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Prevalence of neutropenia in a level IV institution in the city of Barranquilla, Colombia

Prevalencia de la neutropenia en una institución de cuarto nivel en la ciudad de Barranquilla, Colombia

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ABSTRACT

Introduction: Neutropenia, a decrease in the absolute count of circulating neutrophils, compromises the immune response and increases susceptibility to infections, from mild skin conditions to fatal systemic complications. This study analyzes the clinical, sociodemographic characteristics and prevalence of neutropenia in patients of the Bonnadona Prevenir Clinical Organization between 2021 and 2022. **Methods:** We conducted a cross-sectional study using data from the Bonnadona Prevent Clinical Organization laboratory. Patients with an absolute neutrophil count < 1,000 cells/µL in the period 2021-2022 were included. **Results:** 213 subjects were included (average age 50 ± 19 years), 33.3% men and 66.7% women. 70.4% presented moderate and 29.6% severe neutropenia. Age, gender, origin, and affiliation regime did not show significant associations with the type of neutropenia ($p > 0.05$). The most frequent diagnosis was breast cancer (33.3%). The most common treatments were cyclophosphamide + doxorubicin, followed by carboplatin + paclitaxel. High blood pressure (HTN) and HTN + diabetes mellitus (DM) were the most frequent comorbidities. **Conclusion:** Neutropenia is a relevant complication in patients with cytotoxic and immunosuppressive therapies, especially in hematological diseases. We observed a high incidence of moderate and severe neutropenia, with a higher incidence in women, potentially due to the prevalence of breast cancer. These findings highlight the importance of active surveillance and the need for personalized management strategies to mitigate the risk of serious infections and improve patients' quality of life

Keywords: neutropenia, cytotoxic, immunosuppression, chemotherapy, breast cancer.

RESUMEN

Introducción: La neutropenia, una disminución del recuento absoluto de neutrófilos circulantes, compromete la respuesta inmunitaria y aumenta la susceptibilidad a infecciones, desde afecciones cutáneas leves hasta complicaciones sistémicas fatales. Este estudio analiza las características clínicas y sociodemográficas, y la prevalencia de neutropenia en pacientes de la Organización Clínica Bonnadona Prevenir entre 2021 y 2022. **Métodos:** Estudio transversal basado en datos del

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laboratorio de la Organización Clínica Bonnadona Prevenir. Se incluyeron pacientes con recuento absoluto de neutrófilos < 1,000 células/µL en el periodo 2021-2022. **Resultados:** Se incluyeron 213 sujetos (edad promedio de 50 ± 19 años), 33.3% hombres y un 66.7% de mujeres. El 70.4% presentó neutropenia moderada y el 29.6% neutropenia severa. La edad, el género, la procedencia y el régimen de afiliación no mostraron asociaciones significativas con el tipo de neutropenia (p > 0.05). El diagnóstico más frecuente fue cáncer de mama (33.3%). Los tratamientos más comunes fueron ciclofosfamida + doxorrubicina seguido de carboplatino + paclitaxel. La hipertensión (HTA) y la hipertensión + diabetes mellitus (DM) fueron las comorbilidades más frecuentes. **Conclusión:** La neutropenia es una complicación relevante en pacientes con terapias citotóxicas e inmunosupresoras, especialmente en enfermedades hematológicas. Se observó una alta incidencia de neutropenia moderada y severa, mayor en mujeres, posiblemente por la prevalencia del cáncer de mama. Estos hallazgos resaltan la importancia de la vigilancia activa y la necesidad de estrategias de manejo personalizadas para mitigar el riesgo de infecciones graves y mejorar la calidad de vida de los pacientes.

Palabras Clave: neutropenia, citotóxicos, inmunosupresión, quimioterapia, cáncer de mama.

1. Introduction

Neutrophils comprise approximately 70% of the leukocytes in the blood and are crucial in defending the body against bacterial infections [1]. They act as the first line of defense through the phagocytosis of pathogens and the release of antimicrobial factors contained in specialized granules [2,3].

