



RESEARCH ARTICLE

Clinical and laboratory interactions associated with N. Meningitides infection and its relation to disseminate intravascular coagulation (DIC)

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Abstract

Neisseria meningitidis _ is an extremely virulent bacterium that is associated with worsening of clinical cases related to disseminate intravascular coagulation, which together with septicemia will lead to a cascade of pathophysiological events. The objectives of the study emerge from the perspective of elucidating the main parameters linked to the occurrences of the disease/bacteria and with this, based on methodological processes capable of evaluating the subject, based on bibliographic, explanatory, descriptive and documentary mapping, with articles chosen in the time period from 2014 to 2021 in the databases: Scientific Electronic Library Online (SCIELO), National Library of Medicine (PUBMED), and Caribbean Health Sciences (LILACS), to critically and inclusively cover the entire context of literature, from selective, thematic, and conceptual research to the study chosen. Results show that the disease brings severe conditions to humans, in order to detect disseminated intravascular coagulation it is necessary to examine biochemical, hematological and microbiological markers, discussions point to several methods of identification and characterization based on DNA, even so, it is still limited studies against *Neisseria meningitidis* , especially when the DIC reaction stands out in the pathology, making it essential to discover more effective and assertive treatments and medications for case resolutions. It can be concluded that *Neisseria meningitis* affects a large part of the population, and presents high mortality when associated with DIC, requiring a clear and concise diagnosis for the resolution of clinical cases.

Keywords: Meningococemia. Bacterial meningitis. Consumption coagulopathy. Fulminant purple. Homeostatic dysfunctions.

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1 | INTRODUCTION

Neisseria meningitidis _ is a gram-negative bacterium that belongs to the Neisseriaceae family, and was first described by Marchiafava and Celli in cerebrospinal fluid in 1884 and isolated 3 years later by Weichselbaum (GIANCHECCHI et al., 2015). It is a commensal bacterium, found naturally in the respiratory mucosa, where the unusual host is the human being. Meningococcal disease can affect the individual with unequal intensities, causing extremely serious injuries, leading to the patient's appearance of irregularities, perivascular instabilities, leaks and consequent thrombotic syndrome, arising from the cause of infection (DOS SANTOS, 2015; RAMOS, 2019).

Disseminated Intravascular Coagulation (DIC) can be caused by the septicemia of the bacterium *N. meningitidis*, characterized as a consumption coagulative syndrome. This must be diagnosed early and immediately, resolutely and specifically, because the resulting risks induce precipitation of thrombosis, promoting conditions such as seizures resulting from obstetric and surgical complications, trauma, platelet and coagulative deficiency, in addition to hyperfibrinolysis that is responsible for the elimination of blood clots (HJORLEIFSSON et al., 2015).

According to the World Health Organization (WHO), the infection is very prevalent, being common and reaching about 500,000 cases worldwide, in addition to providing a global average attributed to 50,000 deaths within this percentage. Since many of the cases are asymptomatic and are strongly associated with bacterial meningitis followed by sepsis, bringing numerous pathophysiological complications to the patient with comorbidity. Requiring a specific approach, especially in cases that promote DIC, as excessive/uncontrolled bleeding causes several manifestations throughout the body system (BELTRAN, 2014).

Thus, the biomedical area is fundamental in the laboratory area for the outcome of clinical cases affected by this comorbidity. When a condition is well diagnosed and performed in the first moments

of hospitalization, the patient's situation can be reversed early, keeping the patients' lives protected and without sequelae. Also requiring greater prophylaxis in hospital environments and reinforcement in the issue of immunization to reduce cases (ROCHA, 2019). This article aims to present you factors in risk related The infection per neisseria meningitidis analogous The coagulopathy in Consumption (DIC), understand the diagnostic criteria associated with *Neisseria meningitidis* and correlate the clinical and laboratory interactions intrinsically associated with Disseminated Intravascular Coagulation.

2 | THEORETICAL FRAMEWORK

2.1. GENERAL ASPECTS OF *N. meningitidis*

Neisseria meningitidis _ is a commensal bacterium, which is found naturally in the respiratory mucosa, where the unusual host is the human being, being a Gram-negative bacterium, of the genus *Neisseria*, belonging to the family Neisseriaceae and phylum proteobacteria . This bacterium is aerobic, requiring oxygen to survive, in addition to being immobile, non-sporulating, encapsulated and can measure about 0.6 - 1.0 µm (DOS SANTOS, 2015; RAMOS, 2019).

Meningococcal disease can affect the individual with different intensities, and this infection comes from the bacterium *Neisseria meningitidis* . This bacterium has a great ability to spread and adapt to the host system in an effective and virulent way, providing inflammatory signs to the patient and for presenting cellular invasion mechanisms, bringing consequences and difficulties to face this bacterial species (SLEIMAN et al. ., 2019).

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N. meningitidis – appears in the capillary endothelial cells of the entire body system, in which it directly encompasses the emergence of complications directed to thrombi and hemorrhages in the blood-brain system due to its interaction in microvessels (COUREUIL et al., 2019). According to Ramos (2019), one of the crucial factors that allow infection is the intrinsic modification that the bacterium is able to perform, tampering with the genome through genetic alterations, invading human cells, falling into the bloodstream, and regularly promoting meningococcemia. And sepsis, both linked to meningitis.

