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Demographic and clinical characteristics and hematologic alterations in adult patients with dengue fever

Características demográficas, clínicas y alteraciones hematológicas en pacientes adultos con dengue

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ABSTRACT

Introduction: Dengue is an infectious, systemic and dynamic disease, in which there are alterations in hematological variables which can result in severe complications of the disease. In Pinar del Río, in spite of the high incidence of this arbovirosis, there are few reports of the hematological alterations that occur in this disease.
Objective: To describe the main demographic and clinical characteristics and hematological alterations in patients with dengue fever from the Raúl Sánchez health area admitted to the León Cuervo Rubio Teaching and Surgical Clinical Hospital in Pinar del Río province in 2019.
Methods: An observational, descriptive and cross-sectional study was carried out, which included 141 patients. The information was obtained from medical records and databases of the statistical departments. Descriptive statistics of absolute and relative frequencies were applied to the data obtained.
Results: Hospitalization for dengue fever was more frequent in patients between 41 and 50 years of age (26,2 %), men (54,6 %) and white-skinned (85,1 %). The most prevalent symptom was fever (92,2%) and complications were effusion (19,1 %) and bleeding (18,4 %). 59,6 % of patients with dengue fever presented hematological alterations, more frequent in patients over 50 years of age (31,2 %) and white skin. Leukopenia predominated (39,6 %), followed by hemoconcentration (19,9 %) and thrombocytopenia (15,6 %).
Conclusions: Dengue presented demographic and clinical characteristics similar to national and international reports, and hematologic alterations were found in more than half of the patients included in the study.

Keywords: Dengue; Complications; Blood Platelets; Platelet Count.

RESUMEN

Introducción: el dengue es una enfermedad infecciosa, sistémica y dinámica, en la que se presentan alteraciones en las variables hematológicas, las cuales pueden resultar en complicaciones graves de la enfermedad. En Pinar del Río, a pesar de la alta incidencia de esta arbovirosis, existen escasos reportes de las alteraciones hematológicas que se presentan en esta enfermedad.
Objetivo: describir las principales características demográficas, clínicas y alteraciones hematológicas en pacientes con dengue del área de salud Raúl Sánchez, ingresados en el Hospital Clínico Quirúrgico Docente León Cuervo Rubio de la provincia Pinar del Río, en el año 2019.
Métodos: se realizó un estudio observacional, descriptivo, y transversal que incluyó a 141 pacientes. La información se obtuvo de las historias clínicas y las bases de datos de los departamentos estadísticos, a los datos obtenidos se les aplicaron estadística descriptiva del tipo de frecuencias absolutas y relativas.
Resultados: la hospitalización por dengue fue más frecuente en pacientes entre 41 y 50 años, hombres y de piel blanca. El síntoma más prevalente resultó la fiebre, como complicaciones el derrame y el sangramiento. El 59,6 % de los pacientes con dengue presentó alteraciones hematológicas, más frecuentes en mayores de 50 años y de piel blanca. Predominó la leucopenia, seguido de la hemoconcentración y la trombocitopenia.
Conclusiones: el dengue presentó características demográficas y clínicas similares a los reportes nacionales e internacionales constatándose alteraciones hematológicas en más de la mitad de los pacientes incluidos en el estudio.

Palabras clave: Dengue; Variables Hematológicas; Complicaciones; Plaquetas; Recuento de Plaquetas.

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INTRODUCTION

Among the emerging infectious diseases affecting humans and constituting a global health problem is Dengue, which along with other arbovirosis is transmitted by the Aedes Aegypti mosquito (main vector transmitter).[1] It generally presents as an epidemic, with a wide spectrum of clinical pictures, among the most characteristic symptoms and signs are: fever, headache, myalgia and arthralgias among others.[2] The main hematological alterations that occur are leukopenia, hemoconcentration and especially thrombocytopenia (with figures below 150x109/l), due to the suppression of hematopoiesis and increased vascular permeability, among other causes, constituting one of the warning signs of Dengue infection.[3]