Neutropenia is defined as a reduction in the absolute neutrophil count (ANC) in the bloodstream. Typical ANC values vary by age, but neutropenia is generally defined as ANC < 1,500 cells/µL. Clinically, it can be classified as mild (1,000 - 1,500 cells/µL), moderate (500 - 1,000 cells/µL), or severe (< 500 cells/µL). Severe neutropenia, with its consequent reduction in the ability to mount a systemic inflammatory response, increases the risk of infections, especially those of endogenous origin such as skin and gastrointestinal tract [4].

The severity of neutropenia increases the risk of infections, primarily those caused by endogenous flora from the skin and gastrointestinal tract. Profound neutropenia (ANC < 100 cells/µL for more than 7 days post-cytotoxic therapy) has been associated with more significant complications and the need for treatment adjustments, such as dose reductions or delays in chemotherapy, which significantly affect clinical outcomes [5,6].

There are several mechanisms that can cause neutropenia, for instance, decreased marrow production, sequestration, and increased destruction of neutrophils in the blood, whether congenital or acquired [4,7,8].

The lack of local epidemiological data on neutropenia has limited clinical decision-making in our setting, given that it is a prevailing problem associated with morbidity and even mortality [3]. Therefore, the Research Group of the Bonnadona Prevenir Clinical Organization (OCBP) aimed at conducting a study to characterize these patients, including associated diseases, used cytostatic regimens, and comorbidities. The goal was to generate evidence that enables timely and appropriate therapeutic adjustments by anticipating the onset of neutropenia and optimizing clinical management of these patients.

2. Design

A retrospective descriptive cross-sectional study was conducted using data obtained from the clinical laboratory database of the OCBP. The study included patients who had laboratory tests performed at the institution and presented an absolute neutrophil count (ANC) < 1,000 cells/µL during the 2021-2022 period, with a hematologic oncology diagnosis after receiving chemotherapy treatment.

2.1 Population and Sample

Inclusion criteria applied to patients of all ages and both sexes with an ANC < 1,000 cells/µL admitted to OCBP during 2021-2022, with hematologic diagnoses (breast cancer, cervix, colon, lymphoma,

acute lymphoid leukemia, and multiple myeloma), regardless of associated comorbidities. Exclusion criteria considered patients with recurrent neutropenia and those lacking demographic or clinical information in their medical records. Cases were classified according to the severity of neutropenia: moderate and severe.

2.2 Data Collection

Patients diagnosed with neutropenia were identified throughout the institutional laboratory database. During the patient selection process, the clinical record of each individual was reviewed to identify sociodemographic variables, clinical conditions, comorbidities, neutrophil counts, and chemotherapy received.

3. Ethical Considerations

The research protocol was approved by the OCBP Research Ethics Committee. This study is considered low-risk, as the source was the institutional clinical laboratory reporting database.

4. Results

Table 1 presents the sociodemographic characteristics of patients in general and by neutropenia classification. The average age of the patients was 50 years, with a standard deviation of ± 19 years. The age variable was categorized into three groups: minors (19 patients, 8.9% of the total), adults between 18 and 64 years (147 patients, 69% of the total), and older adults over 64 years (47 patients, 22.1% of the total). Male patients represented 33.3% of the sample (71 out of 213), while female patients accounted for 66.7% (142 out of 213). Forty percent of the patients came from rural areas, while most were from urban areas. Furthermore, 54.9% reported being affiliated with a contributory health insurance regime.

Table 1. Descriptive analysis of patient diagnoses by sociodemographic factors.

		Neutropenia		
Characteristics	Total (%)	Moderate n (%)	Severe n (%)	P-value*
	213 (100)	**150 (70.4)**	**63 (29.6)**	
Age	49.9±19.4	50.4±19.9	48.6±20.3	
<18	19 (8.9)	13 (8.7)	6 (9.5)	0.891
18-64	147 (69.0)	105 (70.0)	42 (66.7)	
>64	47 (22.1)	32 (21.3)	15 (23.8)	
Gender				
Male	71 (33.3)	46 (30.7)	25 (39.7)	0.203
Female	142 (66.7)	140 (69.3)	38 (60.3)	
Origin				
Rural	85 (39.9)	57 (38.0)	28 (44.4)	0.381
Urban	128 (60.1)	93 (62.0)	35 (55.6)	
Regimen				
Subsidized	96 (45.1)	70 (46.7)	26 (41.3)	0.470
Contributory	117 (54.9)	80 (53.3)	37 (58.7)	

*Chi-square test for p-value calculation; n: part of the sample analyzed; (%): representative percentage of the analyzed sample (n).