2.2. | RELEVANCE OF DISEASE / BACTERIA

According to Coureuil et al. (2019), lesions acquired by *N. meningitidis* are extremely serious, and may lead to the patient having perivascular irregularities and dysregulations, leaks and possible thrombotic syndrome present at the site of infection. With meningococcal adhesion, blood vessels undergo a reallocation in their cells and with that the appearance of disorders in blood homeostasis, also arising from pro-coagulant and intentional conditions in the endothelium. Which trigger activities and clinical conditions specific and well characteristic of septicemia, disseminated intravascular coagulation and inflammation.

Through Santos et al. (2016), *Neisseria meningitidis* is divided into 12 serogroups that are responsible for pathogenicity, but the most prevalent are in serogroups A, B, C, Y, W and X. These serogroups classify the bacterial strains that cause the disease. According to the author, controlling the disease is still a challenge, since it has a high mortality rate and risks to society.

Some of the characteristics associated with the pathogen's virulence mechanisms are: the capsule, LPS, FHBP, adhesins and MINOR. Among these mechanisms, the capsule is responsible for allowing the protection of the microorganism in the exercise

of the infection, and this factor is the main factor for the attack carried out by the immune system in an attempt to reverse the infectious condition. On the other hand, LPS is the element present in Gram-negative bacteria, capable of promoting the adhesion of *N. meningitidis* and allow it to evade the immune system. The FHBP is the subsidy that allows the proliferation and resistance of meningococcus in the blood. Adhesins are related to the condition in which bacteria interact with target cells acting at various sites in the body, allowing greater diversification of cell invasion. Finally, MINOR promotes the expression of virulent strains through colonization and amplification of the bacteria, being present in more than 50% of clinical cases (RAMOS, 2019).

2.3. | DISEMINATE INTRAVASCULAR COAGULATION

Disseminated intravascular coagulation is a pathological disorder resulting from obstetric and surgical complications, trauma, platelet and coagulative deficiency, in addition to hyperfibrinolysis that is responsible for the elimination of blood clots. This condition is extremely serious and can cause lack of oxygen to the affected tissues, hemorrhage due to heavy bleeding, and multiple organ failure (Hjorleifsson et al., 2015).

Coagulative syndrome, which if not controlled can lead to risks of thrombosis, generating excessive bleeding, developed from underlying problems. This bleeding is conditioned by the alteration and inability to reduce the formation of thrombin causing the dysfunction, all of which promotes a cascade of events until the appearance of hemorrhage. The process begins with impulsive thrombin generation, inducing platelet activation and consumption of natural coagulation inhibitors. As a result, there is an increased risk of developing a hypercoagulable state and probably thrombosis. For Andrade et al. (2021), the

diagnostic forms are effective and accurate, but investigations and actions are still needed aimed at monitoring DIC, as the pathology brings a series of complications and devices secondary to the patient's basic condition, thus requiring resolute devices. More specific, able to cure the beginning of the infection even in the primary form, strongly reducing the risks of misdiagnosis and mortality. Therefore, the importance of knowing the aspects that cover all cases in which DIC is present and its possible disorders.

According to Iba et al. (2019), with disseminated intravascular coagulation, the immune system induces responses by receptors which are evaluated from coagulation markers. Associating sepsis, damage to the microcirculation is observed, which can also be associated with meningococemia present in these cases.

2.3.1. | PATHOPHYSIOLOGY

According to Iba et al. (2019), coagulation changes associated with DIC in the intrinsic environment occur from the imbalance between the fibrinolytic and coagulation systems. Note the increase in thrombin formation, suppression of physiological anticoagulant mechanisms and decay of fibrin removal affected by the infection of the bacterium *N. meningitidis*, leading to a process of septicemia. With the activation of TAFI (inhibitor), there is a decrease in fibrinolysis and fibrin formation, crucial for deposition in the microvasculature and consequent failure of multiple organs, the last step of the process being evidenced by the consumption of platelets, clotting factors, fibrinogen and activation of fibrinolysis causing hemorrhage (PAPAGEORGIOU et al., 2018).

As a departure from this, one of the main clinical problems affected by DIC is called purpura fulminans, which is considered a thrombotic subtype of DIC, a life-threatening condition characterized by progressive purpuric skin lesions of unexpected onset and symmetrical acral necrosis. With typical skin observation and acral

necrosis, purpura fulminans is characterized by fever, hemorrhage from multiple sites, and shock. It is classified as neonatal, idiopathic and infection-induced, whereas acute infectious purpura fulminans is caused by several pathogens, including *Neisseria meningitidis*. (IBA et al., 2019).