Bleeding is the most frequent complication of this entity, as well as effusions and shock.[4,5] The severity and evolution of the cases depend on host, virus and environmental factors. Risk factors include age, especially children and the elderly, white race, female sex, the patient's immune status, the virulence of the infecting strain and some chronic diseases, among others.[6]

The WHO estimates that more than 390 million human beings fall ill annually, of which 2,5 % die,[7] a figure that could underestimate the real incidence if asymptomatic cases that are not quantified are taken into account.[2] All this explains why it becomes a serious health dilemma for humanity, with a very high cost, taking into account that the medical care provided is in addition to the control measures and the working hours lost by the patients. Dengue is the most frequent and rapidly progressing infectious disease in the world [8].

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Since the middle of the last century, the virus has been spreading in Central and South America,[9] due to several economic and social factors, such as travel, migration, climate change and inadequate environmental hygiene [10], in addition to the ecological characteristics of this region.[11]

In Cuba, the first epidemic was reported in 1981, which affected all the provinces,[10] there is still a risk of Dengue transmission since population practices that favor it persist, in spite of the fact that our health system has taken strategies for more than 20 years, managing to increase the level of knowledge of the population about this disease and its prevention.[12] Surveillance is maintained because the transmitting mosquito still exists in the country and a significant number of travelers and collaborators who visit, reside or work in African countries, where outbreaks are still frequently reported. Outbreaks have been reported in several provinces of our country in the last decades, including Pinar del Rio.[13,2]

Dengue is a viral disease of growing importance for human health, so that knowledge of the main symptoms, hematological alterations and complications associated with the course of the disease is essential for the proper management of these patients. In Pinar del Río, in spite of the high incidence of the disease, few studies have been carried out in this sense.

Therefore, the aim of this study is to describe the main demographic and clinical characteristics and hematological alterations in patients with dengue fever from the Raúl Sánchez health area admitted to the León Cuervo Rubio Teaching and Surgical Clinic Hospital in Pinar del Río province in 2019.

METHODS

An observational, descriptive and transversal study was carried out in the Teaching, Clinical, Surgical Hospital León Cuervo Rubio, in the year 2019. Universe: The universe was represented by all patients admitted to that institution during that year, belonging to the Raúl Sánchez health area, with a confirmed diagnosis of Dengue (492 patients). Sample: A non-probabilistic purposive sampling was carried out and the sample (n = 141 patients) was represented by all patients who met the inclusion criteria defined for this research.

Inclusion criteria: Patients with a confirmed diagnosis of Dengue, belonging to the Raul Sanchez health area, adults (over 18 years of age), with no history of suffering from hematological diseases whose clinical history allowed the collection of all the variables to be studied.

Exclusion criteria: Patients with missing information in the clinical histories.

Definition and operationalization of variables: Qualitative variables (sex, skin color, clinical manifestations, hematological alterations, complications) and quantitative variables (age, hematocrit, leukocyte count, platelet count) were identified based on previous knowledge.

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Operationalization of variables

Variable	Classification	Scale	Indicator
Age	Discrete quantitative	19 to 30 years of age 31 to 40 years 41 to 50 years From 51 to 60 years old 61 to 70 years old Older than 71 years	Absolute frequency (AF) y and relative frequency (RF).
Skin color	Qualitative nominal polytomous	White, black, mestizo	Absolute frequency (AF) and relative frequency (RF)
Sex	Qualitative nominal dichotomous	Male Female	Absolute frequency (FA) and relative frequency (FR)
Clinical manifestations	Qualitative nominal polytomous	Fever Headache Arthralgia Myalgia Pruritus Exanthema Abdominal pain	Absolute Frequency (AF) and Relative Frequency (RF)
Complications	Qualitative nominal polytomous	Stroke Bleeding Shock	Absolute frequency (AF) and relative frequency (RF)
Hematocrit	Quantitative continuous Discretized	Normal: In man from 0,41 to 0,54 L/L In woman from 0, 37 to 0,47 L/L Altered: Above (hemoconcentration) or below (anemia) normal reference values for both sexes	Absolute Frequency (AF) and Relative Frequency (RF)
Total leukocyte count	Quantitative continuous Discretized	Normal: 5 to 10 x 109/L Altered: below 5 x 109/L (leukopenia) or above 10 x 109/L (leukocytosis)	Absolute Frequency (AF) and Relative Frequency (RF)
Platelet count	Quantitative continuous Discretized	Normal: 150 to 350 thousand x 109/L Altered: below 150 x 109/L (thrombocytopenia) or above 350 thousand x 109/L (thrombocytosis)	Absolute Frequency (AF) and Relative Frequency (RF)
Hematologic alterations	Qualitative nominal dichotomous	No: When the hematocrit, platelet count and total leukocyte count values	Absolute Frequency (AF) and Relative Frequency (RF)