Regarding the type of neutropenia, Table 1 shows that 150 patients (70.4%) had moderate neutropenia, and 63 (29.6%) had severe neutropenia. When analyzing sociodemographic factors, it was observed that among patients with moderate neutropenia, 8.7% were minors, 70% were in the 18–64-year-old age group, and 21.3% were older than 64 years. Regarding gender, 30.7% of patients with moderate neutropenia were male, and 69.3% were female. Rural-origin patients with moderate neutropenia represented 38%, while urban-origin patients comprised 62%. Regarding the insurance regime, 46.7% of patients with moderate neutropenia were under the subsidized regime, and 53.3% were under the contributory regime.

For patients with severe neutropenia, 9.5% were minors, 66.7% were in the 18–64-year-old age group, and 23.8% were older than 64 years. Regarding gender, 39.7% of patients with severe neutropenia were male, and 60.3% were female. Regarding origin, 44.4% of patients with severe neutropenia came from rural areas, and 55.6% came from urban areas. As for the insurance regime, 41.3% of patients with severe neutropenia were under the subsidized regime, and 58.7% were under the contributory regime.

Finally, an association analysis was conducted using the chi-square test for each sociodemographic factor concerning the type of neutropenia. Results indicated that age, gender, origin, and insurance regime showed no significant associations (p-value > 0.05) with the type of neutropenia. Therefore, it can be stated that these sociodemographic factors are not related to the type of neutropenia with a 95% confidence level.

Figure 1 shows that breast cancer was the most frequent diagnosis among the patients (33.3%), followed by lymphomas (10.8%), colon cancer (7.0%), acute lymphoid leukemia (5.6%), cervical cancer (4.2%), multiple myeloma (3.8%), and anemia. When analyzing the figure by gender, it was found that all the patients with breast cancer were female, representing 32.9% of the diagnoses. Similarly, 4.7% and 3.8% of the patients were male with lymphoma or colon cancer, respectively. Likewise, when analyzing by age, it was observed that most of the patients with breast cancer were 64 years old or younger, while the percentage of patients with breast cancer older than 64 years was 8%. The percentage of patients older than 64 years with lymphoma or colon cancer was 1.9% and 2.3%, respectively. Finally, regarding the origin of the patients, breast cancer and colon cancer were more common in patients from urban areas. In contrast, those from rural areas were primarily affected by lymphomas, acute lymphoid leukemia (ALL), and multiple myeloma.

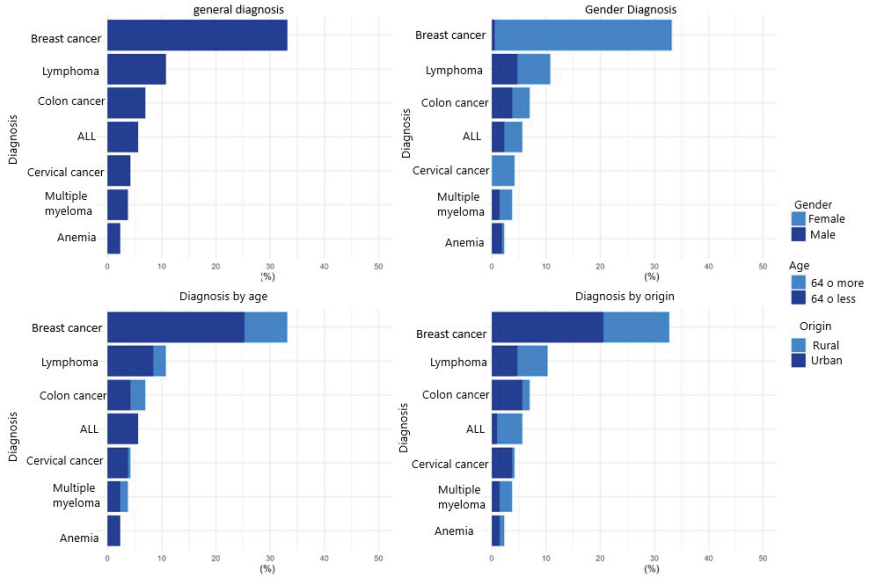

Figure 1. Common diagnoses in general and by sociodemographic factors.

