reported being heterosexual, while men were more variable, with the majority being bisexual. Three clinical syndromes were identified at admission. The frequency of focal syndrome was dominant in women, but was not significantly different from the others. In men, meningeal syndrome and focal syndrome were the dominant ones, significantly exceeding non-focal syndrome. Ten neurological complications were identified, cerebral toxoplasmosis was the most frequent, followed by cerebral cryptococcosis and meningeal tuberculosis. Considering all patients in general, their typical hospital stay was 11 days with a range between 2 and 56 days. Of the 42 patients evaluated, it was only possible to measure the CD4 status for 27.

**Conclusions:** the young male population with employment in the city of Santa Cruz with aberrant sexual behavior was the most affected. Focal syndrome was the most frequent form of presentation, in the form of

cerebral toxoplasmosis. Severely low levels of immunosuppression were found in the study population. Hospital stay is variable and is longer in cases of focal syndrome and meningeal syndrome. We consider it important to continue the present study, which will allow us to increase the sample size.

**Keywords:** Neurological Complications; Human Immunodeficiency Virus Infection; Focal Neurological Syndrome; Meningeal Syndrome.

## RESUMEN

**Introducción:** la afectación neurológica es frecuente entre los pacientes que padecen infección por Virus de la Inmunodeficiencia Humana (VIH). Entre un 40 a 60 % desarrollará en algún momento complicaciones neurológicas sintomáticas con alta morbi-mortalidad.

**Objetivo:** analizar las características clínicas-epidemiológicas de los pacientes con infección por VIH que desarrollan complicaciones neurológicas en el Hospital Japonés de Santa Cruz de la Sierra en el periodo entre marzo del 2019 y febrero del 2022.

**Métodos:** estudio observacional, descriptivo, prospectivo, transversal. Universo y Muestra: Pacientes que ingresen por servicio de Emergencia del Hospital Japonés con diagnóstico confirmado de Enfermedad por Virus de la inmunodeficiencia Humana durante el periodo comprendido entre marzo de 2019 a febrero de 2022

**Resultados y discusión:** se evaluaron 42 pacientes en total de los cuales la mayoría fueron varones, quienes, presentaron una menor edad promedio. Para ambos sexos, la mayoría de los pacientes indicaron tener una fuente laboral. Respecto a su orientación sexual, casi la totalidad de las mujeres indicaron ser heterosexuales mientras que en los varones existió una mayor variabilidad, siendo la mayoría bisexuales. Se identificaron tres síndromes clínicos de ingreso. La frecuencia del síndrome focal fue dominante en mujeres pero, no se diferenció significativamente de los demás. En varones, el síndrome meníngeo y el síndrome focal fueron los dominantes superando significativamente al síndrome no focal. Fueron 10 las complicaciones neurológicas identificadas, Toxoplasmosis cerebral fue la más frecuente seguida de Criptococosis cerebral y Tuberculosis meníngea. Considerando todos los pacientes en general, su estadía hospitalaria típica fue de 11 días con un rango entre 2 y 56 días. De los 42 pacientes evaluados, solo fue posible medir el estado del CD4 para 27.

**Conclusiones:** la población joven del sexo masculino con vínculo laboral de la ciudad de Santa Cruz con conducta sexual aberrante fue la más afectada. El síndrome focal fue la forma de presentación más frecuente, en forma de Toxoplasmosis cerebral. Se encontraron grados severamente bajos de inmunosupresión en la población estudiada. La estadía hospitalaria es variable y se prolonga más en casos de síndrome focal y síndrome meníngeo. Consideramos importante dar continuidad al presente estudio, lo cual permitirá aumentar el tamaño de la muestra.

**Palabras clave:** Complicaciones Neurológicas; Infección por Virus de Inmunodeficiencia Humana; Síndrome Neurológico Focal; Síndrome Meníngeo.