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		are within the normal values described for these variables. Yes: When the values of hematocrit, platelet count and total leukocyte count are altered	
Type of hematological alteration	Qualitative nominal polytomous	Alterations in hematocrit: Anemia or hemoconcentration. Leukocyte alterations: Leukopenia or leukocytosis. Platelet alterations: Thrombocytopenia and Thrombocytosis	Absolute frequency (AF) and relative frequency (RF)

Methods of data processing and analysis:

Empirical (observation, documentary review), theoretical (analysis and synthesis and logical historical) and statistical (descriptive) methods were used for the research. In order to obtain the necessary information, an analysis of the protocols for the care of patients with Dengue fever was carried out to learn about the current situation.

With the previous knowledge, qualitative and quantitative variables were identified, which allowed the application of elements of descriptive statistics.

The procedure for the collection of information was as follows: the medical records of the affected patients were reviewed, as well as the databases of the statistical departments of the León Cuervo Rubio Surgical and Clinical Teaching Hospital in order to obtain the necessary data and incorporate them into a database in Microsoft® Excel 2010.

Statistical processing: The information obtained from the patients' medical records was stored in a database created with Microsoft® Excel 2010 software and processed with SPSS version 22 working on Windows XP.

For the statistical analysis of said information and given the characteristics of the same, the final results were processed and presented in distribution tables and frequencies (absolute and relative %), and figures, for better understanding.

This research complied with the basic ethical principles of the research process. A research project was prepared, discussed and approved by the Scientific Council of the Faculty of Medical Sciences "Dr. Ernesto Guevara de la Serna" and its corresponding Ethics Committee. All data obtained were used for strictly professional purposes, respecting the identity and confidentiality of the information collected.

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RESULTS

Table 1. Distribution of patients taking into account age, sex and skin color. León Cuervo Rubio Teaching Clinical Surgical Hospital, 2019.

| Age (years)	Sex				Skin color						Total	
	Female		Male		White		Mestizo		Black			
	No.	%	No.	%	No.	%	No.	%	No.	%		
De 19 a 30	8	5,7	20	14,2	25	17,7	1	0,7	2	1,4	28	19.9
De 31 a 40	11	7,8	6	4,3	15	10,6	0	0,0	2	1,4	17	12.1
De 41 a 50	19	13,5	18	12,8	27	19,1	1	0,7	9	6,4	37	26.2
De 51 a 60	16	11,3	13	9,2	26	18,4	0	0,0	3	2,1	29	20.6
De 61 a 70	8	5,7	12	8,5	18	12,8	0	0,0	2	1,4	20	14.2
Mayor de 71	2	1,4	8	5,7	9	6,4	0	0,0	1	0,7	10	7.1
Total	64	45,4	77	54,6	120	85,1	2	1,4	19	13,5	141	100.0

Source: Medical Records.

Table 1 shows that the most represented age group was 41 to 50 years old (26,2 % of the sample); the presence of patients older than 71 years old with dengue fever was less frequent (7,1 %). Men (54,6 %) and white skin color (85,1 %) were more frequent in the group of patients studied.