Figure 2 shows the most common treatments applied to the patients in this study, both in general and by sociodemographic factors. The most frequent treatment was cyclophosphamide plus doxorubicin (19.7%), followed by carboplatin plus paclitaxel (8.9%). The treatment graph by gender highlighted a notable disparity in the number of treatments applied between genders. Regarding

the age group, it was observed that the most common treatments were applied to patients under 64 years of age. Finally, a higher frequency of these treatments was observed in patients from urban areas, except for those who received R-CHOP, which was more frequent in patients from rural areas.

Figure 3 shows the most frequent comorbidities in general and by sociodemographic factors. It was observed that hypertension (HTN) was the most common comorbidity overall (13.6%), followed by diabetes mellitus (DM) or the combination of both (HTN + DM). When analyzing comorbidities by gender and age group, it was observed that most of the patients with HTN were female and 64 years or younger. Regarding the origin of the patients, the prevalence of HTN was similar in both rural and urban areas.

Figure 4 shows the classification of neutropenia in general and by sociodemographic factors; 70.4% of the patients had moderate neutropenia, while 29.6% had severe or mild neutropenia. When analyzing neutropenia classifications by age group and place of origin, it is evident that most patients with severe neutropenia were 64 years or younger or came from urban areas. Additionally, the majority of patients with moderate or severe neutropenia were female.

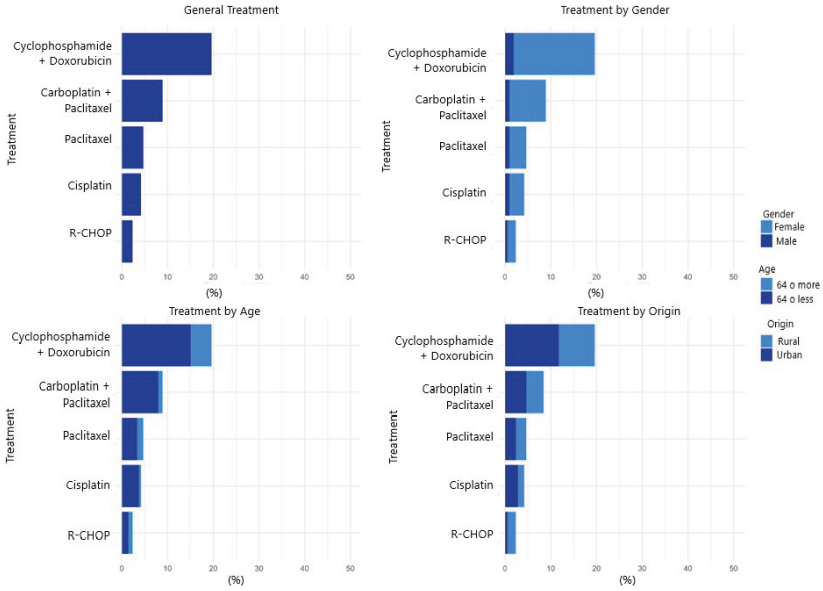

Figure 2. Common treatments in general and by sociodemographic factors.