2.3.2. | CLINICAL AND LABORATORY MANIFESTATIONS PRESENT

The most frequent clinical manifestations of a patient with meningitis are: fever, muscle pain, vomiting, nausea, irritability, lethargy, food refusal, headache and respiratory difficulty. It should be noted that these symptoms change according to age and the duration of the disease from the transient to the fulminant phase, leading to the death of the patient in a few hours. When it comes to more severe cases, the patient may present shock and disseminated intravascular coagulation (DIC), defining what is called the Waterhouse- Friderichsen syndrome, which is related to about 15% to 20% of patients diagnosed with meningitis. (SOUZA, 2020).

Meningococcus can multiply rapidly in the bloodstream, leading to severe forms of septic shock. Clinical onsets involve acute onset fever, disseminated intravascular coagulation, hypotension petechiae, purpura or maculopapular rash, multiple organ failure, demonstrating the systemic character of the infection (SOUZA, 2020).

According to WU et al. (2020), carriers of the infection may also develop cases of maculopapular rash (exathema) with petechiae indications, in addition to ecchymotic lesions. Associating *N. meningitidis* infection with DIC, the author also presents a study in which the patient presents a severe condition of sepsis and multiple organ failure, showing a cascade of events that affect the immune system, activating defense cells, which release substances that modify blood clotting, and post-infectious immune responses, triggering thrombosis,

disseminated intravascular coagulation and increased cytokines. According to LEVI (2018), disseminated intravascular coagulation (DIC) manifests itself from a latent and compensated activation of coagulation with acute hemostatic dysfunction and the potential increase in thrombotic risk. This phase is characterized by an imbalance between activation and inhibition of the coagulation system. It may be accompanied by fever, sudden drop in body temperature (hypothermia), shortness of breath, tachycardia, pressure drop and metabolic acidosis, clinically associated with an inflammatory response, and dysregulation of hypercoagulative homeostasis. In most cases, bleeding is due to reduced hemostatic capacity, a side effect of excessive consumption of clotting factors and platelets during clotting activation, a condition that is also known as consumption coagulopathy.

2.4. | EPIDEMIOLOGY

According to Souza et al., (2020), the incidence rate is higher in males, however the case fatality rate is higher in women in Brazil, meningococcal disease is endemic, with epidemic outbreaks occurring in some locations, with a stable incidence of 1.8/100,000 inhabitants. As many diseases are reported without identifying the etiologic agent, the real incidence remains uncertain in our country. It is also observed that about 50% of cases are in children under 5 years of age. In endemic periods, there are no peaks of incidence in adolescents, unlike what happens in North America and Europe. The lethality of meningococcal disease in Brazil is around 20%, but when meningococcemia is present, it can reach 50%. The cases of meningococcal infection are worldwide, but it is not divided equally between countries, the study shows that in only 10% of the population has the infection in developed countries in non-epidemic situations. It is noted that the infection is seen in the USA with a higher prevalence in children under six months of age, however, the infection case rates are well highlighted in areas where there are camps, homes, military and university dormitories, that is,

environments that provide more contact between individuals presenting significant percentages and with lethality of up to 55% when coming from sepsis, 25% when associated with sepsis and meningitis and 5% in cases only of meningitis without other associated complications (SURVEILLANCE GUIDE IN HEALTH, 2017).

According to the study by DAZZI et al. (2014), where a verification of the cases of meningitis that occurred in Brazil between the years 2009 to 2012 was carried out, and with this, the prevalence of cases in male patients with reported ages of children/adolescents in a category from 1 to 9 was observed. Years, and from 20 to 39 years, with ethnicities focused on the white color and with seasonality in the Southeast region.

2.5. | TESTES AND EVALUATIONS

Sleiman et al. (2020) brings a clinical case, where the patient presented meningococcemia directly associated with purpura fulminans, septic shock and severe acute myocarditis. The main laboratory findings present in the case, with samples obtained from venous blood, it was noted an increase in C-reactive protein, hyperleukocytosis, acute renal failure, and finally it was noted that the patient had a picture of non-obstructive acute renal failure when analyzing the serum creatinine of 3.46 mg/dL, and creatinine clearance of 24 mL per minute. Other laboratory tests were performed, such as the laboratory analysis of CSF (cerebrospinal fluid), glycemia, proteins, both normal. Gram staining was not noted for the presence of bacteria, nor pleocytosis in the cerebrospinal fluid.

According to the author, meningitis was not yet certain in the case, but the patient needed to be hospitalized, and with that, the condition worsened with clinical signs of disseminated intravascular coagulation, which was diagnosed from tests such as the prothrombin time where obtained an increase of 26%, low fibrinogen, thrombopenia, also high aPTT, imminent D-dimers, hypotension, decreased coagulation factor V, in addition to presenting acute pulmonary edema, increased PCT,

and thus, with the blood culture performed after 15 hours, the condition with meningococemia associated with purpura and septic shock was found and diagnosed. In addition to a biopsy performed from the purpura in the patient's skin, which identified thrombi in the capillaries, and acute myocarditis, hypokinesia, ST wave elevation and hypersensitive troponin Ic.

Laboratory tests are essential for the evaluation of disseminated intravascular coagulation. Among the anticoagulants responsible for the degradation of fibrin in clots formed, there is tissue plasminogen activator. The coagulogram exam is essential, as it will directly evaluate all the factors involved in hemorrhages (VASCONCELOS, 2022).

