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Main Hematological Alterations Found in Patients Affected by New Coronavirus Infection

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Abstract: Covid-19 is a highly infectious disease caused by the new Coronavirus, which was identified in Wuhan in China and caused covid-19, 11,821 cases and 259 deaths were recorded in the first 30 days of infection, it is known that the disease causes clinical changes, so hematology is a type of test that analyzes information about the types and amounts of components in the blood as: Red blood cells; White blood cells; Platelets. The present study aimed to present the main hematological alterations found in patients hospitalized by Covid-19. The most prevalent mild symptoms include fever and cough, while in severe patient's respiratory failure occurs, so it is possible to observe in the blood test a significant decrease (10% - 20%) of oxygen saturation. However, it was observed that there was a prevalence of changes related to leukocytes and platelets, however, lymphopenia was also present in reports made by authors.

Keywords: Covid-19. Epidemiology. Hematology. Clinical Manifestations

1. Introduction

Covid-19 is a highly infectious disease caused by the new Coronavirus associated with severe acute respiratory syndrome 2 (SARS-CoV-2). In December 2019, this new virus was transmitted, which was identified in Wuhan, China and caused Covid-19, and then spread and transmitted quickly from person to person worldwide (VIEIRA, 2020).

Since 2019, when the first case arose, the virus has spread rapidly, in the first 30 days, China recorded 11,821 cases and 259 deaths. (SAMPAIO, 2020). In January 2020, the World Health Organization (WHO) considered the disease as an important international health crisis (HALLAL *et al*, 2020).

In relation to the first reported and confirmed cases, in Brazil occurred in February, and several actions were used with the intention of reducing the progress of the disease. On February 3, 2020, the country declared A Public Health Emergency of National Importance (ESPIN), in March, who said there was a global pandemic with about 118,000 cases in 114 countries and territories, in April the number of new cases was already approaching 2 million in almost all countries, and more than 100,000 confirmed deaths worldwide (HALLAL *et al*, 2020; BRAZIL, 2020).

A few months after the discovery of the virus, the number of confirmed cases worldwide reached more than 23 million people, and just over 800,000 deaths by the end of August 2020. In the same period, the United States led the world ranking, both of confirmed cases (5,755,002), and of deaths, (177,773), and Brazil occupied the 2nd position in total cases (3,622,861), and 2nd position in total deaths (115,309) (LIMA *et al*, 2021).

Covid-19 causes clinical changes that vary according to each individual's organism, the most prevalent and mild symptoms include fever and cough, while the most serious symptoms are respiratory failure and chest pains. Diagnosis can be made through a medical consultation, but for better confirmation it is necessary to perform laboratory tests. Hematology is one of the crucial tests in this investigation, it studies the elements that make up blood such as: Red blood cells; Leukocytes; Platelets; The objective of hematological analysis is to identify if there are changes in these elements, such as lymphopenia, lymphocytosis and thrombocytopenia. In addition to its use to establish a diagnosis, it is used for the follow-up of patients diagnosed with Covid-19 (AZEVEDO, 2020).

The choice of the theme proposed a differentiated look at Hematology because this area of activity is extremely important for concrete diagnoses, considering that this technology is also present in the follow-up of patients hospitalized by Covid-19. This literature review aimed to present the main hematological alterations found in patients affected by infection of the new coronavirus, and to report the most prevalent symptoms of Covid-19.

2. Methodology

This is a bibliographic review study, that is, a survey of theoretical reference from scientific publications, which is nationally and internationally involving the main clinical manifestations and hematological effects found in patients affected by infection of the new coronavirus.

The data collection occurred through the Coordination for the Improvement of Higher Education Personnel (CAPES) and Google Academic.

The research began in April 2020 by the inclusion criteria: works in English and Portuguese, published in the last five years, which deal with topics related to involving the main clinical manifestations and hematological effects found in patients affected by infection of the new coronavirus. These, available for free online. Exclusion criteria include: works whose text is not available in full, duplicated, review, meta-analysis, and also works that, after reading, were not related to the research objective.

