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PREDISPOSING FACTORS FOR DYSBIOSIS AND BACTERIAL INFECTION IN THE DEVELOPMENT OF FOURNIER'S SYNDROME: A SYSTEMATIC REVIEW

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Abstract: Fournier syndrome is considered a clinical emergency due to its rapid progression and high morbidity and mortality rates. It should be noted that the studies reported on Fournier syndrome lack continuous monitoring or follow-up in the research, therefore, the availability of literature is limited to a geographical distribution of cases, without confinement to a specific location. The objective of this review was to systematically analyze the predisposing factors of dysbiosis and bacterial infection in the development of Fournier's syndrome, identifying the pattern of bacterial infections associated with the syndrome, differentiating between mono-infections and poly-infections, as well as determining the main body area affected by Fournier's syndrome in the systematic review. The systematic review was conducted according to the PRISMA methodology, with searches in the Google Scholar, PubMed, Scielo, National Institutes of Health (NIH), and El Sevier databases, articles published by universities, hospitals, scientific journals, and research institutes over the last five years in English, Spanish, and Portuguese. The results showed a predominance of monomicrobial infections (60%) over polymicrobial infections (40%), It was also demonstrated that the predisposing factors for dysbiosis and bacterial infection in the development of Fournier's syndrome were diabetes mellitus, renal failure, acquired human immunodeficiency, and hypertension. It was shown that the main body area affected in Fournier's syndrome was the perianal area. In conclusion, knowing the predisposing factors and th s of the patient allows us to determine the appropriate treatment for each patient and highlights the importance of using sterile surgical equipment and asepsis.

Introduction

Fournier's syndrome, also referred to as Fournier's gangrene and identified in some studies as "flesh-eating disease," is defined as a rapidly progressive necrotizing fasciitis of sporadic occurrence, predominantly affecting males, especially older adults. This process develops as a result of a synergistic polymicrobial infection; in the clinical setting, it is known as a urological emergency that mainly affects the genital and perineal areas.

In recent decades, Fournier's syndrome has been overlooked due to its low prevalence, accounting for 0.02% of total hospital admissions, occurring in approximately 1.6 cases per 100,000 people and in 0.25 women per 100,000 people per year, affecting both sexes, but mostly men (Auerbach et al., 2020). The lack of information on a recurrent pathology is unusual in the clinical setting; however, in the case of Fournier's syndrome, the lack of information is alarming, probably due to its low reported prevalence. Preventing the population from contracting infections is a challenge, but investigating rare pathologies in greater depth would benefit the minority of the population that presents them, improving their quality of life. As they are largely unexplored, complications often affect those with comorbidities.

The literature mentions that Fournier's syndrome is of polymicrobial origin, falling into the type I category of necrosis. Therefore, the pathophysiology is caused by the entry of commensal bacteria into the affected area. Some of the bacteria reported are *Escherichia coli, Staphylococcus* spp., and *Streptococcus* spp. (Córdova-Molina et al., 2023).

Fournier's syndrome is recurrent in the genital area, considering that trauma to these areas can be the entry point for some micro s that, over time, can become more virulent and, therefore, cause an alteration in immunity.

Methodology

Eligibility criteria:

Inclusion criteria:

- Studies conducted in populations with Fournier's syndrome
- Publications in English, Spanish, and Portuguese
- Studies published between 2020 and 2025
- Studies, scientific articles, clinical reviews, websites, case reports related to Fournier syndrome

Exclusion criteria:

- Removal of articles and cases in which the patient will not develop Fournier's syndrome and/or does not present predisposing factors for the syndrome. Similarly, articles that do not meet the 2020-2025 publication range were excluded.

Sources of information:

- A systematic review of scientific articles, clinical reviews, and case reports was conducted using databases such as Google Scholar, PubMed, Scielo, National Institutes of Health (NIH), and El Sevier, as well as articles published by universities, hospitals, scientific journals, and research institutes over the last five years in English, Spanish, and Portuguese.

Search strategy:

- A systematic search was conducted in the Google Scholar, PubMed, Scielo, National Institutes of Health (NIH), and El Sevier databases, studies, scientific articles, clinical reviews, scientific journals, and research institutes using the following terms:
  - Fournier syndrome, idiopathic gangrene, Fournier gangrene, polymicrobial disease.
  - Clinical studies on Fournier's syndrome.
  - Dysbiosis in polymicrobial diseases.
- The search was conducted in English, Spanish, and Portuguese, in the publication ranges of 2020-2025.

Study selection process:

- All literature published between 2020 and 2025 was selected according to the inclusion and exclusion criteria. The literature was organized based on Fournier's syndrome factors using the Notion tool.