According to Santos (2019), other aspects arising from meningococcal infection interposed in meningeal irritation are linked to signs of characteristic signs of the disease, such as kernig's sign and Brudzinski's sign. Kernig's sign can be assessed in response to trunk flexion, and Brudzinski's sign on thigh flexion in parallel with the patient's head and pelvis. The author reports that, in children up to 9 months of age, they present with signs of stress, recurrent crying linked to meningeal crying, lack of appetite, vomiting and even seizures. With the accurate assessment of N. meningitidis cases with disseminated intravascular coagulation, the opinion of a decrease in cases resulting from severe complications and in mortality rates is notably evident.

According to Hjorleifsson et al. (2015), to be able to diagnose disseminated intravascular coagulation, it is necessary to carefully evaluate the biochemical markers, and as already mentioned, another part of the patient's prognosis is based on the alpha-2-antiplasmin response. Santos (2020), brings that there is a specific system for determining the findings, a report in which DIC I, DIC II, and DIC III are distributed, where DIC I means that there is a compensated coagulative activation, DIC II means that there is a decompensated coagulative activation and DIC III that is fully declared, evaluated from tests that if obtained results above or equal to five, will define the proceeding of the case, being this greater or equal to five, being able to conclude that there is presence of DIC III, needing to do the

control every day, but if the algorithm is less than 5, it means that it may not have a direct link with DIC III, needing to repeat the biochemical tests again for the diagnosis to be fully manifested.

2.5.1. | LABORATORY / DIFFERENTIAL / GENETIC DIAGNOSIS

For Santos (2019), the diagnosis of the disease can be made by several types of laboratory tests, such as in culture from the cerebrospinal fluid (CSF), which is the most appropriate due to its specificity, but there are also other types of tests. Diagnostic tests, such as the chemocytological examination of the CSF, which allows the counting and differential of cells, and others with a low degree of specificity, such as direct bacterioscopy using the staining technique. For the genetic diagnosis of N. meningitidis, several methods are used for detection, such as pulsed field gel electrophoresis, PCR, MLEE and MLST. It is noted that the diagnosis of PFGE (multilocus enzyme electrophoresis) is based on the electrophoretic detection of DNA through the chromosomal digestion of the bacterium formulated with restriction endonuclease, which allows the identification of epidermal waves derived from the bacterium. Multilocus enzyme electrophoresis (MLEE) evaluates the electrophoretic transmutations of cytoplasmic enzymes, based on gel kinesis and allelic factors, crucial for the life of the bacterium. MLST (Multilocus Sequence Typing) directly evaluates polymorphisms and alleles by locus (RAMOS, 2019).

According to Vasconcelos et al. (2018), for the laboratory diagnosis of meningitis, it is necessary to evaluate the CSF through blood culture, scraping of petechiae, urine, feces, puncture of the liquid removed from the lumbar region, preferably located in the L1 and S1 vertebrae, is also performed. In addition to tests such as direct bacterioscopy, culture, CIE, latex agglutination and chemo cytology. Normality is evidenced from the colorless liquid, with an amount of 80

to 150 ml. The progression is very fast and the differential diagnosis will depend on the manifestation of the disease, where the clinical state of bacteremia will indicate the analysis of the upper respiratory tract, and with the causative agent itself. Accurate diagnosis and with primary care is necessary for a better stability of the cases, being noticed in the laboratory analysis the presence of pleocytosis, neutrophilia, hyperproteinorrhaquia, Gram tests are also slightly used, culture and hypoglycorrachia. These tests are preferably obtained before the start of antibiotic treatment (BATISTA, 2021).

For the diagnosis of DIC, there are some parameters that are necessary for detection, such as thrombocytopenia, platelet count that, if reduced to a number below 100,000/ul, is already suggestive of disseminated intravascular coagulation, there is also prothrombin time, activated partial thromboplastin time, thrombin, fibrinogen (reduced), fibrin, D-dimer and schizocyte presentation in the blood (HERNANDEZ et al., 2017).

2.6. | HOSPITAL INFECTION

Ministry of Health Ordinance No. 930, of August 27, 1992, determines that "all hospitals in the country must involuntarily maintain a Hospital Infection Control Commission (CCIH) of the nature of the sponsoring institute". On January 6, 1997, Law No. 9,431 was enacted, providing for the mandatory maintenance of the hospital infection influence program by hospitals in the country. The causative sources of particles capable of carrying microorganisms inherent to nosocomial infections can be classified as internal and external, thus requiring greater inspection and hospital care. Among the indoor sources are people, fans, air conditioners, nebulizers and humidifiers, floors and potted plants and certain types of food. As for the external sources, we have soil, water, decomposing organic material, dust from constructions and renovations, which routinely influence the hospital environment (GUIMARÃES et al., 2021).

Hospital infection is a major aggravator of

comorbidities related to hospitalized patients, demanding interposed and crucial activities for the implementation of control measures to avoid HI, making prophylaxis permanent and intrinsically related to hygiene, biosecurity and adoption of programs that ensure protection. And improvements in the internalized environment and patient health (GIROTI, et al., 2018).

