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Clinical-epidemiological characterization in patients diagnosed with immune thrombocytopenic purpura at "Vladimir Ilich Lenin" General Hospital

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ABSTRACT

Introduction: immune thrombocytopenic purpura is a bleeding disorder characterized by an isolated decrease in platelets, not associated to any other recognizable pathology. The management of immune thrombocytopenia is a matter of discussion regarding its evolution, diagnosis, prognosis and treatment. Objective: to characterize the patients diagnosed with immune thrombocytopenic purpura clinically and epidemiologically at "Vladimir Ilich Lenin" General Hospital, from 2015 to 2020. Method: an observational, descriptive, cross-sectional study was carried out at the "Vladimir Ilich Lenin" General Hospital, in the province of Holguín, Cuba. The study period ranged from 2015 to 2020. The universe consisted of 30 patients who met the inclusion criteria of the research. The entire universe was studied. Results: female sex (63,3 %) and the age group from 40 to 49 years old (46,7 %) predominated. At the time of admission, 43,3 % of the studied patients presented slight bleeding, and 46,7 %, a platelet count with moderate thrombocytopenia. 56,7 % had a complete response to first-line treatment. Conclusions: female patients, between 40 to 49 years old predominated with mild bleeding and moderate thrombocytopenia at the time of admission. The largest number of patients had a complete response to first-line treatment and progressed to chronicity.

Keywords: Autoimmunity; Bleeding; Thrombocytopenia; Thrombocytopenic purpura.

Immune thrombocytopenic purpura (ITP) is a disorder characterized by an isolated platelet decrease (less than 100 x 10^9/L), not associated to any other recognizable pathology such as heparin-induced thrombocytopenia, disseminated intravascular coagulation, vitamin B9/B12 deficiency, splenic sequestration, portal hypertension, myelodysplasia, congenital thrombocytopenia or lupus erythematosus[1,2,3].

This hemato-immunologic condition is also known as autoimmune, immunologic or primary thrombocytopenic purpura. The term idiopathic thrombocytopenic purpura was used for several years but nowadays should not be used, as it is considered erroneous and ambiguous, due to the importance of the immunological mechanisms of platelet destruction mediated by autoantibodies and T lymphocytes and/or impaired platelet production in its pathogenesis[4,5,6].

The first description of a purpuric syndrome compatible with ITP was made by Avicenna in 1025, but it was not until 1735, when Paul Gottlieb Werlhof described its clinical picture in depth. Therefore, this condition is also called Werlhof disease[7,8].

This hemorrhagic disease is characterized by the premature destruction of platelets by antibodies that are directed against antigens (glycoproteins) that coat platelets, megakaryocytes and cytotoxic mechanisms are involved1.

The most common symptoms of ITP are petechiae, hematomas and ecchymosis after minor blows, which the patient usually does not remember, as well as epistaxis, hematuria, melena, menorrhagia, hematemesis and gingivorrhagia. In more severe cases, spontaneous hemorrhages increase and the probability of central nervous system bleeding is very high[1].

It has a worldwide incidence of 3,3/100 000 adults per year. Newly diagnosed ITP has an annual incidence of 2 to 4 cases per 100 000 population; while the prevalence of chronic ITP in adults is 9,5 to 23 cases per 100 000 population[2,9].

In Europe, the annual incidence is estimated at 2,68 cases per 100 000 adults. One of the highest rates in the Americas is in the United States with about 1,6 ca-

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Conflict of interests
The authors declare that they have no conflict of interest.

ses per 100 000 adults. Data on the incidence of this disorder in Cuba are not entirely clear[2,10].

Although the mortality of this disease is very low, ranging between 0,016 and 0,038 patients per year, it increases with age and the presence of comorbidities, affecting the quality of life in the areas of physical functioning and mental health[2,10].

The management of immune thrombocytopenia is a matter of discussion regarding evolution, diagnosis, prognosis and treatment. Several guidelines have been published expressing different expert opinions, but there is still no worldwide consensus on the most appropriate management of the disease[11].