Data extraction process:

- Data were collected from the Google Scholar, PubMed, Scielo, National Institutes of Health (NIH), El Sevier databases, studies, scientific articles, clinical reviews, scientific journals, and research institutes.

- The authors of the selected literature were not contacted for additional information.
- The data was organized using the Notion tool for effective control in accordance with the items required for this purpose.

List of data:

- **Outcomes of interest:**
  - Affected areas, treatment, Gram-positive bacteria, Gram-negative bacteria, predisposing factors, diabetes in Fournier's syndrome, renal failure in Fournier's syndrome, urinary tract infections in Fournier's syndrome.

Assessment of risk of bias in individual studies:

Synthesis methods:

- A search of the scientific literature was conducted using the inclusion and exclusion criteria mentioned above, for which a flowchart was created for their classification.

Background

Jean Alfred Fournier, a French doctor specializing in dermatology, documented specific cases in patients with progressive gangrene of the genitals, of idiopathic origin, mainly in healthy young men. In 1883, he published an article on the subject, and from that date onwards, the condition became known as Fournier's gangrene or Fournier's syndrome.

There are several terms associated with this syndrome, such as necrotizing fasciitis, idiopathic gangrene, and progressive gangrene. This particular condition is significant due to its rapid progression, leading to multiple organ failure, altering patients' quality of life, and affecting both sexes, although mainly the male population, causing infections in areas such as the perineum, scrotum, urinary tract, external genitals, and adjacent tissues (Villafuerte et al., 2024).

Dysbiosis

Microorganisms can have both a symbiotic and pathogenic relationship with the host. However, it should be noted that when these microorganisms, or in this case bacteria, are in harmonious balance, this term is referred to as eubiosis. However, a disruption of the bacterial balance in our body leads to a decrease in beneficial bacteria in our microbiota and, therefore, the growth of pathogenic bacteria, which is known as dysbiosis. Similarly, dysbiosis is attributed to lesions that trigger types of skin and even soft tissue infections such as subcutaneous abscesses, since several of these lesions harbor pathogenic microorganisms that, when given a favorable environment such as temperature, contribute to the spread and thus cause dysbiosis in the skin and, as a consequence, the development of various pathologies or traumas.

Affected areas

Fournier's syndrome is considered a pathology in which the area of localization is mainly confined to the genital area of affected patients; these areas are accompanied by lesions or abscesses, most of which present necrosis that spreads rapidly, contributing to bacterial spread.

Skin lesions/trauma allow bacteria to enter, causing inflammation and tissue destruction; these pathogens promote thrombosis of certain subcutaneous vessels, adding to the state of necrosis. This can affect oxygen levels, contributing to their destruction and an increase in bacterial infections.

Sometimes Fournier's syndrome can begin with nonspecific symptoms such as discomfort affecting only one region or even the entire body, inability to sit, and limited movement. Escudero-Sepúlveda (2022) explains that after limited movement, these signs evolve into pain, swelling, redness, fever, local heat, crepitus, and erythema.

Researchers Husna, K., & Novida (2021) explained that a systemic inflammatory response, sepsis, edema in the skin area, necrosis, crepitus, and purulent discharge are observed in the affected area. Crepitus in Fournier's syndrome is due to microorganisms in the affected area, such as anaerobic bacteria, which, as the author explains, are bacteria that produce exotoxins that cause gas and necrosis. In addition, they indicate that in the anorectal area, some include: perianal abscess, anal fissure, and intestinal perforation due to colorectal lesions or neoplasms, diverticulitis, and appendicitis. In the urogenital tract, they include infection of the bulbourethral gland, urethral injury, iatrogenic injury secondary to manipulation of urethral strictures, epididymitis, orchitis, or lower urinary tract infection.

In Brazil, a study described by Moreira (2022) indicated that the areas of subcutaneous tissue, superficial and deep fascia, mainly of the scrotum, perianal space, perineum, and external part of the genitals, are predominant, and in addition to having a high lethality rate, the infectious process spreads rapidly.

Martínez et al. (2024) explain that a genital or perineal injury, ranging from an abrasion to a urinary tract infection, localized cellulitis, or a perineal abscess, results in the production of endotoxins and enzymes that cause tissue destruction and microthrombosis of the subcutaneous vessels. However, Bangash et al. (2024) mention that complications such as disseminated intravascular coagulopathy or severe sepsis and multiple organ failure have a mortality rate of up to 45%. Taking this into account and considering that it occurs in perineal areas, Abdelmoneim (2024) emphasizes that if the infection spreads to the abdomen, thrombi may form, which are most commonly found in the deep circumflex iliac artery and the superficial inferior epigastric artery. Although the scrotum is the most affected, the testicles are generally not affected, as they receive more direct blood supply from the aorta.