Regarding the data appreciation, this was performed qualitatively, prioritizing the analysis of micro processes, understanding, interpreting and dialing these findings, inter-relating them, through the established criteria.

Therefore, all rules related to ethics and copyright were obeyed, since as a result of the bibliographic characteristic of this study, it was not necessary to evaluate by the Research Ethics Committee.

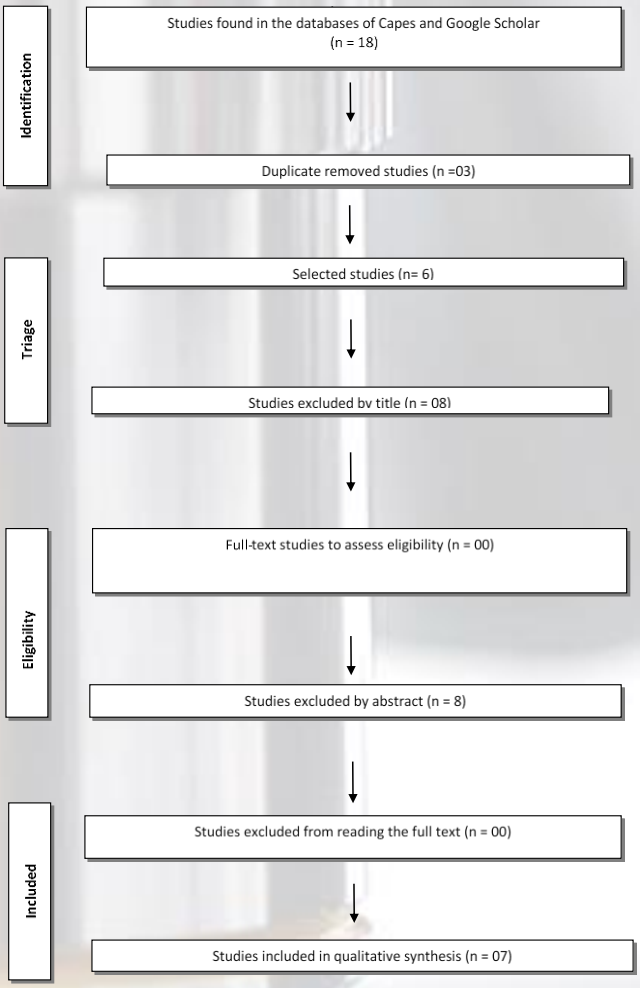

Figure 1. Flowchart of Selection Criteria and inclusion of studies

3. Results and Discussion

Regarding the results found, a total of 18 works were analyzed, but only 07 works were included in the research, respecting the inclusion criteria.

No.	Date	Title	Authors	Periodic	Goals	Findings
1	2020	Predictive factors for severe evolution of the patient with COVID-19	Lucas Antônio Garcia de Carvalho; Abner Fernandes da Silva; Anna Luiza Campos de Castro; Bruno Severo de Castro Lippe; Felipe Yoneda Reyes; Gabriel Yoshiaki Hata; Isabella de Moura Magalhães; Marina Mattuella Debenetti; Matheus Lorenzetti Peron; Victory of Moura Magalhães.	Dissertation published in a journal by the national journal in Curitiba, through the Undergraduate Program in Medicine by the Pontifical Catholic University of Minas Gerais.	Discuss through a review of the literature, the main alterations to physical examination, laboratory and imaging tests that suggest an unfavorable evolution for patients affected by COVID-19.	A meta-analysis with 13 studies and 2,738 symptomatic patients, among which 2,386 had alterations in chest CT of thin sections, the most found standard of matte glass 85.49% (CI: 64.74%-97.89%), being associated with consolidations in 58.42% (CI: 48.46%-67.58%). Other relevant patterns found that corroborate the severe evolution of patients are interlobular septal thickening in 48.46% (CI: 11.44%-86.19%), pleural thickening in 52.46% (CI: 15.53%-87.54%) and air bronchogram in 46.46% (CI: 17.76%-76.95%). The distributions of these pulmonary lesions were observed to be bilateral in 81.80% (CI 73.94%-88.51%). It also points out that chest X-ray has no sensitivity to diagnose frostglass opacities, being normal at the beginning of the disease.
2	2020	Hematological Repercussions on COVID-19 Infection	M.V.C. Azevedo; C.M.C. Milk; A.C.C.F.S. Melo; P.G.L. Gonçalves; J.A.H. Soares; L.C. Bruno; E.S.D.S. Lelis; M.E.S.O. Araújo; R.D.N. Welcome; M.F.M. Soares.	Dissertation published in a journal by the international journal in Teresina, through the Uninovafapi University Center.	Describe the main hematological repercussions scientifically proven in patients infected with COVID-19.	An exuberant inflammatory response similar to cytokine release syndrome was observed in patients with severe COVID-19 infection. This picture corroborates the evolution of hematological complications, the most frequent being hypercoagulability with disseminated intravascular coagulation (IVC), associated with thromboembolic accidents and hemophagocytic lymphohistiocytosis