## INTRODUCTION

The Joint United Nations Program on Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), known as UNAIDS, in presenting the situation of the disease at the end of 2016, states that 36,7 million people were living with HIV worldwide of these, 2 million were in Latin America and the Caribbean; likewise, approximately 100 000 new infections and 50 000 deaths from AIDS-related causes were recorded.<sup>(1,2,3,4,5)</sup> AIDS is a pandemic characterized by profound immunosuppression, which leads to the development of opportunistic infections, neoplasms, and, fundamentally, neurological manifestations.<sup>(6,7,8)</sup>

In Bolivia, up to June 2018, patients with this condition are concentrated in the central area of the country, 45,4 % in Santa Cruz, 21,5 % in La Paz, and 19,3 % in Cochabamba, while in the remaining six departments, the figure is 13,8 %. In terms of age groups, the highest number of people suffering from this disease are between 15 and 39 years old. The ratio is two men for every woman. At the Japanese Hospital in Santa Cruz de la Sierra, neurological complications are frequently treated in patients with Human Immunodeficiency Virus infection, with a significant mortality rate; however, the clinical and epidemiological characteristics are unknown. The present study is proposed to respond to the scientific problem caused by the lack of knowledge of the clinical and epidemiological variables of patients with immunodeficiency acquired by the Human Immunodeficiency Virus (HIV) who develop neurological complications.<sup>(9,10,11,12)</sup> There is a need to characterize the behavior of these complications in our environment and their clinical and epidemiological manifestations to achieve timely diagnosis and impose treatment that improves survival since most of them are potentially treatable pathologies.<sup>(13,14)</sup> Characterization would benefit the HIV-positive population. It was carried out at the Japanese Hospital in

Santa Cruz de la Sierra, which has the necessary material and human resources to deal with it. It lasted three years, starting in March 2019, and is part of the lines of research of the Neurology Department of that center. The study was carried out with ethical aspects in mind and without any conflicts of interest or legal aspects that could be imputed.

## METHOD

**Type of study:** Observational, descriptive, prospective, cross-sectional study. **Universe and Sample:** Patients admitted through the Emergency Department of the Japanese Hospital with a confirmed diagnosis of Human Immunodeficiency Virus Disease from March 2019 to February 2022. **Inclusion criteria:** any patient aged 18 years or over with CNS involvement admitted through the Hospital Japonés emergency department. Patients with a confirmed diagnosis of human immunodeficiency virus disease with neurological manifestations. **Exclusion criteria:** Patients with neurological manifestations without a confirmed Human Immunodeficiency Virus Disease diagnosis. Patients who die before the type of neurological complication can be determined.

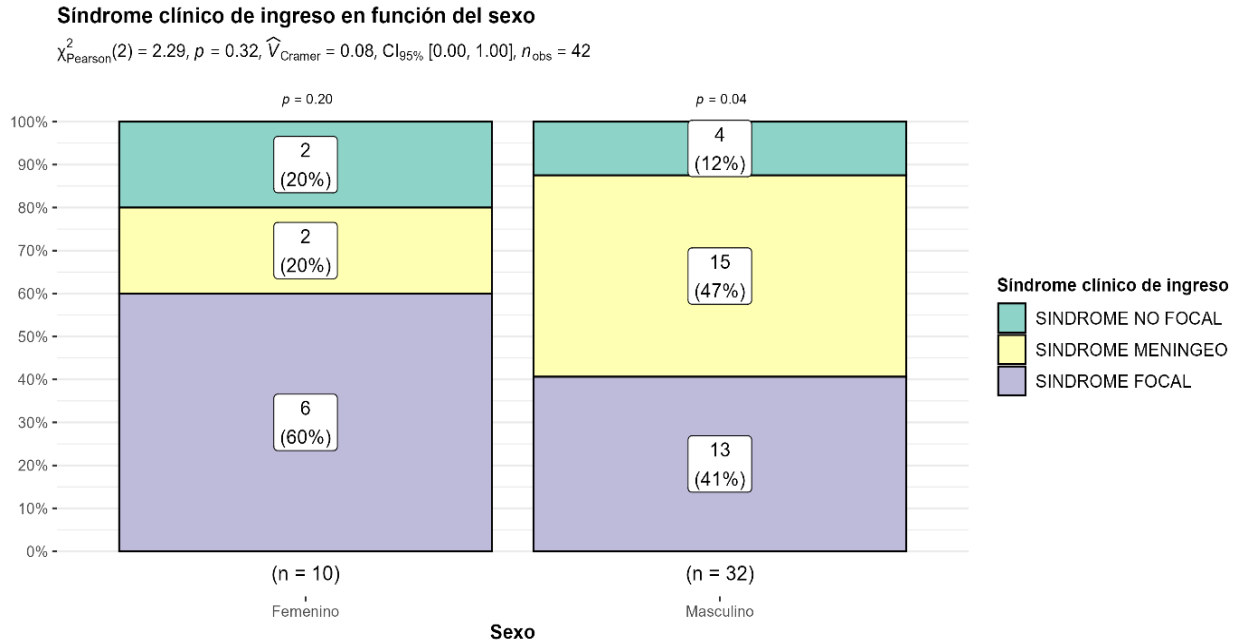
**Techniques and instruments.** Data collection will be done using an individual data collection form and medical record registration. The data was analyzed using R software and will be presented using Microsoft PowerPoint. **Procedure.** Patients aged 18 years and over who are admitted to the emergency department with neurological signs and symptoms that are confirmed by a rapid test for HIV are included in the study, as are all those who have been admitted with a history of HIV disease and meet the inclusion criteria—completion of the data record on admission. Once the HIV disease diagnosis has been confirmed, the patient is included in the study. Otherwise, they are excluded. Request the latest CD4 count and viral load data. Perform Computed Axial Tomography and Lumbar Puncture. Send samples for Cytochemistry, Gram stain, Nielzi stain, India ink, Genexpert, and Culture for BAAR and Fungi. Observation and data collection of clinical evolution, diagnosed neurological complications, hospital stay, and conditions at discharge. At discharge, collection of data from the epicrisis and previously prepared file.