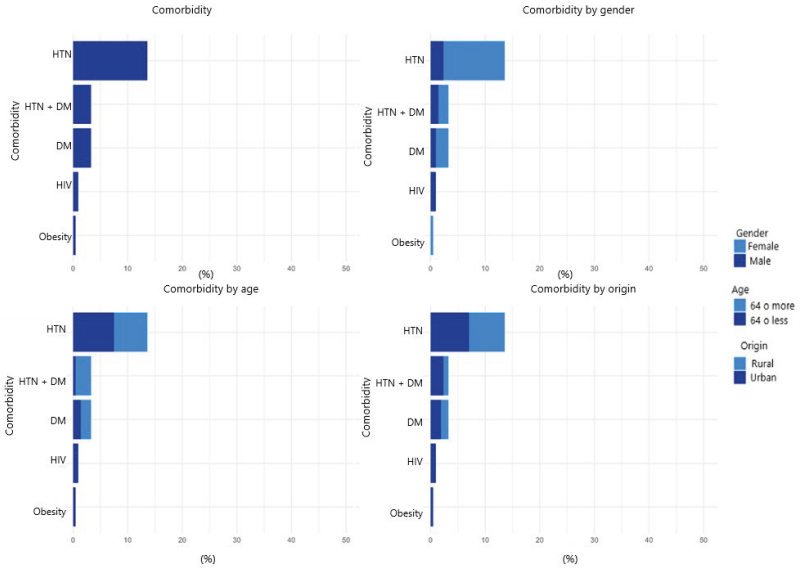

Figure 3. Common comorbidities in general and by sociodemographic factors.

Figure 5 presents the classification of neutropenia related to the patient's most frequent diagnoses, treatments, and comorbidities. It was observed that most patients with breast cancer had a moderate neutropenia; similarly, the majority of patients with lymphoma or colon cancer had moderate neutropenia. When analyzing the treatments provided and the patient's comorbidities, it was found that most patients who received cyclophosphamide plus doxorubicin as treatment had moderate neutropenia. Furthermore, approximately 83% of patients with hypertension (HTN) had a moderate neutropenia, while most (57.1%) of the patients with DM or HTN had a severe neutropenia.

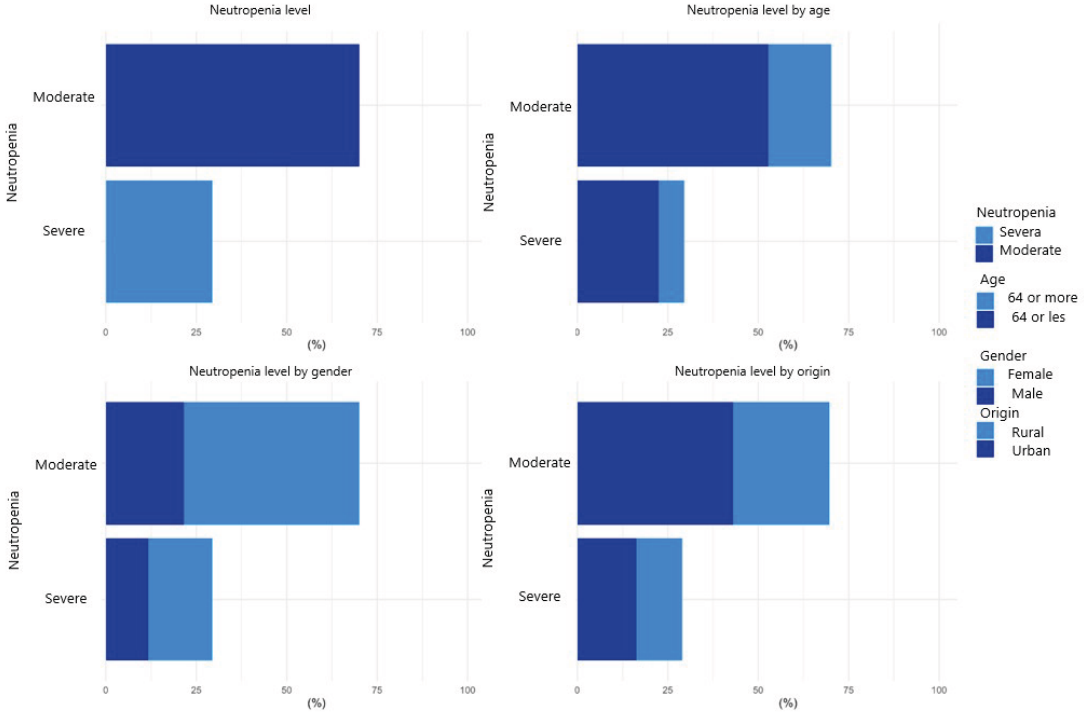

Figure 4. Neutropenia classification in general and by sociodemographic factors.