According to Bonadonna (2021), it is recognized that the hands of health professionals, visitors and patients may represent the most common vector of infections acquired in hospitals. In these environments, hand hygiene should be considered the primary measure to reduce the risk of infections. Numerous studies have also shown that white coats and uniforms worn by healthcare professionals are often contaminated.

The author reports that droplets larger than 5 µm are produced mainly by coughing, sneezing, singing or talking. In healthcare facilities, certain medical practices such as fluid aspiration and bronchoscopy can also cause particles of this size to diffuse. The most relevant infections transmitted by droplets are measles, chicken pox, tuberculosis, meningococcal disease, *Mycoplasma pneumoniae*, SARS-CoV-2 (Severe Acute respiratory syndrome coronavirus 2) and influenza. In general, airborne transmission of infection only concerns microorganisms with a low infectious dose and occurs after the release of large amounts of microorganisms into the air. The main factors that influence the level of microbial load in the indoor air of a healthcare facility include the number of occupants and the level of relative humidity, which in turn is associated with the specific arrangement of the healthcare facility's rooms. It is evident that close to 5% of the hospitalized population is affected by hospital infection in developed countries, whereas in Brazil this rate increases and the indicators reach 15.5%, proving that Brazil needs reinforcements in the fight against hospital infections, especially and as a result of highly pathogenic and transmissible microorganisms.

Sepsis, for example, can occur through infection caused by *N. meningitidis*, as it can also be linked to HI, resulting from genetic predisposition, clinical status, vulnerability and susceptibility of the host (QUEIROZ, 2019).

One of the certainly most important factors affecting indoor air is the efficiency of air handling systems, which can be not only an effective way to prevent airborne disease transmission, but also a way to reduce the spread of chemical contaminants and physicists. In addition, air treatment systems, human activities in the various areas and the presence of individuals with health problems can also influence the quality of circulating air. This is also a consequence of the technical choices concerning these systems, sometimes dictated by design choices that are unsuitable or unsuitable for hospital environments (BONADONNA, 2021).

2.6.1 | SUSCEPTIBILITY AND COMPLICATIONS

According to Ramos (2019), one of the reasons that lead to the development of susceptibility to the pathology is fostered in aspects such as the immune status, immunocompromise of the patient, bacterial resistance to certain antibiotics, in addition to complications linked to hospital infection that end up making treatment and monitoring difficult. of meningococcal disease attributed to the patient's clinical condition. The author emphasizes that the installation of the infection can be recurrent from contaminated particles, being linked to the malignancy of the strain, and emphasizes the importance of the lifestyle and strengthening of the immune system at this time, since it releases antibodies interposed by the complement system, promoting thus, the killing of the bacterium through cell lysis and phagocytosis. According to the author, responses characteristic of cellular injury associated with the release of cytokines and harmful substances to the patient are observed in the inflammatory process of the meninges, thus

causing fires through the production of LPS, IL-I and tumor necrosis factor, both mediated by the central nervous system.

For Sleiman et al. (2020), *N. meningitidis* can spread either in the typical form of meningitis, directly reaching the cerebrospinal fluid and later the meninges, as well as rapidly spreading in the blood and causing septicemia, endotoxemia, shock, dysfunction, urinary system infections, panophthalmitis, pericardial infection, arthritis, pneumonia and even conjunctivitis.

There are many susceptibilities for the patient to present clinical worsening and development of possible complications, among them, there is the antimicrobial susceptibility, where the drugs used before were replaced in response to bacterial resistance, which makes it a concern for health professionals, because, if the wrong antibiotic is used, the patient can develop even more serious conditions due to the spread of resistant strains. And in this case, to define susceptibility, it is important to use the CMI (minimum inhibitory concentration) through the E-test. The patients who survive always develop some sequelae resulting from the infection, whether physical, auditory, scars, amputations, and even psychological, such as seizures and speech disharmonies (RAMOS, 2019).

2.7. | IMMUNIZATION AGAINST MENIGOCOCCOS

According to Nunes (2017), because meningococcal disease has characteristics of rapid evolution, severity, lethality and has a potential epidemic character, vaccines are considered the best strategy developed by public health to prevent its occurrence. The first mode of prevention for meningococcal disease was the non-conjugated vaccines, which are divided into bivalent (serogroups A and C) and tetravalent (serogroups A, C, Y and W135), but have been

much less used today for several reasons. One of the main reasons is the inadequate immune response, especially when it comes to serogroup C bacteria for children under the age of 2 years of age, due to a failed response to antigens for being T independent in this age group. These vaccines also have a short duration compared to other vaccines, as they do not induce immunological memory and have hyperresponsiveness when administered later doses of the vaccine (SANTOS, 2019).

In 2015, the vaccine against serogroup B was validated in the country, but it is not yet part of the national vaccination plan. According to data from the Ministry of Health, from 2010 to 2016 there were considerable decreases in cases and deaths of meningococcal disease in the country, which is related to the control and promotion of vaccination in the vaccination plan (SANTOS, 2019).