The ITP has a highly variable clinical course in terms of duration and severity, and the response to conventional treatments is not predictable. Treatments are divided into first-line treatments consisting of corticosteroids, intravenous immunoglobulin (IV Ig) and anti-D immunoglobulin, and second-line treatments consisting of splenectomy and other therapeutic agents[10,12].

Having made the above considerations and taking into account that this pathology despite its importance has been a subject little addressed[9], the present research was conducted with the aim of characterizing the patients diagnosed with immune thrombocytopenic purpura clinically and epidemiologically at "Vladimir Ilich Lenin" General Hospital, from 2015 to 2020.

METHOD

Type of study: an observational, descriptive, cross-sectional study was conducted in patients diagnosed with immune thrombocytopenic purpura at "Vladimir Ilich Lenin" General Hospital, Holguín, Cuba, in the period from 2015 to 2020.

Universe and sample: the universe was composed of 30 patients who fulfilled the inclusion criteria of the research. All patients aged 30 years or older, with a diagnosis of ITP during the study period, and with complete clinical histories were included in the research. The entire universe was studied.

Variables and data collection: the following variables were extracted: sex, age, degree of bleeding on admission (no bleeding, mild bleeding, moderate bleeding, severe bleeding), platelet count on admission (mild thrombocytopenia, moderate thrombocytopenia, severe thrombocytopenia, very severe thrombocytopenia), response to first-line treatment (complete response, response, no response) and evolution to chronicity. Data were collected from the review of medical records.

For the degree of bleeding, it was considered that mild bleeding is the loss of less than 25 % (less than 1 500 mL) of blood volume, moderate bleeding from 25 % to 35 % (between 1 500 mL and 1 750 mL) and severe bleeding greater than 35 % (greater than 1 750 mL). In the case of thrombocytopenia, platelet count figures between 50 x 10^9/L and 100 x 10^9/L are considered mild, moderate between 30 x 10^9/L and 50 x 10^9/L, severe between 10 x 10^9/L and 30 x 10^9/L and very severe figures lower than 10 x 10^9/L. Response to first-line treatment was measured 7 days after the initiation of steroid therapy. Patients with a complete response were those, whose platelet count was greater than or equal to 100 x 10^9/L and there was no bleeding; with response when the platelet count was greater than or equal to 30 x 10^9/L with an increase greater than twice the initial value and no bleeding; and without response when the platelet count was less than 30 x 10^9/L or there was an increase of less than twice the initial value, or the presence of bleeding.

Statistical processing: a model was prepared for data collection, which was processed in a Microsoft Excel database 2013, where it was analyzed by means of descriptive statistics. The data were processed in the Epidat program version 4.0 to obtain relative and absolute frequencies.

Ethical standards: approval for the study was requested from the Medical Ethics Committee and the Scientific Council of the hospital institution, which granted the necessary permissions. The ethical principles of beneficence, non-maleficence, justice and autonomy in scientific research were complied with at all times.

RESULTS

Of the total number of studied patients, 46,7 % were in the age range of 40 to 49 years old. Of the total number of analyzed patients, 63,3 % were women (Table 1).

Table 1. Distribution of patients diagnosed with immune thrombocytopenic purpura according to age and sex. General Hospital "Vladimir Lenin". 2015-2020

Age	Female		Male		Total	
	No.	%	No.	%	No.	%
30 – 39	3	10,0	1	3,3	4	13,3
40 – 49	9	30,0	5	16,6	14	46,7
50 – 59	1	3,3	2	6,7	3	10,0
60 – 69	4	13,3	2	6,7	6	20,0
70 – 79	2	6,7	1	3,3	3	10,0
TOTAL	19	63,3	11	36,7	30	100

Source: Individual Clinical History (Patient Medical Records).

Of the total number of patients, 43,3 % presented mild bleeding at the time of admission (Table 2).

Of the total number of patients, 46,7 % had a platelet count with moderate thrombocytopenia on admission (Table 3).