Table 2. Distribution of patients according to clinical manifestations.

Clinical manifestations	No.	%
Fever	130	92,2
Headache	110	78,0
Arthralgia	97	68,8
Myalgia	79	56,0
Retro orbital pain	74	52,5
Pruritus	47	33,3
Exanthema	45	31,9
Abdominal pain	39	27,7

Source: Clinical Histories.

On studying the wide range of symptoms and signs present in the patients, it was found that 92,2 % of the patients presented fever, this being the most frequent symptom, followed by headache and arthralgia, observed in 78,0 % and 68,8 % of the patients studied, respectively.

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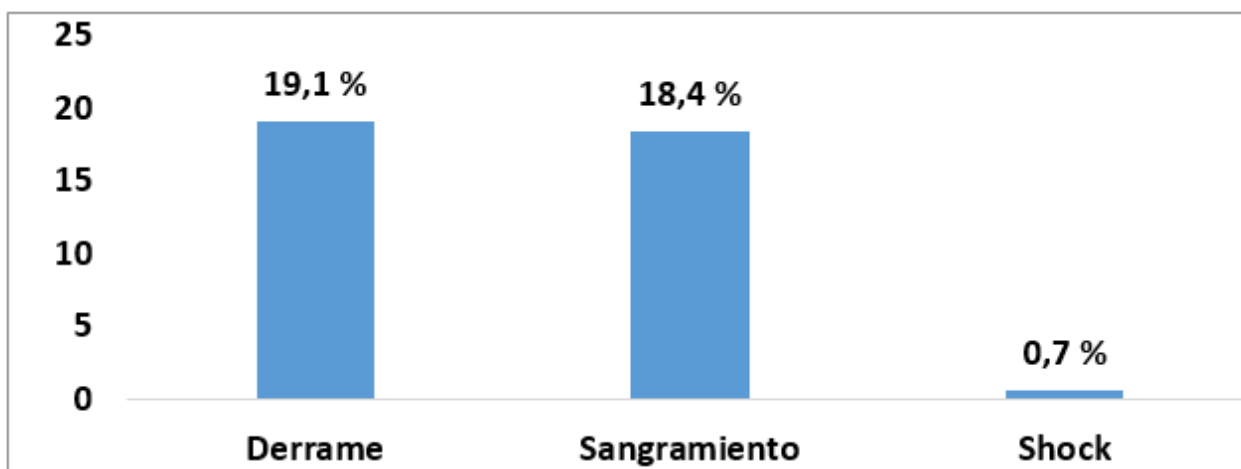
Source: Clinical Histories.

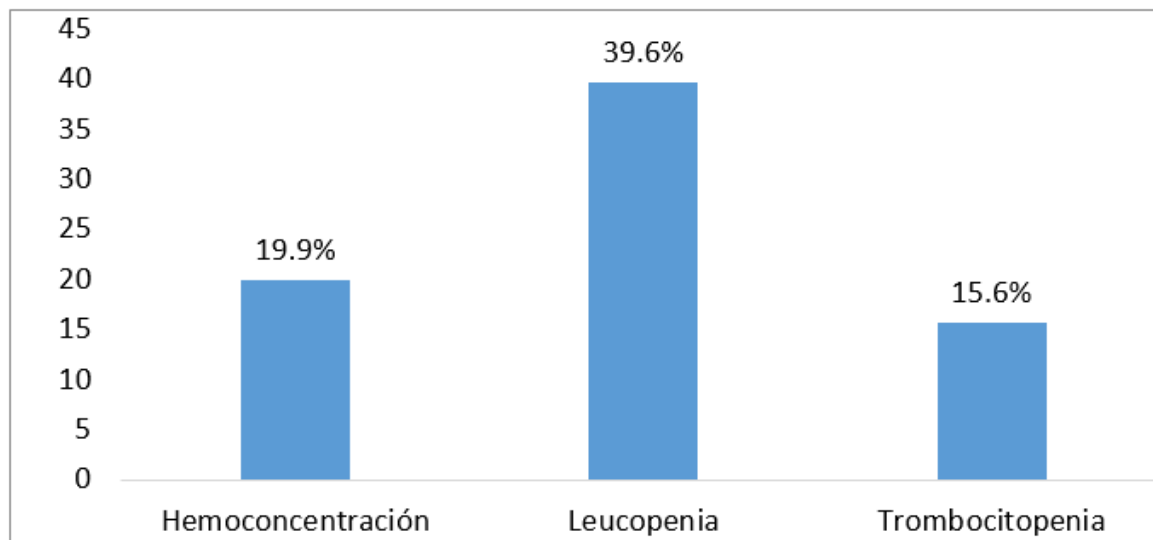**Fig. 1** Frequency of complications in the series studied.