Risk factors

Age and male sex

Fournier's syndrome mainly affects older males; with advancing age, beneficial bacteria tend to decrease, which can result in an immune disorder that triggers bacterial infections. In males, according to Rueda et al. (2023), Fournier's syndrome mainly involves the male genitals, due to anatomical differences in the drainage of pelvic secretions, which in females reduces susceptibility to Fournier's syndrome.

Predisposing pathologies

Diabetes mellitus

Diabetes mellitus is a metabolic condition characterized by elevated blood glucose

levels. Over time, failure to treat it properly leads to complications in the body, affecting quality of life.

It is classified into three categories:

Type 1 diabetes mellitus, characterized by the elimination of pancreatic β cells, which is mediated by the immune system. Type 2 diabetes mellitus, a chronic type caused by the gradual loss of insulin secretion, resulting in physical disability due to multi-organ difficulties. Gestational diabetes mellitus developed in some pregnant women (Chávez-Reyes et al., 2021).

The diabetic population is more prone to infections and, as a result, complications due to their immunosuppressed state and poor healing. In addition, Pandiaraja, J., & Shalini, (2024), add that hyperglycemia decreases cellular immunity, altering chemotaxis and phagocytosis, facilitating the onset of serious infections. Some of the most recurrent infections they present are: urinary, respiratory, dermatological, fungal, and bacterial infections; genitourinary disorders; and trauma or injuries to the genital area, among others.

Hypertension and Acquired Human Immunodeficiency

Rosario-Castro et al. (2023) conducted a study showing that hypertensive patients may have less microbiota diversity compared to the healthy control group. Two main types of bacteria were found: in hypertensive patients, bacteria of the genus *Prevotella*, and in the control group, the genus *Bacteroidetes* predominated. These results suggested that people with an increase in this non-symbiotic bacterial group (*Prevotella*) always had extremely high numbers in relation to Fournier's syndrome. In Fournier's syndrome, HIV patients are more susceptible to opportunistic infections. Therefore, Ortiz et al. (2021) state that this may be a risk factor for the development of this infection, since the impaired immune system is unable to regulate the spread of the disease, leading to a more severe progression of this syndrome.

Renal failure and diabetes mellitus

Voordeckers et al. (2020) mention that diabetes mellitus in combination with end-stage renal disease is the most frequent cause of Fournier's syndrome, as it triggers secondary hyperparathyroidism, i.e., a decrease in blood calcium levels, which leads to a decrease in blood flow. On the other hand, Alcarraz (2024) explains that diabetes and renal failure are interconnected through shared factors and their metabolic complications and are characterized by a progressive decline in renal function, leading to a state of immunosuppression and metabolic disorders that increase susceptibility to serious infections, such as Fournier's syndrome.

Alcoholism

Liver cirrhosis is one of the most common factors, in which it presents with progression and immunosuppression with bacterial infections. Bourceanu et al. (2023) presented a case of a male patient with alcoholic liver cirrhosis who presented with fever and pain in the perineal area. They explained that the consequences of alcohol consumption cause progressive damage to liver function and immunosuppression with

polymicrobial infections that can sometimes lead to necrotizing fasciitis.

Bacteria

Gram-negative bacteria . in Fournier's syndrome

Gram-negative bacteria play a fundamental role in the development of Fournier's syndrome, mainly *Escherichia coli*, causing some types of thrombosis in various tissues, leading to necrosis. Also predominant on the list are *Pseudomonas aeruginosa*, *Corynebacterium* spp., and *Klebsiella pneumoniae*, the latter being particularly prevalent in patients with trauma who have perianal abscesses or abscesses in the genital area in general. Bacteria that do not predominate in the list for the syndrome but have been reported include *Bacteroides ovatus*, *Prevotella denticola*, *Actinomyces* sp, and *Enterococcus faecalis*.

Gram-positive bacteria . in Fournier's syndrome

The most predominant bacteria in Fournier's syndrome are of the genus *Staphylococcus* and *Streptococcus*. Some bacilli characterized by spore production also predominate, which can affect older adults due to their weakened immune systems. In addition, according to Sanchés et al. (2020), some cases of *Clostridium* sp. bacteria have been reported in Fournier's syndrome, where one of the treatments is with a hyperbaric chamber, as this reduces systemic toxicity.

Diagnosis and treatment

The diagnosis of this syndrome ideally begins with a physical examination of the affected area, where necrotic tissue is expected to be observed in the genital regions. With the help of imaging methods, edema and emphysema in soft tissues that are correlated with Fournier's syndrome can be detected (Ortiz et al., 2021).