## RESULTS AND DISCUSSION

A total of 42 patients were evaluated, the majority of whom were male ( $n= 32$ ; 76 %); they had a lower average age (37 years;  $\pm 11$ ) compared to women. For both sexes, the majority of patients indicated having a job. Regarding their sexual orientation, almost all of the women stated that they were heterosexual ( $n=8$ ; 80 %), while among the men, there was more significant variability, the majority being bisexual ( $n=12$ ; 37,5 %). Finally, most patients generally indicated the city of Santa Cruz de la Sierra as their current residence (table 1).

Socio-demographic characteristics	Sex	
	Feminine (n= 10)	Masculine (n= 32)
Age		
Average (standard deviation)	41 ( $\pm 14$ )	37 ( $\pm 11$ )
Employment relationship		
Yes	7 (70 %)	20 (62,5 %)
No	3 (30 %)	12 (37,5 %)
Sexual orientation		
Heterosexual	8 (80 %)	3 (9,37 %)
Homosexual		8 (25 %)
Bisexual		12 (37,5 %)
No answer	2 (20 %)	9 (28,13 %)
Current place of residence		
Santa Cruz de la Sierra	6 (60 %)	23 (71,86 %)
Warnes	2 (20 %)	
Cotoca	1 (10 %)	4 (12,49 %)
Yapacaní	1 (10 %)	
Monteagudo		1 (3,13 %)
Montero		1 (3,13 %)
Pailón		1 (3,13 %)
San José de Chiquitos		1 (3,13 %)
San Julián		1 (3,13 %)

Three clinical syndromes were identified on admission: i. Focal (n= 19; 45,24 %), ii. Meningeal (n= 17; 40,48 %) and iii. Non-focal (n= 6; 14,28 %). The frequency of focal syndrome was dominant in women (n=6; 60 %) but did not differ significantly from the others (p>0,05). In men, meningeal (n=15; 47 %) and focal (n=13; 41 %) syndromes were dominant and significantly exceeded non-focal (p<0.05). However, in general terms, no statistically significant association (p>0,05) was found between the clinical syndromes and sex; the relationship between the two variables was very weak ( $V_{\text{Cramer}}=0,08$ ). Therefore, it is possible to infer that the form of clinical presentation of the patients evaluated occurred independently of their sex (figure 1). However, based on the confidence intervals (CI 95 %) of the effect size, the above assessment should not be considered conclusive. Given the low precision demonstrated by the analysis, it is recommended to increase the sample size (mainly for women) to obtain more robust results.<sup>(15)</sup>



**Figure 1.** Inferential contrast of clinical admission syndromes according to sex

Ten neurological complications were identified (table 2); cerebral toxoplasmosis was the most frequent (n=13; 30,95 %), followed by cerebral cryptococcosis (n=9; 21,43 %) and meningeal tuberculosis (n=7; 16,67 %). No statistically significant association was found between the types of neurological complications and sex ( $\chi^2(9) = 7,92; p > 0,05; V_{\text{Cramer}} = 0,00; \text{CI}_{95\%} [0,00; 1,00], n = 42$ ).