					(HLH) or macrophagic activation syndrome (MAS). Among the changes in the blood count, we highlight the significant increase in the cell volume of monocytes, leukopenia, lymphopenia (83.2%), neutrophilia, thrombocytopenia, ferritin increase, DHL, C-reactive protein (60.7%), D-dummer (43%), TAP, TTPa, fibrinogen, procalcitonine, IL-6 and troponin. In relation to the factors of worse prognosis in patients infected with SARS-CoV-2, it is important to highlight the elevation of Dd (DD) greater than 3.0 ug/mL and prolongation of prothrombin time (PT), especially if 1.5 times higher than the reference value.	3	2020	The Covid-19 Pandemic: A Narrative Review of The Main Aspects Related to the New Coronavirus.	Isabela Cristina Lima Aroeira.	Research paper presented as a mandatory requirement for obtaining a Bachelor's degree in Medicine from the Pernambuco School of Health - FPS	Conduct a narrative review on the main epidemiological, pathophysiological, clinical and diagnostic topics of COVID-19.	A study conducted from the analysis of the first 425 confirmed cases in Wuhan described some epidemiological characteristics of COVID-19. The results showed that the mean age of the infected was 59 years and 56% belonged to the male gender [3]. Regarding the severity of the infection caused by the new coronavirus, the CDC of China recorded, until February 11, 2020, 44,672 cases, 80.9% mild or moderate cases, 13.8% severe cases, and 4.7% critical cases. The overall mortality rate was 2.3%, and 81% of deaths occurred in patients over 60 years of age. In critical cases, this

						rate was 49%							
4	2020	Immune Thrombocytopenia Associated with Sars-COV 2 infection.	J.R.B. Franco; M.W. Kings; J.P.P. Silveira; K.A.S.S. Lopes; L. Medeiros; T.S. Datoguia; E. Boturão Neto; J.E. Nicholas.	Dissertation published in a journal by the international journal, by UniRV Campus Aparecida GO, Brazil; and also, by the Goiano Institute of Oncology and Hematology (INGOH), Goiânia, GO.	Coronavirus disease (COVID-19) was characterized by the World Health Organization as a pandemic in March 2020. Symptoms of cough, progressive dyspnea, fever, and myalgia are commonly present. However, the clinical spectrum covers involvement of various organs and systems. Hematological changes have been described in SARS-Cov2 infectio	Male patient, 31 years old, health professional, reports exposure to possible source of contamination on 20/06/2020. See that a data of onset of his symptomatology occurred on 23/06/2020 (D1) and consisted of odinophagia, followed by high fever and astherin. He has diabetes mellitus, hypertension and dyslipidemia, all under control with medication. He sought the emergency service, with a fall in oxygen saturation and aquipnea on 07/02/2020 (D9) and was admitted to the ICU, requiring NIV. Chest tomography showed pulmonary involvement in 30-50% of the pulmonary					n. Retrospective studies identified leukopenia in 25% of patients, lymphopenia in 63% of cases, and thrombocytopenia in 33%, and platelet levels below 100,000/mm3 are observed in less than 5% of cases.	parenchyma and showed no changes in renal function, no signs of sepsis, IVC, or multiple organ failure. I was on ceftriaxone, cefepima, methylprednisolone, intermediate-dose anticoagulant (0, 5 mg / kg 12 / 12h) and convalescent plasma therapy (03/07/2020, D10). The patient is blood type A positive. The two transfused bags were corrected from the same donor, a 55-year-old man, with IgM quantification of 3.7 AU/mL and IgG: 82.1 AU/mL (CLIA methodology - chemiluminescence). The patient reports that one day after receiving the plasma, he already presented the significant improvemen