As it is considered a surgical-urological emergency, the treatment of choice is triple antibiotic coverage and extensive surgical debridement of necrotic and non-viable tissue until healthy tissue is found, removing any areas suspected of infection in order to control the affected area (Escudero-Sepúlveda, 2022).

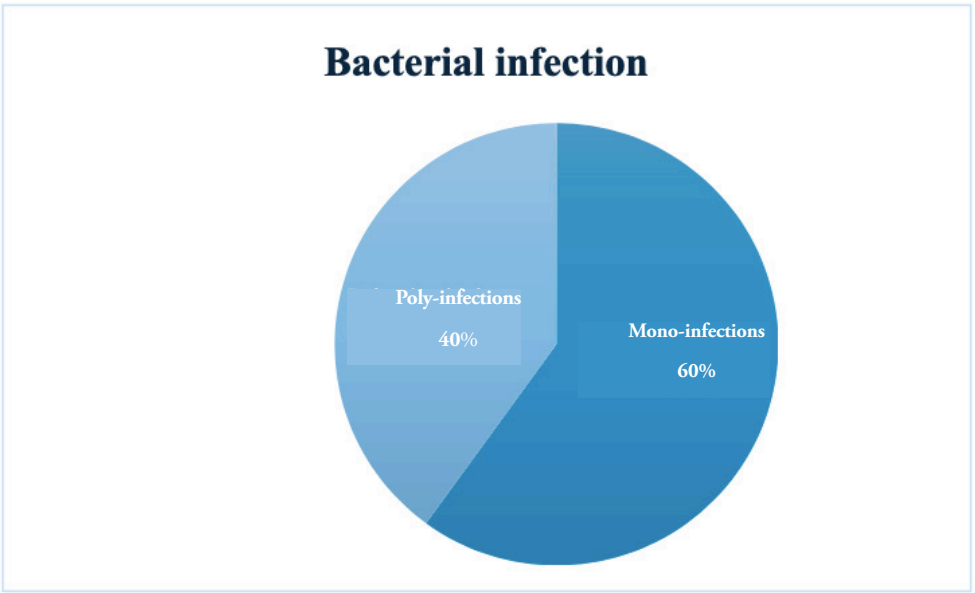
Results

Reference	Predisposing pathology
(Luvsannyam et al., 2022)	Diabetes mellitus
(Husna & Novida, 2021)	Diabetes mellitus
(Córdova Molina et al., 2023)	Diabetes mellitus and renal failure
(Elbeddini et al., 2020)	Diabetes mellitus
(Sánchez et al., 2020)	Hypertension
(Herrera Ortiz et al., 2021	HIV
(Arce Chavez et al., 2023)	Hypertension, diabetes mellitus
(Toral Santos et al., 2023)	Hypertension
(Zakariya-Yousef Breval et al., 2021)	Diabetes mellitus
(Padilla et al., 2020)	Kidney failure

Table 1: *Systematic analysis of predisposing factors for dysbiosis and bacterial infection in the development of Fournier's syndrome*

Reference	Gram classification +/-	Identified bacteria
(Luvsannyam et al., 2022)	Gram-negative bacilli	*Enterococcus faecalis*
(Husna & Novida, 2021)	Gram-negative bacilli and Gram-positive cocci	Klebsiella pneumoniae, Staphylococcus aureus, and Staphylococcus pasteuri,
(Córdova Molina et al., 2023)	Gram-negative bacilli	*Escherichia coli*
(Elbeddini et al., 2020)	Gram-negative bacilli, Gram-positive bacilli	*Bacteroides ovatus, Prevotella denticola, and Actinomyces* sp.
(Sánchez et al., 2020)	Gram-negative bacilli	*Klebsiella* sp.
(Herrera Ortiz et al., 2021)	Gram-negative bacilli	*Escherichia coli*
(Arce Chavez et al., 2023)	Gram-positive cocci	*Staphylococcus aureus*
(Toral Santos et al., 2023)	Gram-positive cocci and Gram-negative bacilli	*Coagulase-negative Staphylococcus and Escherichia coli*
(Zakariya-Yousef Breval et al., 2021)	Gram-positive diplococci and cocci	Acidaminococcus intestini and *Streptococcus gallolyticus*
(Padilla et al., 2020)	Gram-negative bacilli	Serratia marcescens

Table 2: Bacteria reported in selected articles



* Monomicrobial: (, (Córdova Molina et al., 2023), (Yulier et al., 2020), (Herrera Ortiz et al., 2021),(Arce Chavez et al., 2023) , (Padilla et al., 2020). Polymicrobial:(Husna & Novida, 2021) , (Elbeddini et al., 2020) , (Toral Santos et al., 2023), (Zakariya-Yousef Breval et al., 2021) .