Public policies are also related to the purchasing power of immunizations, because with them it is possible to guarantee the prevention of infection and thus reduce the risks of lethality, promoting an intermittent and effective social condition, reducing transmissibility and possible epidemic outbreaks inherent to the pathology in question. Not to mention that with vaccines, there is the promotion, strengthening and prevention of the spread of N.meningitidis, becoming a categorical reference and of great social relevance for countries (LIMA, 2017).

3. METHODOLOGY

The present study was based on the type of bibliographic, explanatory, descriptive and documentary research, of a basic nature and with a qualitative approach defined from interpretations, and scientific evidence which were analyzed and evaluated (MARCONI, 2017). Evidencing critically and including the entire context of the literature, from selective, thematic and conceptual research to the chosen study, to achieve the presented objectives (SOUZA et al., 2018). The theoretical framework was carried out through the survey of articles, using the following databases: Scientific Electronic Library Online (SCIELO), National Library of

Medicine (PUBMED), and Latin American and Caribbean Literature on Health Sciences (LILACS), serving as consecutive support for constant observations, reading and interpretations of the various articles available from these databases. Neisseria meningitidis, disseminated intravascular coagulation, clinical and laboratory diagnosis were used in the research project, with Bolivian operators such as Neisseria meningitidis) AND (disseminated intravascular coagulation), (Neisseria meningitidis) OR (disseminated intravascular coagulation). The inclusion criteria used to carry out the course conclusion work are: articles chosen from 2014 to 2021, in languages such as Portuguese, Spanish and English, focusing on topics related to N. Meningitidis / Disseminated Intravascular Coagulation / Disseminated Intravascular Coagulation related to Diagnosis / Diagnosis / Laboratory/clinical diagnosis associated with consumption coagulopathy.

The exclusion criteria are based on articles, which excluded the origin of DIC attributed to N. meningitidis and the chances of complications arising from it, or just bring the subject linked to an opinion article or abstracts which have little scientific evidence. 57 articles available on digital platforms were analyzed, 26 of which were chosen, 16 in Portuguese and 10 in a foreign language.

4. | RESULTS AND DISCUSSION

4.1 RESULTS

From the methodological search, 57 articles were found, separated from the databases, 20 of them in the Virtual Health Library (VHL), 02 in LILACS (Latin American and Caribbean Literature in Health Sciences), and 35 PUBMED articles (National Library of Medicine). The documents were read, evaluated and of these, 26 articles were selected within the inclusion and exclusion

criteria until the arrival of the results presented below:

The tables exemplify findings on risk factors, diagnostic criteria associated with infection, and clinical and laboratory interactions intrinsically associated with disseminated intravascular coagulation. In the tables below, the parameters evaluated are followed in chronological order with information such as: author/year, title, and main results.

Table 1: Risk factors and diagnostic criteria associated with *Neisseria meningitidis* infection linked to the secondary condition of DIC.

AUTHOR/YEAR	TITLE	MAIN RESULTS
Herzog et al. (2010)	Disseminated Intravascular Coagulation, Meningococcal Infection, and ischemic changes affecting the Lower Extremities: A Case Study.	Faced with the adversities coming from DIC linked to infection by the bacterium <i>Neisseria meningitidis</i> , results show that the disease brings severe, pathogenic and invasive diseases to humans, the process triggers a cascade of inflammations that cause bacteremia, septic shock, fever, petechiae, FMO, thrombosis, bleeding and necrosis.
Parpagierou et al. (2018)	Disseminated Intravascular Coagulation: An Update on Pathogenesis, Diagnosis, and Therapeutic strategies	Among the diagnoses linked to <i>Neisseria meningitidis</i> and DIC, it was validated that tests such as: platelet count, plasma fibrinogen, PT, fibrin, D-dimer, thrombin-antithrombin complex, plasmin-antiplasmin, are essential to evidence the disease, that are inserted from clinical situations of a systemic inflammation that affects all blood homeostasis and body balance.
Levi. (2018)	Clinical characteristics of disseminated intravascular coagulation in patients with solid and hematological cancers.	Other findings refer to disseminated intravascular coagulation (DIC), with associated risk factors from a latent and compensated activation of coagulation with acute hemostatic dysfunction and the potential increase in thrombotic risk. DIC may be accompanied by fever, hypothermia, dyspnea, tachycardia, hypotension and metabolic acidosis, and is clinically associated with an inflammatory response and dysregulation of hypercoagulable homeostasis.
Branches. (2019)	<i>Neisseria meningitidis</i> characteristics and epidemiology of meningococcal disease.	There are several DNA-based identification and characterization methods, the most used in the case of <i>N. meningitidis</i> are the polymerase chain reaction, (PCR) polymerase chain reaction, pulsed-field gel electrophoresis, (PFGE) pulsed-field gel electrophoresis, multilocus sequence typing (MLST) multilocus sequence typing and multilocus enzyme electrophoresis gene sequencing, (MLEE) multilocus Enzyme Electrophoresis.
Wu, Meng-Yu et al. (2020)	<i>Neisseria meningitidis</i> Induced Fatal Waterhouse – Friderichsen Syndrome in a Patient Presenting with Disseminated Intravascular Coagulation and Multiple organ Failure.	<i>N. meningitidis</i> invades the bloodstream will directly target non-ciliated epithelial cells and activate immune cells, causing endothelial injury. Endotoxin activates the complement system to deregulate clotting factors, which directly causes endothelial injury. All these factors will have a direct influence on the brain, lung, heart, adrenal system and body limbs through ischemia.