In the series studied, effusion was the most frequent complication with 19,1 %, followed by bleeding with 18,4 % and less frequent shock with only 0,7 %.

Table 3. Distribution of patients taking into account the presence or absence of hematological alterations according to age, skin color and sex.

Age	Hematological alterations					
	No		Yes		Total	
	No.	%	No.	%	No.	%
From 19 to 30 years of age	14	24,6	14	16,7	28	19,9
From 31 to 40 years	9	15,8	8	9,5	17	12,1
41 to 50 years of age	19	33,3	18	21,4	37	26,2
51 to 60 years old	7	12,3	22	26,2	29	20,6
61 to 70 years	6	10,5	14	16,7	20	14,2
Older than 70	2	3,5	8	9,5	10	7,1
Total	57	40,4	84	59,6	141	100
Skin color						
B	47	82,5	73	86,9	120	85,1
M	1	1,8	1	1,2	2	1,4
N	9	15,8	10	11,9	19	13,5
Sex						
F	27	47,4	37	44,0	64	45,4
M	30	52,6	47	56,0	77	54,6

Source: Medical Records.

The table shows that, out of a total of 141 patients, 59,6 % presented hematological alterations, with 26,2 % corresponding to patients in the 51-60 years age group followed by the 41-50 years age group with 21,4 %, with these alterations also predominating in patients with white skin color (86,9 %) and male sex (56,0 %).

Source: Medical records.

Fig. 2 Frequency of hematological alterations in the series studied

The figure shows that in the present study leukopenia predominated followed by hemoconcentration and thrombocytopenia, with 39,6 %, 19,9 % and 15,6 % respectively.

DISCUSSION

Dengue virus infection is one of the most important public health problems in tropical countries, affecting a large number of population of different ages, sex and race.

In the present investigation, the most represented age group was 41 to 50 years old (26,2 %) and the male sex with 54,6 % of the sample, which could be related to the greater exposure to the vector in the early morning and evening hours, as well as to the place and type of work performed by the person, with men being more prone to be out of the home at these times and to perform night work. These results correspond with studies conducted by Baitha[14] in similar studies.

In the study, patients with white skin color predominated with 85,1 %, which can be explained by the predominance of white skin in the population group to which the sample belongs. This aspect is not referred to in the literature reviewed.

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Dengue presents a variation in its clinical presentation depending on the patient and the incubation period, where the most frequent symptoms are fever and headache, with myalgias, arthralgias, retroorbital pain, pruritus, exanthema and sometimes abdominal pain.[15,16] Accordingly, in the present investigation 92,2 % of the patients studied had fever and 78,0 % and 68,8 % had headache and arthralgia, respectively.

Fever is a clinical manifestation that accompanies a large number of diseases, especially infectious diseases. In the particular case of dengue fever, the entry and replication of the virus in the cell provokes a powerful immune response with the release of proinflammatory cytokines such as IL-1β and IL-6 that induce the production of prostaglandins (PGE2) by the pre-optic area of the hypothalamus, which are directly responsible for triggering the mechanisms of temperature elevation, increasing the hypothalamic thermostat set point, creating a new balance between heat production and heat loss by the organism. The presence of fever in these patients is reported in more than 90 % of cases in multiple investigations, accompanied in most cases by headache, arthralgias and/or myalgias.[14,17,18]

Bleeding by different routes, pleural effusion and shock are usually the most frequent complications in patients with dengue, mainly due to the hematological alterations mentioned above. Hemorrhage or bleeding may be the result of the previously described vascular endothelial lesion that causes an alteration of hemostasis (physiological mechanism of protection against blood loss), thrombocytopenia or platelet malfunction that may cause aberrant coagulation or a combination of both factors, which supports the results presented in the present investigation.