**Table 2.** Neurological complications presented by the patients studied

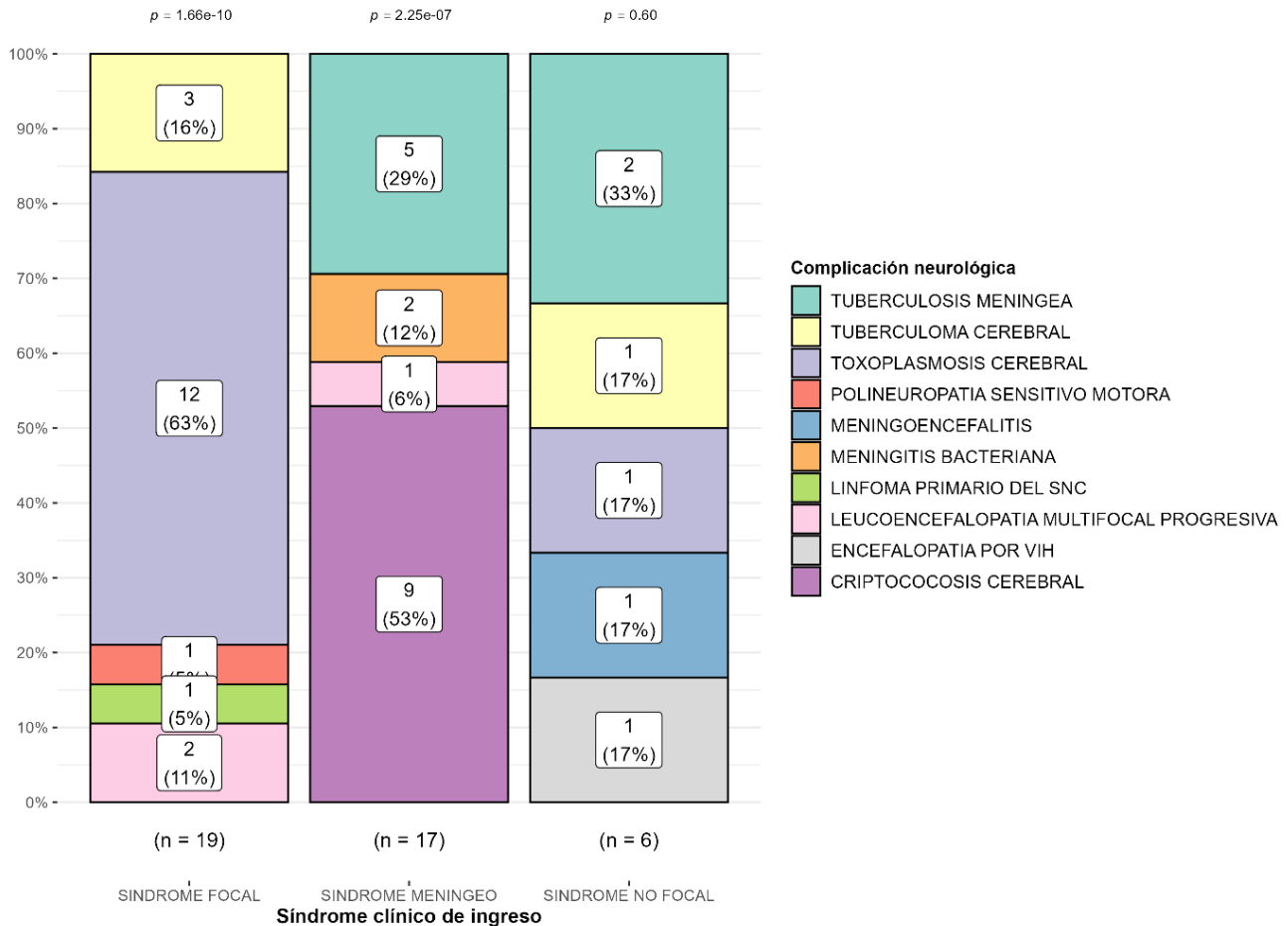
No	Neurological complications	n	%
1	Cerebral toxoplasmosis	13	30,95
2	Cerebral cryptococcosis	9	21,43
3	Meningeal tuberculosis	7	16,67
4	Cerebral tuberculoma	4	9,52
5	Progressive multifocal leukoencephalopathy	3	7,14
6	Bacterial meningitis	2	4,76
7	HIV encephalopathy	1	2,38
8	Primary CNS lymphoma	1	2,38
9	Viral meningoencephalitis	1	2,38
10	Sensory-motor polyneuropathy	1	2,38
Total		42	100