						t of symptoms, and hospital discharge on 07/07/2020 (D14), asymptomatic. It states that it did not have adverse effects on therapy. already had significant improvement in symptoms, and high hospital discharge on 07/07/2020 (D14), asymptomatic. It states that it did not have adverse effects on therapy. already had significant improvement in symptoms, and high hospital discharge on 07/07/2020 (D14), asymptomatic. It states that it did not have adverse effects on therapy.				Federal University of Juiz de Fora-MG, Brazil.	ng cardiovascular, kidney, gastrointestinal and hematological manifestations. In addition to laboratory alterations that reflect an increase in inflammatory activity, blood count and coagulation parameters are also frequently deregulated in severe COVID-19. The objective of this work is to summarize and review the main hematological manifestations of infection by the	bepresent, especially in cases with secondary bacterial infection or cytokine storm. In coagulation, it is frequent to increased-dummer, prothrombin time, activated thromboplastin time and fibrin degradation products, also with prognostic implications. The occurrence of thromboembolic, venous and arterial events is quite common, especially in the severe patient.
5	2020	Hematological manifestations in COVID-19	S.T.F. Grunewald	Research work presented as a mandatory requirement to obtain the undergraduate degree by the	Covid-19 is a multisystemic disease with several extrapulmonary manifestations, includi	In the blood count, the most frequent changes are lymphopenia and thrombocytopenia, both with prognostic value. Neutrophilia may also						

					new corona virus.	
6	2020	COVID-19 and the hematology laboratory: a review of recent literature	Mark Fleury Kneip	Review article published by the international journal, and the Federal University of Rio de Janeiro (UFRJ).	COVID-19 manifests itself mainly as a respiratory tract infection. However, a huge number of studies shows characteristics of a systemic disease with repercussions on the cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic and immunological systems	COVID-19 presents important alterations of the hematopoietic system and is often associated with a state of hypercoagulability. Careful evaluation of laboratory indices at the onset of the disease and during evolution can help the clinical staff to formulate a treatment approach adapted to the situation, besides allowing special attention to those patients who are most in need.
7	2020	A Report of Experience of Professionals Inserted in the Expanded Center of Interprofessional Care During the Emergence of COVID-19.	Cleverson Felipe da Silva Ferreira; Bruna Kérsia Vasconcelos Santos; Jane Eduarda of Lira Moura; Monalisa Ferreira de Vasconcelos; Lysrayane Kerullen David Barroso; Ana Lorena Madeiro de Lima;	Paper Published by E-Publish-Science & Health: Updates on COVID-19.	The objective of this work is to reflect on the multiprofessional performance in the Expanded Interprofessional Care Center (NACI), in a Psychiatric Hospitalization Unit in the city of Sobral-CE	In the experience report, it is discussed about the creation and composition of NACI, as well as the use of care management during activities and experiences from interprofessionality.

Therefore, it is noticed that there is no predilection about the choice of the journal for publication on the theme chosen in the period studied. In addition, it was observed that the papers dealing with the subject were scientific articles.

Finally, in the following sections we have the main points that the authors consulted discuss about the main clinical manifestations and hematological effects found in patients affected by infection of the new coronavirus.

Regarding the record of the first case confirmed by Covid-19 in Latin America, this occurred in Brazil, a 61-year-old Brazilian who had visited Lombardy in northern Italy, returned to the country, specifically to São Paulo on February 21, 2020, one month after the first confirmed case in the country, all states reported cases of the new Coronavirus (FERREIRA NETTO, 2020).