Table 2. Degree of bleeding in patients diagnosed with immune thrombocytopenic purpura

Degree of bleeding at admission	No.	%
No Bleeding	7	23,3
Mild Bleeding	13	43,3
Moderate Bleeding	8	26,7
Severe Bleeding	2	6,7
TOTAL	30	100

Table 3. Behavior of platelet count in patients diagnosed with immune thrombocytopenic purpura

Platelet Count	No.	%
Mild thrombocytopenia	5	16,6
Moderate thrombocytopenia	14	46,7
Severe thrombocytopenia	8	26,7
Very severe thrombocytopenia	3	10,0
TOTAL	30	100

Of the total studied patients, 56,7 % showed a complete response to treatment (Table 4).

Table 4. Response to first-line treatment in patients diagnosed with immune thrombocytopenic purpura

Treatment Response	No.	%
Complete Response	17	56,7
Response	9	30,0
No Response	4	13,3
TOTAL	30	100

DISCUSSION

In a study conducted by Palmezano *et al*.13 in Colombia, with the aim of estimating the prevalence of autoimmune diseases, it was found that the average age was 46,6 years and there was a higher prevalence in women with 71 %. According to the data of this research, immune thrombocytopenic purpura ranked fourth among all the autoimmune diseases studied with a total of 128 patients, representing 8,8 % and a prevalence of 33 cases per 100 000 patients.

In another study by Palmezano *et al*.14 conducted with the aim of observing clinical variables in a cohort of patients with immune thrombocytopenic purpura, 128 cases were analyzed, of which 73 % of the patients were women, with a median age of 42 years.

In the thesis of León *et al*.[9] carried out with the aim of finding out the clinical, laboratory and evolutionary characteristics of immune thrombocytopenia in adult patients, there was a predominance of the female sex with 82,01 % and a mean age of 45,2 ± 17,3 years old.

The results of the distribution according to age and sex in the present study are in agreement with the three previously cited studies[9,13,14]. Likewise, the studies by Nina *et al*.[10] and Petro *et al*.[15] showed a notable predominance of female sex, but there was no correspondence in terms of mean age, since in both studies this variable was higher than previously described, with values of 59,9 years and 61 years old, respectively.

The cause of the higher proportion of female patients with the disease is still unknown, despite being a common element of several autoimmune diseases[13]. It can be speculated that this is due to an intimate interrelationship between immunological, hormonal and environmental factors inherent to this sex, which would also explain its high incidence in women of late reproductive age.

Although the predominance of female sex is a constant in many studies, the same is not true for the age of the patients, since this element has a wide spectrum of presentation. In elderly patients, in addition to the conjugation of the aforementioned factors, systemic deterioration may play an important role in the manifestation of this condition.

In the study by Nina *et al*.[10], all patients presented some hemorrhagic manifestation at the time of diagnosis, being more frequent at nasal and cutaneous level with 82,60 % and 56,50 % respectively; while in the study by Palmezano *et al*.14, 56 % presented some hemorrhagic manifestation, ecchymosis (40 %), petechiae (39 %), gingivorrhage (26 %) and epistaxis (22 %).

According to León *et al*.[9], minor bleeding was the most frequent clinical expression, with a predominance of cutaneous bleeding, petechiae and ecchymosis with 56,12 % and 52,52 %, respectively.

In the present study, although most of the patients presented bleeding on admission, this was not a common element, as suggested by Nina *et al*.[10] in their study. Most of the attended patients presented mild bleeding, corresponding to the oral cavity, nasal cavity and skin. This data is quite close to those of Palmezano *et al*.[14] and León *et al*.[9].

Although 76,7 % of the patients presented some hemorrhagic manifestation, there was a considerable percentage that did not develop them (23,3 %). The platelet count often serves as a predictor of bleeding severity, but in these cases, no statistically significant correspondence was found to support this, since there were patients without bleeding with moderate and severe thrombocytopenia.

It is likely that these patients had come to the hospital for consultation regarding other reasons, and through the application of clinical methods and laboratory techniques, the diagnosis of ITP was concluded. The non-appearance of bleeding is a peculiar fact, but it should be taken into account that, despite a decrease in platelets in healthy individuals, hematopoietic mechanisms act to compensate that decrease.