However, a significant and influential association ( $p < 0,05, V_{\text{Cramer}} = 0,65$ ) was found between neurological

complications and clinical syndromes at admission (figure 2), specifically for focal and meningeal syndromes. For focal disease, cerebral toxoplasmosis was the most frequent neurological complication (n=12; 63%), significantly outnumbering the others presented within this syndrome (p<0,05). On the other hand, cerebral cryptococcosis was the complication that widely and significantly dominated within the meningeal syndrome (n=9; 53%, p<0,05). For patients with non-focal syndrome, no neurological complication was significantly dominant (p> 0,05).

**Complicación neurológica en función del síndrome clínico de ingreso**

$\chi^2_{\text{Pearson}}(18) = 51.94, p = 3.82e-05, \hat{V}_{\text{Cramer}} = 0.65, CI_{95\%} [0.00, 1.00], n_{\text{obs}} = 42$



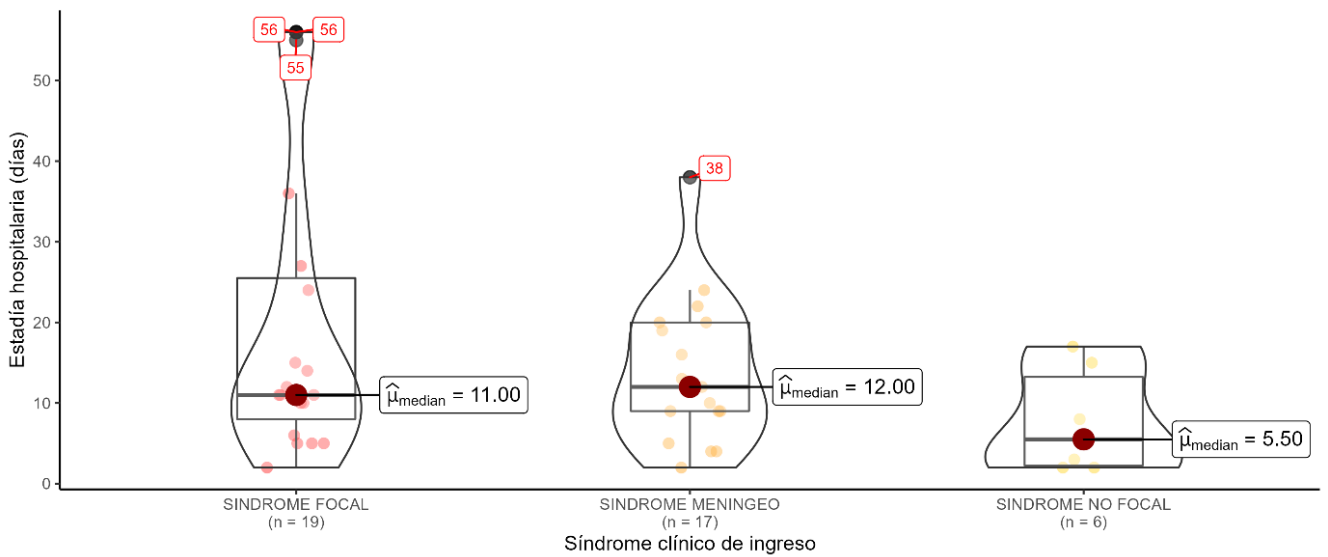
**Figure 2.** Inferential contrast of neurological complications according to clinical syndromes at admission

Considering all patients, their typical hospital stay was 11 days, ranging between 2 and 56 days. The length of stay was not significantly different between the sexes (WMann-Whitney= 153,00; p>0,05; rank biserial= -0,04; CI95 % [-0,43; 0,35], n= 42). However, relating hospital stay with clinical syndromes on admission, although no statistically significant differences were detected (p>0,05), a medium effect size was found (ε2=0,08), and based on its confidence intervals (CI<sub>95%</sub>), the possibility that, with an increase in the sample size, significant differences may arise between the length of time patients stay and the clinical syndrome with which they are admitted to hospital (figure 3). In this regard, a trend was observed whereby patients with focal and meningeal syndrome have a more extended hospital stay in contrast to those with non-focal syndrome.