5. Discussion

This study addresses the prevalence of neutropenia in a tertiary-level institution specialized in managing hematologic and oncologic diseases and providing care for patients with other conditions. Neutropenia is a critical complication in patients undergoing cytotoxic and immunosuppressive therapies, particularly with agents such as anthracyclines and taxanes, due to their considerable impact on morbidity and mortality [2].

Our results showed that the average age of patients with neutropenia was 50 ± 19 years, consistent with previous studies investigating febrile neutropenia in hematologic and oncologic neoplasms [9,11]. The predominant diagnosis was breast cancer, present in 33.3% of the cases, all in female patients. This proportion can be attributed to the morbidity profile of the institution, where breast cancer constitutes 29% of the total treatments. This could explain the higher prevalence of neutropenia in women, with a ratio of 1.6:1 [12,13].

Literature has documented the risk of neutropenia associated with various chemotherapy regimens. For example, it has been reported that regimens combining anthracyclines and taxanes can carry a risk of neutropenia of up to 20% in specific diagnoses, as mentioned in the study by Sobrevilla et al. [14]. Our findings corroborate this association, as cyclophosphamide plus doxorubicin was the most frequent treatment (19.7%), followed by carboplatin plus paclitaxel, both commonly used in breast and cervical cancer patients.

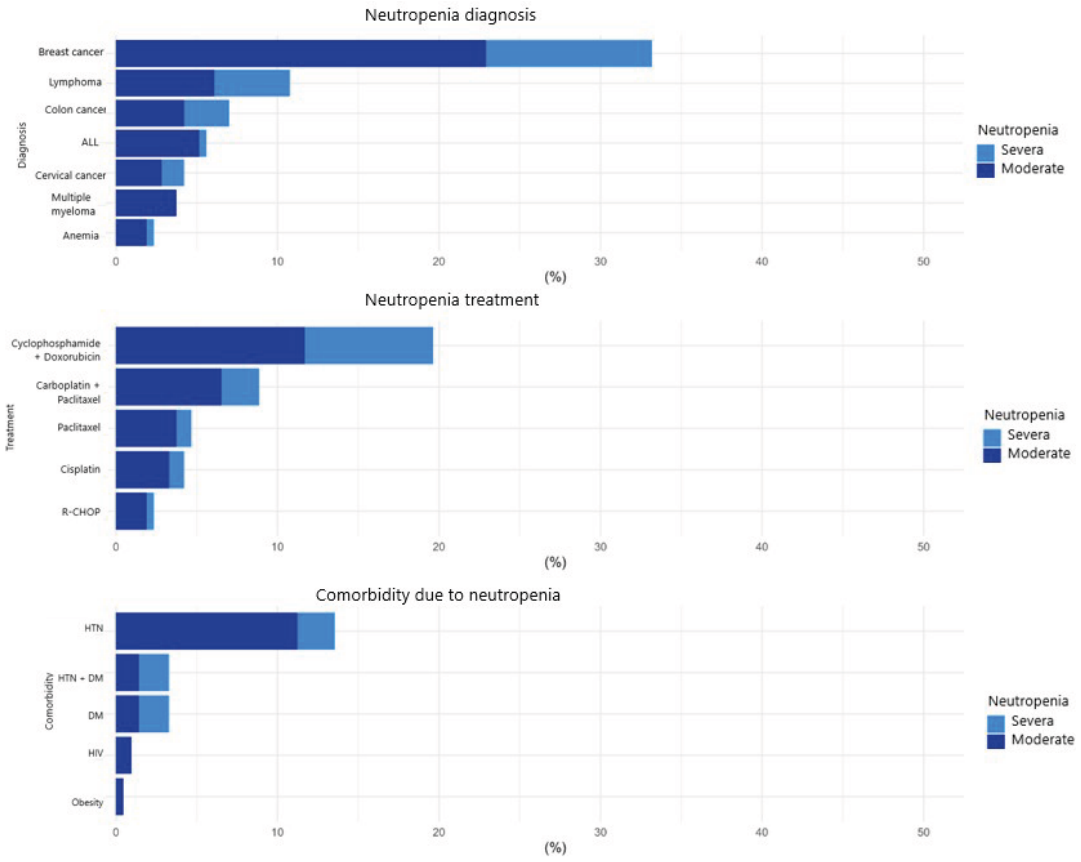

Figure 5. Type of neutropenia according to the most frequent diagnoses, treatments, and comorbidities.