In the investigation by León *et al.*[9], at the time of diagnosis, an average platelet count of 58 x 10^9/L is shown, which constitutes mild thrombocytopenia. In contrast, in Nina *et al.*[10], the platelet count at diagnosis averaged 26 x 10^9/L, which can be classified as severe thrombocytopenia. The same happens to the study conducted by Petro *et al.*[15], where the median platelet count on admission to the institution was 12 x 10^9/L.

The results of the present study do not coincide with any of the previous investigations, as patients with moderate thrombocytopenia predominated. Patients with mild and severe thrombocytopenia accounted for 16,6 % and 26,7 %, respectively. These values are lower than those previously mentioned.

As it has been shown, there is often a correspondence between the degree of bleeding and platelet count values. When platelet levels fall sufficiently low to be considered moderate thrombocytopenia (platelets between 30 x 10^9/L and 50 x 10^9/L), this is generally the precise moment when bleeding begins to manifest itself, being the most frequent reason for admission.

The response to first-line treatment was 86,7 %, where 56,7 % and 30 % of patients had a complete response or response to treatment, respectively; behaving similarly to the study by Nina *et al*[10]. In this study, the response to treatment was 96 %, with 61 % and 35 % of patients having a complete response or response to treatment, respectively.

According to Escamilla *et al.*[1], the first-line treatment is prednisone, a corticosteroid that should not be administered until the platelet count increases. Its use cannot be prolonged due to adverse side effects such as Cushing's syndrome, obesity, hyperglycemia, hypertension, acne, osteoporosis and increased infections. At the psychological level it can produce anxiety, emotional instability, irritability, depression, memory alterations and psychosis.

For patients who did not respond to first-line treatment, it was necessary to resort to strategies belonging to the second line of treatment which includes: splenectomy, immunosuppression (mainly with rituximab) and in recent years, thrombopoietin receptor agonists: romiplostim and eltrombopag. The latter have changed the management of chronic ITP, minimizing the risk of bleeding and achieving a long-lasting response with fewer side effects[15].

CONCLUSIONS

There was a predominance of female patients, between the ages of 40 and 49 years old, with mild bleeding and moderate thrombocytopenia at admission. Most patients had a complete response to first-line treatment.

AUTHORSHIP

FMHV: formal analysis, research, methodology, writing-original draft.
DMFS: research, methodology, writing-revision and editing.
BCSR: conceptualization, research, methodology, writing-revision and editing.
RJPH: conceptualization, research, methodology, monitoring, validation.

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Caracterización clínico-epidemiológica de pacientes diagnosticados con púrpura trombocitopénica inmune en el Hospital General "Vladimir Ilich Lenin"

RESUMEN

Introducción: la púrpura trombocitopénica inmune es un trastorno hemorrágico caracterizado por una disminución de plaquetas aislada, no asociado a otra patología reconocible. El manejo de la trombocitopenia inmune es motivo de discusión en lo concerniente a evolución, diagnóstico, pronóstico y tratamiento. Objetivo: caracterizar clínico-epidemiológicamente a los pacientes diagnosticados con púrpura trombocitopénica inmune en el Hospital General "Vladimir Ilich Lenin", en el periodo de 2015 a 2020. Método: se realizó un estudio observacional, descriptivo de corte transversal en el Hospital General "Vladimir Ilich Lenin" de la provincia de Holguín. El periodo de estudio comprendió desde el 2015 hasta 2020. El universo estuvo constituido por 30 pacientes que cumplieron con los criterios de inclusión de la investigación. Se trabajó con la totalidad del universo. Resultados: predominó el sexo femenino (63,3 %) y el grupo de edad de 40 a 49 años (46,7 %). Al momento del ingreso, el 43,3 % de los pacientes estudiados, presentó sangramiento leve y el 46,7 % un recuento plaquetario con trombocitopenia moderada. El 56,7 % tuvo una respuesta completa al tratamiento de primera línea. Conclusiones: existió un predominio de pacientes del sexo femenino, entre las edades de 40 a 49 años, con sangramiento leve y trombocitopenia moderada al momento del ingreso. La mayor cantidad de pacientes tuvo una respuesta completa al tratamiento de primera línea y evolucionaron a la cronicidad.

Palabras clave: Autoinmunidad; Hemorragia; Púrpura trombocitopénica; Trombocitopenia.