Six months after the first recorded case of Covid-19 in China, 216 countries were hit by the new Coronavirus, in 2020 in June, the 22nd, the world recorded 8,860,331 cases and 465,740 deaths. Among the many countries most affected were the United States, on this same date, recorded 119,923 deaths and 2,275,645 of contaminated people (MARTIN *et al*, 2020).

When analyzing the regions of America in 2020, in April, May and June, it was observed that the United States,

Ecuador and Canada had the highest number of cases in April. Brazil and Chile had the highest number of cases in June. In relation to deaths, in the United States there were more deaths in April, while in Canada and Ecuador there were more deaths in May, Chile and Brazil occurred more deaths in June (Table 1) (GOMES *et al*, 2020).

Table 1- Representation of the number of cases and deaths in April, May and June by the reviews of America in 2020.

REGIONS	CASES/MONTH	DEATHS/MONTH
Brazil	25,690/June	989/June
Canada	1,468/April	132/May
Chile	5,296/June	155/June
Ecuador	754/April	May 79
United States	28,778/April	1,668/April

Source: Adapted from GOMES, Guilherme Gallo Costa *et al*. Epidemiological profile of the New Infectious Disease of Coronavirus-COVID-19 (Sars-Cov-2) in the world: Descriptive study, January-June 2020.

The degree of epidemiology of Covid-19 differs according to the country and its regions, because each country, state, and city, establish its preventive measures, the regions of Brazil, for example, the southeast region has always led with the highest number of cases, already the northeast region in second place, following the north, south and Midwest (SOUZA *et al*, 2021).

A study with a goal of analysis involving the clinical status of patients from different studies showed the following symptoms: fever (88.3%); cough (68.6%); myalgia (35.8%); expectoration (23.2%); dyspnea (21.9%); headache (12.1%); diarrhea (4.8%) and nausea (3.9%) (Table 2). It was observed that fever was the symptom that was most present in most patients, while diarrhea and nausea were not prevalent symptoms (XAVIER, 2020).

Table 2- Percentage of symptoms presented by patients in the study with ameta-nalysis.

Symptoms	Percentage
Fever	88,3%
Cough	68,6%
Myalgia	35,8%
Expectoration	23,2%
Dyspnoea	21,9%
Headache	12,1%
Diarrhoea	4,8%
Nausea	3,9%
Total	100%

Source: Own author, 2021.

Another study evaluated the symptoms in 1117 children under the age of 18 years, in view of the clinical manifestations, the symptom that was most present was fever (47.5%), followed by cough (41.5%), runny nose (11.2%), diarrhea (8.1%), nausea (7.1%), fatigue (5.0%) and respiratory difficulty (3.5%). Some more severe symptoms were identified, 145 children were diagnosed with pneumonia and 43 had their upper airways infected (ALMEIDA, 2021).

Regarding infection, children have the same probability as adults, however, symptoms present differently, in infected children the symptoms of Covid-19 present mildly and often the infection is asymptomatic. When symptomatic children present mostly low fever and cough associated with some gastrointestinal symptoms including abdominal pain diarrhea and nausea, usually recovery lasts on average 14 days (ZIMMERMANN, 2020).

Usually, 80% of infected people recover without needing hospital treatment, usually clinical manifestations start as a common cold and soon after the individual has fever, cough, headache, fatigue, throat infection, headache, myalgia, loss of taste and smell, however, the most common symptoms reported by authors are fevers and cough. On average 25% of cases occur to atypical pneumonia and respiratory deterioration, in addition to respiratory symptoms, some patients in mild state present digestive manifestations (GOULARTE,2020).

Hematology is a type of test that analyzes specific information about the types and amounts of components in the blood, such as: Red blood cells (red blood cells); White blood cells (leukocytes); Platelets (blood clotting). It is known that coronavirus mainly affects the lungs, however, it causes laboratory changes that can be perceived in a blood count. Initially in the first week of infection, lymphocytes are the main affected by the virus, in the second week this change becomes even more worrying, even in the first 14 days the patient may present albumin fall due to increased permeability of blood capillaries resulting from the inflammatory process (FLEURY, 2020).