Of the 42 patients evaluated, measuring the CD4 count for 27 was only possible. Of these, the typical value was generally 48 (range between 7 and 442). No statistically significant differences were recorded in the CD4 values between the sexes (WMann-Whitney= 62,00; p>0,05; rrank biserial= -0,02; CI<sub>95%</sub> [-0,50; 0,48], n= 27). Similarly, CD4 values were not significantly associated with the clinical syndromes at admission (p>0,05; V<sub>cramer</sub>=0,00); patients with CD4 values below 50 were proportionally dominant for all syndromes, but they did not differ significantly from patients with other values (p>0,05; figure 4).

Estadía hospitalaria en función del síndrome clínico de ingreso

$\chi^2_{\text{Kruskal-Wallis}}(2) = 3.30, p = 0.19, \hat{\epsilon}^2_{\text{ordinal}} = 0.08, \text{CI}_{95\%} [0.02, 1.00], n_{\text{obs}} = 42$



Pairwise test: **Dunn test**, Comparisons shown: **only significant**

Figure 3. Descriptive and inferential contrast of hospital stay and clinical syndromes on admission

CD4 en función del síndrome clínico de ingreso

$\chi^2_{\text{Pearson}}(6) = 2.02, p = 0.92, \hat{V}_{\text{Cramer}} = 0.00, \text{CI}_{95\%} [0.00, 1.00], n_{\text{obs}} = 27$

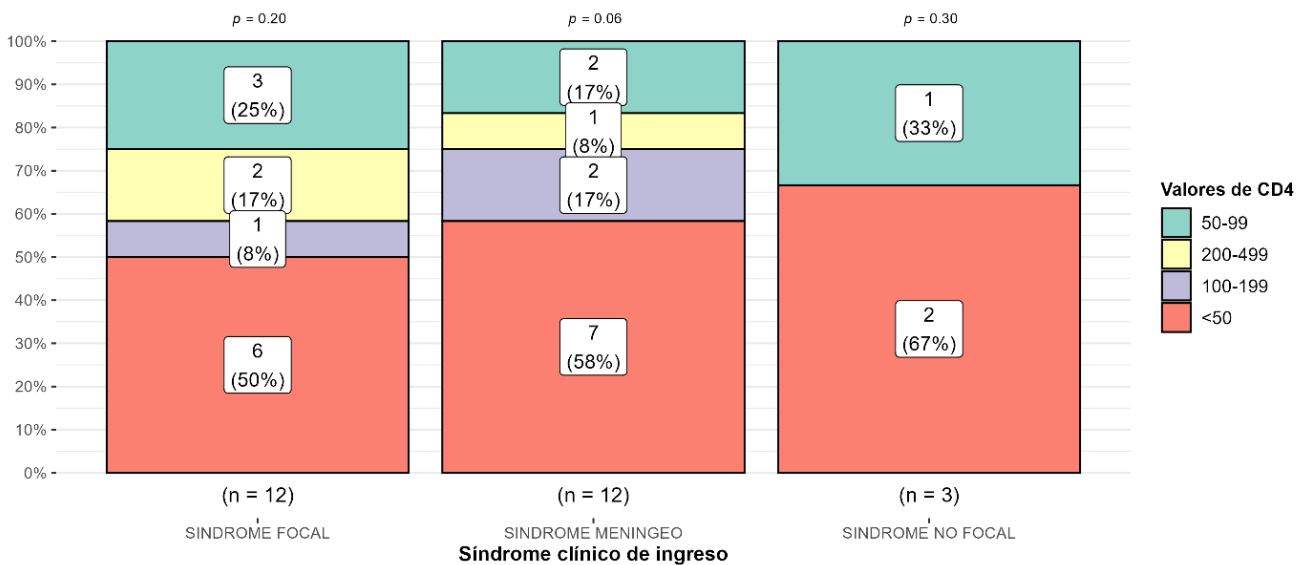


Figure 4. Inferential CD4 count contrast according to clinical admission syndromes

**CONCLUSIONS**

Young males with employment ties in the city of Santa Cruz with aberrant sexual behavior were the most affected. The most frequent form of presentation was focal neurological syndrome in the form of cerebral toxoplasmosis. Severely low levels of immunosuppression were found in the population studied. Hospital stays vary and are longer in focal and meningeal syndrome cases.

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## **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

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