Table 2: Correlations between clinical and laboratory interactions intrinsically associated with disseminated intravascular coagulation.

AUTHOR/YEAR	TITLE	MAIN RESULTS
Hjortleifsson et al. (2015)	Prediction of survival in patients suspected of disseminated intravascular coagulation.	In order to detect disseminated intravascular coagulation, it is necessary to examine the biochemical markers in detail, and part of the patient's prognosis is based on the alpha-2-antiplasmin response, which is the main physiological inhibitor of the serine protease plasmin, responsible for the dissolution of fibrin clots.
Vasconcelos et al. (2018)	meningitis bacterial	Laboratory relationships present: • Analysis of CSF (L1 /S1) by blood culture; • Petechiae scraping; • Urine; • Feces; • Direct bacterioscopy; • CIE; • Agglutination by latex; • Chemo cytology
Sleiman et al. (2019)	Meningococcal purpura fulminans and severe myocarditis with clinical meningitis but in the meningial inflammation - a case report	In the case report, the study in question brings the main laboratory results arising from the diagnosis of meningococemia, purpura fulminans, septic shock and severe acute myocarditis: • High C-reactive protein; • Hyper leukocytosis; • Non-obstructive acute renal failure; • Creatinine- 3.46 mg/ dL; • Creatinine Clearance - 24 ml/minute; • normal blood glucose; • High lactate - 5.8 mmol/L; • LCR analysis- bacteria/ pleocytosis; • hypokinesia; • ST wave elevation; • Hypersensitive troponin IC.
Andrade et al. (2021)	Disseminated intravascular coagulation: a diagnostic approach.	Although the diagnosis based on the clinical and laboratory perspective is preponderant, studies are still needed for better targeting and investigation of DIC conditions, since the treatment is very individualized and depends on the patient's prognosis. Studies show that methods of preventing the clotting cascade are effective in conjecturing pathology.
Vasconcelos. (2022)	Coagulogram: Hemostasis: Coagulation mechanisms and laboratory evaluation.	Among the clinical applications of diagnostic tests to evaluate DIC were found: • Platelet count: evaluates thrombocytopenia and platelet infections; • Prothrombin Time: evaluates problems in the extrinsic and common pathway; • Activated Partial Thromboplastin Time: evaluates the functioning of intrinsic and common pathways; • D-Dimer: identifies if there is thrombosis; • Platelet aggregation test: monitoring of coagulation simultaneously.

4.2 | DISCUSSION

N. meningitidis infection he can be associated with disseminated intravascular coagulation, and thus bring irreparable and consecutive harm to the patient's body. In this case, the clinical, laboratory and differential diagnosis of the patient is of fundamental importance, through knowledge fostered and evaluated in the specificity of clinical cases. Thus, studies have shown that the pathology is aggressive and challenging, as it is a bacterial infection that can trigger other dysfunctions, such as disseminated intravascular coagulation, affecting all body and organs homeostasis (ANDRADE et al., 2021).

For Dutazaka et al. (2021) the clinical manifestations of meningococcal disease affected

by *N. meningitidis* can range from transient fever to bacteremia to fulminant illness, with death reported within hours of the onset of clinical symptoms. The bacterium releases endotoxins, the main toxin being the outer membrane glycolipid, lipopolysaccharide, causing intravascular pathology. This leads to intravascular coagulation, loss of capillary integrity, blood leakage into the dermis and underlying tissue and, eventually, ischemic lesions causing thrombotic events in the microvasculature and resulting dysfunctions.

In similarity to the study by Hollinshead (2019), the author points out that, although the bacterium is normally colonized in the human nasopharynx, the patient can still end up developing the pathology, depending on the levels of susceptibility of the host. Therefore, identification methods are essential for diagnosis, both clinical and laboratory, in the best way to avoid mortality rates.

Calvacante et al. (2017), emphasizes the pathogenesis of *Neisseria* strains, which are highly contagious, directly sensitizing the patient's nasopharynx by colonizing it, reaching the vast majority of children, as they still do not have a significant line of defense to fight the infection, the bacteria need an incubation period ranging from 2 to 10 days until it enters the bloodstream, and thus, whether or not to promote meningococcal disease. Cases that can be reported, from direct contact with the infected person.