It is important to note that neutropenia is one of the most common complications in patients with oncologic and hematologic conditions, with the potential to interrupt cytotoxic treatment, negatively affecting therapeutic response and quality of life [6,14]. In our study, most neutropenia cases were moderate (70.4%), a finding that aligns with existing literature, which suggests that in the general population, neutropenia tends to present as mild to moderate [13]. However, even moderate forms of neutropenia can increase the risk of opportunistic infections, particularly in immunocompromised patients due to their underlying disease.

Finally, no significant associations were found between the severity of neutropenia and factors such as age, gender, or geographical origin of the patients. This finding underscores that, despite demographic differences, the severity of neutropenia seems to be more influenced by factors intrinsic to the disease and treatments received than by the sociodemographic characteristics of the patients.

6. Conclusions

Neutropenia, a prevalent complication in patients undergoing cytotoxic or immunosuppressive therapies, showed a higher incidence in women; it is attributed to the high prevalence of breast cancer, the most frequent pathology both in the institution and nationally and globally. According to the Pan American Health Organization, more than 491 thousand cases are diagnosed annually in the Americas, and in 2023, the High-Cost Account reported that 49.94% of the 58,813 new cases in the country corresponded to breast cancer (15).

Neutropenia increases the risk of opportunistic infections, as neutrophils, responsible for phagocytosis and releasing bactericidal proteins such as cathepsins and lysozyme, which generate extracellular traps (NETs). Uncontrolled inflammation can lead to excessive NET formation during sepsis, thus causing multiple

organ dysfunction (16). Early diagnosis and appropriate treatment strategies were crucial, especially in outpatient settings.

Early identification of neutropenia helped prevent severe infectious complications that could threaten patients' lives. Factors such as demographics and treatment type influenced severity and prognosis and highlighted the importance of preventive measures, active surveillance, and monitoring protocols to optimize clinical management.

This study underscores the need to continue research and develop strategic guidelines that individualize the management of neutropenia based on hematologic-oncologic diagnosis, stage, and comorbidities.

7. Administrative information

7.1 Additional files

None declared by the authors.

7.2. Acknowledgements

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7.3. Author contributions

Dr. Anillo: Made significant contributions to the statistical analysis and interpretation of the results of the study on the prevalence of neutropenia. Her experience in applied biostatistics was crucial to ensure a rigorous analysis of the data and to obtain relevant conclusions. **Dr. Ángel, Dr. Osorio:** Actively participated in the design of the study and in the collection of data related to the prevalence of neutropenia at the institution. In addition, they contributed with a critical review of the intellectual content of the manuscript. **Dr. Ángel, Dr. Ibáñez:** They were involved in the conception of the study and the interpretation of the clinical data. Their experience in hematology allowed to evaluate the clinical relevance of neutropenia in patients. **Dr. Mieles:** Coordinator of pre-transfusion management, supported the collection and analysis of data related to neutropenia, providing her technical expertise **Dr. Gillian:** From her perspective in clinical epidemiology and hematology, she participated in the design of the study and in the interpretation of data on the prevalence of neutropenia. **Dr. Villegas:** Contributed his experience in clinical effectiveness and data management, supporting the study design, data interpretation, and integration of technological innovations in the analysis. **Drs. Rosado, Osorio T., Cantillo, Arroyo, González, and Padilla:** As physicians at the institution, they made significant contributions to the collection and analysis of data from patients with neutropenia.

7.4. Financing

No author has received direct funding from any commercial entity that could influence the results or conclusions presented in this study

7.5. Availability of data and materials

The data used in this study were collected at our institution with the due authorization of the coordinators of the areas involved. The bibliographic review included related studies, but a small amount of literature specific to our region was found.

7.6. Statements

7.6.1. Ethics committee approval

Clinical cases were not needed

7.6.2. Declaration

Authors assume full responsibility for the opinions and conclusions presented in this article. The journal is not responsible for any errors or omissions, nor for the interpretations or applications derived from the information contained herein

7.6.3. Consent for publication

The patient's legal guardian provided written consent for the publication of this clinical case.