The amount of bleeding may vary from mild to severe in dengue hemorrhagic fever, causing in some cases a fatal outcome, and will depend on the degree of endothelial lesion and the state of platelets.[19] The liquid that escapes to the extravascular space accumulates in different cavities (pleural and ascitic effusions) causing, depending on the amount, respiratory difficulty.[20]

Leukopenia is usually a frequent finding in about 68,4 % of patients,[21] or the majority of cases, which corresponds to the present study. In another study of 99 patients, 44 had leukopenia.[20]

When the cell becomes infested with the dengue virus, the infection migrates to the lymph nodes, recruiting monocytes and macrophages which become the target of the infection, which spreads through the lymphatic system, affecting several cells such as splenic and hepatic macrophages. The virus also affects circulating mononuclear cells in the blood, other immune cells may undergo apoptosis, causing leukopenia which predisposes the patient to other infections.[22] Shamsunder reports an incidence of leukopenia of 20 %,[23] lower than in the studies cited above and in this study.

Hemoconcentration, calculated by an increase of 20 % or more in hematocrit, suggests hypovolemia due to increased vascular permeability and plasma extravasation.[24] The magnitude of hematocrit variation may be related to the appearance of hemorrhagic manifestations. The immune response generated by the virus and the activation of monocytes, macrophages and lymphocytes among other defense cells, increase the production of inflammatory cytokines (Interleukins, interferon, tumor necrosis factor and others) and this storm of cytokines together with the activation of complement by the degradation products of the virus injure the endothelial cells increasing vascular permeability, causing fluid to leak from inside the cell, causing cellular dehydration and hemoconcentration. This justifies the results obtained in the study, where the main alteration in hematocrit was hemoconcentration.[25]

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Suwarto and Hidayat in their study report that 16,9 % and 12,1 % of patients had hemoconcentration and thrombocytopenia respectively.[26] Similar result to the present investigation where 19,9 % presented elevated hematocrit values and 15,6 % a low platelet count, in addition to leukopenia in 39 % of cases. Several studies reviewed report the three hematological alterations already described, with high incidence,[27,28] while another study reviewed only coincides with leukopenia in 45,5 % of the cases, but hematocrit was elevated in only 9,8 % of the cases.[29]

In severe infection with increased vascular permeability, decreased blood volume, blood pressure and hemodynamic instability, shock may appear as a complication and frequent cause of death of the patient if not treated adequately and in a timely manner.[30,31]

Hematological alterations are common in the course of dengue infection, due to the pathophysiology of this disease, with a decrease in the number of platelets (thrombocytopenia) and leukocytes (leukopenia), as well as an increase in hematocrit (hemoconcentration), which is consistent with the results obtained in the present study. The appearance of these laboratory findings are frequently reported and are usually between days 3 and 8 of the course of the disease.[27]

CONCLUSIONS

After all the analysis, it can be concluded that hospitalization for dengue fever was more frequent in patients between 41 and 50 years old, male and white, with hematological alterations being more frequent in white patients over 50 years old.

The clinical manifestations included fever, headache and arthralgias. Hematological parameters were modified during admission in most of the patients, with changes in platelet count being related to the subsequent appearance of complications and hematological alterations being responsible for a longer hospital stay.

Conflict of interests
The autors declare that does not exist an interest conflict.

Authorship Contribution
the authors participated in the conceptualization, research, writing – initial draft, writing – revision and editing.

Additional material
Additional material to this article can be consulted in its electronic version available at:
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