In patients in the intermediate phase of the disease, the blood test presents a large decrease in oxygen, which causes an elevation of lactate dehydrogenase (LDH) and lactate. In severe patients, respiratory failure occurs, so it is possible to observe in the blood test a significant decrease (10% - 20%) of oxygen saturation. The lack of oxygen in the blood is a serious condition, which can cause severe tissue damage and, consequently, the risk of death (MARTINS, 2021).

In an analysis performed by (ZANCANARO, 2020), it showed that in leukocyte alterations, 75% of patients with mild symptoms had normal lymphocytes, 31.6% had Lymphopenia (low level of lymphocytes in the blood), and severe patients presented Leukocytosis that can be defined as increasing the number of leukocytes, is a response of the organism to an infection.

Most hematological findings in infections by the new coronavirus are related to leukocytes, our body's defense cells and platelets, coagulation-related cells (Image 1) (CÂNDIDO, 2021). It is possible to observe that changes related to leukocytes and platelets have a higher prevalence, causing leukopenia and thrombocytopenia, respectively.

Tabela 2: Alterações hematológicas mais comuns e com valor prognóstico em casos de infecção por SARS-COV-2. [Hb]: Concentração de hemoglobina. TP: Tempo de protrombina. VHS: Velocidade de Hemossedimentação. (Fonte: Autoria própria).

Parâmetros avaliados	Quantitativo de artigos que relataram alterações para cada parâmetro avaliado		
Sexo dos indivíduos	Mais de 50% dos indivíduos era do sexo masculino	Mais de 50% dos indivíduos era do sexo feminino	Não informado
	6	1	7
Alterações nas hemácias	Diminuição da [Hb]	Aumento da VHS e diminuição da [Hb]	Não informado
	2	2	10
Alterações nas plaquetas	Trombocitopenia		Não informado
	11		3
Alterações nos leucócitos	Linfócitos associados com leucopenia		Aumento dos neutrófilos
	11		5
Alterações na coagulação	D-Dímero	D-Dímero e TP	Não informado
	4	4	6

Figure 2. Representation of the sampling of the study on hematological alterations associated with Covid-19 in Patients. Source: CÂNDIDO, Hematological Alterations Associated with Covid-19 in Patients, 2021.

Patients in severe and critical condition have an insufficient immunological response pattern, however, presents neutral cytosis with morphological changes including changes in granulocytes and monocytes, besides presenting cytopenia lymph (- 20%) in the blood count, because the degradation of the lymphatic system ends up causing morphological changes and lymphocytic dysfunction. Neutrophils and B and T lymphocytes and killer natural cells will produce high levels of pro-inflammatory cytokines and chyosins and thus the inflammatory picture ends up aggravating lymphocytic and tissue dysfunction causing a deficiency in the function of organs affected mainly by the lungs (GRUNEWALD, 2020).

The Chinese population infected with covid-19 has demonstrated the presence of leukopenia, i.e., low levels of white blood cells, besides presenting moderate lymphopenia and may progress too severe. The most frequent hematological alteration is the low level of lymphocytes, that is, lymphopenia, because it functions as a biomarker of the severity of the infection. However, lymphocytes can be used in screening to aid in diagnosis and also in monitoring the evolution of severe cases by covid-19 (PEREIRA, 2021).

5. Conclusion

The study of the main hematological alterations found in patients affected by infection of the new coronavirus, epidemiological data indicate that the virus reached more than 23 million people, and just over 800,000 deaths by the end of August 2020, in this same period the United States was the country that suffered the most from the consequences of the pandemic, occupying the first place in the world ranking of confirmed cases and deaths. In Brazil, the Southeast region led the ranking of cases confirmed by Covid-19.

Therefore, it was observed that symptoms in patients in mild state comprise mostly fever and cough, while in patients in severe condition occurs to respiratory failure. It is known that coronavirus causes hematological alterations that can be perceived in a blood count, from the data collection it was observed that there was a prevalence of alterations related to leukocytes and platelets, however, lymphopenia is defined as low level of lymphocytes, was also present in reports made by authors.

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