When the bacterium invades the bloodstream, a cascade of events takes place, from the activation of the immune system through Macrophages and Neutrophils, which will release proteases and cytokines capable of promoting endothelial damage (tissue factor) and the entire systemic inflammatory process. With this, there is the degradation of fibrin by the fibrinogen inhibitor 1 (PAI-1) and plasmin, the bacterium releases endotoxins capable of promoting the generation of thromboplastin (tissue factor), with this there will be the activation of prothrombin (inactivated) in thrombin (activated) resulting in excessive activation of fibrinogen into fibrin, its fibrinolysis being inhibited by thrombin-activated fibrinolysis inhibitor (TAFI) and by (PAI-1) at high levels,

neutralizing the action of plasminogen by inhibiting plasmin cleavage. Stimulating the complement system, and thus causing dysregulation throughout coagulative homeostasis, leading to endothelopathy, associated with thrombocytopenia, microthrombotic vascular disease, and putting an end to multiple organ failure. These organs, which can be affected from the brain, with dysfunctions in the central nervous system, such as the lung, heart, also affect the limbs with the presence of ischemia, in addition to the Watterhouse-Friderich syndrome, which directly affects the adrenal system (WU et al., 2020).

As for Vasconcelos (2022), the diagnosis for *N. meningitidis* linked to DIC is directed at investigative parameters, capable of identifying the intensity of complications by directly evaluating hemostasis, immunological and inflammatory condition of the patient, since it is a secondary pathology to an existing condition, mainly associated with septicemia caused by bacterial endotoxin, through tests that act strongly on detection such as PT, APTT, Fibrinogen, Fibrin and platelets, D-dimer fundamental for analysis.

On the other hand, Hollinshead (2019) clarifies that genetic methods for characterization are essential, as they evaluate the DNA sequences of *Neisseria meningitidis* and are essential for diagnosis, as they cover the entire lineage and present forms of the bacterium, as mentioned above, MLEE, multilocus / ribosomal MLST and PFGE. Vasconcelos et al. (2018), patent in their study that the clinical diagnosis is made from the symptomatology, while the laboratory diagnosis is more detailed in advance by the analysis of CSF, blood culture, serum, petechiae, direct bacterioscopy, crossed immunoelectrophoresis (IEC), latex and chemocytology forming a precise and decisive investigation network to define the best intervention to be carried out. Hospital infections are also a major aggravator of public health problems, which refer to the worsening of cases associated with meningitis and DIC, strengthening the infection, which can strengthen and accelerate the process of infection from other microorganisms such as

fungi mites, bacteria, worsening the patient's condition (SILVA, 2013).

According to Santos (2019), in Brazil, currently, the vaccine used is the conjugated vaccine against serogroup C (Men C), being used mainly in the first year of life and booster in adolescence. The child uses the first dose in the third month of life, the second dose in the fifth month of life, and a booster at 12 months. At the age of 10 to 19 years, a booster or single dose can be used, in cases of those who had not been vaccinated before, and the patient's vaccination status should always be checked.) The use as prevention of only Meningitis C is justified because this serogroup has been for years the most common to cause meningococcal disease, and booster doses are necessary precisely because of the drop in serum antibodies that fight the bacteria.

Incidence cases studied between 2014 and 2019 in Pará, point out that the infection previously occurs in winter climates, where lethality rates in Brazil as a whole can reach a percentage of approximately 600 deaths, in a population average of 3500 cases in the country. , and in Pará there were increased rates linked to present agglomerations, whether coming from public transport, poor prophylaxis, precarious basic sanitation, lack of information and basic health care, with serogroups A, B and C being the main responsible for the infection, however, the most prevalent in Brazil is the serogroup type B and C (DA SILVA, et al., 2020).

In view of the above, there is a need to evaluate and importance of endemic outbreaks that are the main causes of mortality, subdivided into risk classes, starting with a primary case, starting with a primary case Co, secondary case, carrier, outbreak, outbreak community and institutional outbreak, which can lead to attack rates with cases exceeding 100,000 inhab, and difficult to control, especially in winter climates. Therefore, immunization mechanisms were implemented to promote an improvement in the state. The vaccine being the main strategy to contain the cases, and reduce the occurrences, even if not contemplating the whole picture of

the strains. (RAMOS, 2019; SANTOS et al. 2020).

It is worth mentioning that the drop in the number of platelets is one of the important properties in cases in DIC associated with *Neisseria Meningitidis* sepsis, as platelets circulating are reduced due to a consumption coagulopathy. Data provided by the International Society on thrombosis and Haemostasis (2016), for DIC are useful to identify patients with coagulation triggering, and avoid clinical worsening.

Thus, to alleviate cases of the disease, the secretary of health surveillance/MS (2017), still determines an investigation roadmap to assume the pathology that follows a triage flowchart until its determination, such as, a suspected case, medical assistance , clinical suspicion, notification, which ends with epidemiological surveillance, which suggests all control measures, guidance and closure of cases, thus defining the best decisions to be taken to avoid a new outbreak, and with that the reduction of the cases.

Therefore, the study against *Neisseria meningitidis* is still limited, especially when in the pathology the reaction of Disseminated Intravascular Coagulation stands out, and it is essential to discover more effective and assertive treatments and medications for case resolutions.

5. | FINAL CONSIDERATIONS

Nevertheless, it can be concluded that *Neisseria meningitis* is a severe disease that affects a large part of the population, and presents high mortality when associated with a secondary condition of DIC, thus highlighting the importance of clinical and laboratory diagnosis for the determination and accurate investigation of the disease. Patient's picture.

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