7.6.4. Conflicts of interest

Authors declare that there are no conflicts of interest regarding this manuscript titled "Prevalence of Neutropenia in a Level IV Healthcare Institution in the City of Barranquilla." All authors have independently participated in the development, analysis, and interpretation of data, as well as writing the article.

8. References

1. Eberl M, Davey M. Neutrófilos [Internet]. London: British Society for Immunology; 2023 [cited 2024 Jan 16]. Available from: https://www.immunology.org/public-information/bitesized-immunology/cells/neutrophils
2. Dale DC. Neutropenia [Internet]. Kenilworth, NJ: Manual MSD; 2023 [cited 2024 Jan 16]. Available from: https://www.msdmanuals.com/es-mx/professional/hematología-y-oncología/leucopenias/neutropenia
3. Schwartzberg LS. Neutropenia: etiology and pathogenesis. Clin Cornerstone. 2006;8 Suppl 5:S5–11
4. Boxer LA. How to approach neutropenia. Hematology Am Soc Hematol Educ Program. 2012;2012:174–82.
5. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, et al. Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2011;52(4):e56–93.
6. Lyman GH, Abella E, Pettengell R. Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: A systematic review. Crit Rev Oncol Hematol. 2014 Jun;90(3):190–9.
7. Hashiguchi Y, Kasai M, Fukuda T, Ichimura T, Yasui T, Sumi T. Chemotherapy-induced neutropenia and febrile neutropenia in patients with gynecologic malignancy. Anticancer Drugs. 2015 Nov;26(10):1054–60.
8. Laskey RA, Poniewierski MS, Lopez MA, Hanna RK, Secord AA, Gehrig PA, et al. Predictors of severe and febrile neutropenia during primary chemotherapy for ovarian cancer. Gynecol Oncol. 2012 Jun;125(3):625–30.
9. Garzón JR, Isaza N, Posada A, Méndez R, Arenas J, Ardila MP, et al. Características clínicas y microbiológicas de pacientes con neutropenia febril en un hospital universitario. Infectio. 2019;23(4):347–52.
10. García K, Londoño J, Villegas L, González M, Correa A. Diagnóstico microbiológico en neutropenia febril secundaria a quimioterapia por malignidad hematológica: descripción de una cohorte. Acta Med Colomb. 2020;45(2):71–7.
11. Madrid C, Díaz L, Combariza J, Gálvez K, Olaya V, Ramírez I, et al. Epidemiología de la neutropenia febril en pacientes adultos con neoplasia hematológica, en un período de 26 meses en el Hospital Pablo Tobón Uribe, Colombia. Rev Chil Infectol. 2013;30(2):195–201.

12. González-Leal XJ, Molina-Gamboa J, Bolaños-Meade J, Villela L. Aislamientos microbiológicos en pacientes con neutropenia febril: ¿es apropiado el uso de las guías clínicas internacionales en México? Rev Hematol Mex. 2013;14(3):113–9.

13. Lobatón JF, González ME, Aruachán SE, Meza LA, García M, Borré DP, et al. Caracterización clínico patológica y hallazgos microbiológicos de la neutropenia febril en pacientes oncohematológicos en una clínica privada en la ciudad de Montería-Colombia. Rev Colomb Hematol Oncol. 2020;7(2):33–41.

14. Sobrevilla PJ, Sobrevilla N, Ochoa FJ. Neutropenia inducida por quimioterapia: el punto de vista del oncólogo. Gac Mex Oncol. 2016;15(6):344–9.

15. Organización Panamericana de la Salud. Cáncer de mama [Internet]. Washington, D.C.: OPS/OMS; 2021 [updated 2021 Oct 17; cited 2024 Nov 2]. Available from: https://www.paho.org/es/temas/cancer-mama

16. Godínez-Vidal AR, Carrillo-Esper R, Cabello-Aguilera R. Trampas extracelulares de neutrófilos en sepsis. Med Crit [Internet]. 2020;34(2):156–9. Epub 2022 Aug 8 [cited 2024 Nov 6]. Available from: http://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S2448-89092020000200156. doi:10.35366/93970