Graph 1 Identification of the pattern of bacterial infections associated with the syndrome, differentiating between mono-infections and poly-infections in the review

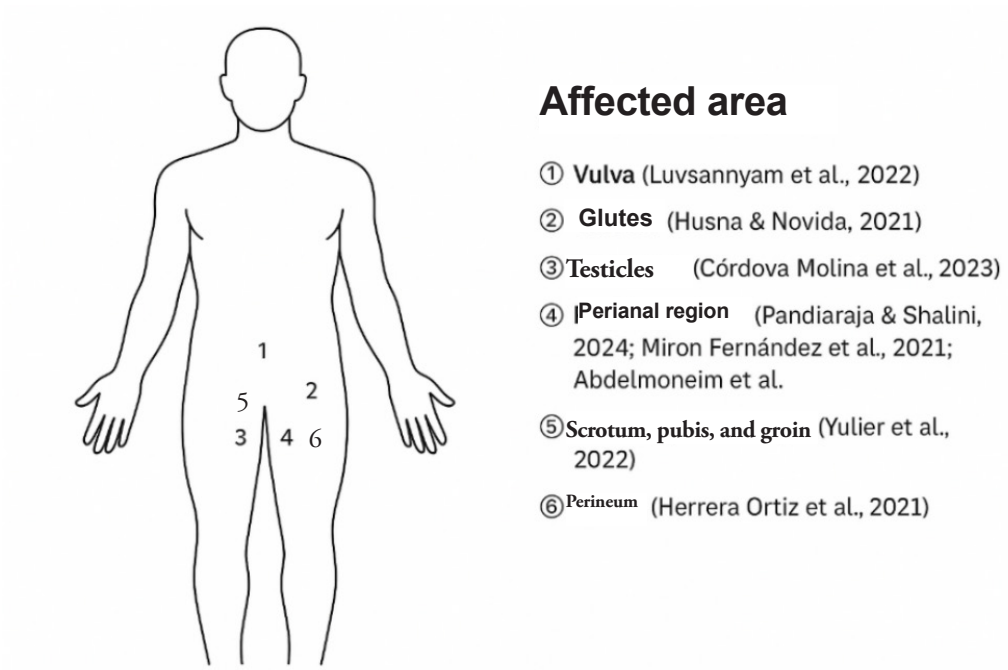


Figure 1 *Areas affected in Fournier's syndrome in systematic review*

Source: *own elaboration*

Discussion

Fournier's syndrome, being an infectious pathology of necrotic origin, is characterized by the appearance of pathogenic microorganisms, mainly Gram-negative bacteria, affecting genital areas, surgical complications, and predisposing diseases. Taking the above into account, there are several factors that can trigger this syndrome, including age and, in some cases, the gender of the patient.

It is also important to note that diseases can be associated with complications, and Fournier's syndrome is no exception. As shown in Table No. 1, these are related to predispositions or conditions directed towards others, such as diabetes mellitus, which is one of the most prevalent pathologies in the world, mainly affecting the elderly population. Diabetes mellitus is characterized by problems with wound healing and even surgical interventions, where recovery is often prolonged, making it a key focus for the spread of bacteria, mainly pathogens. In these cases, aging in the population is not only associated with physical changes, but also with a predisposition to certain pathologies or comorbidities that can be chronic or in n some cases. Therefore, infectious diseases can become complicated and even fatal in some scenarios.

However, hypertension, acquired human immunodeficiency, renal failure, and some heart diseases, despite being rarely documented as predisposing factors for Fournier's syndrome, do not rule out the evolution or progression that they can trigger. Many of the pathologies mentioned above are related to the immunosuppression presented by patients.

Microorganisms, specifically bacteria, have developed countless mechanisms or strategies to demonstrate adaptive conditions, which is one of the most worrying health emergencies for the future. It should be mentioned that, in these patients with compromised immune systems, many of their organs present functional alterations depending on the stage of their disease. If it is already in an advanced stage, they sometimes require assistance with medical equipment for proper functioning in the body, such as valves or catheters. These devices can create an ideal environment for bacterial growth if not managed properly. This is often referred to as biofilms, which form a kind of mesh or net that traps bacteria. This accumulation then forms colonies that constantly progress with different metabolic requirements and conditions, creating a protective barrier against antimicrobials. In accordance with the above, this process of biofilm generation can begin intraluminally or extraluminally. the intraluminal route refers to the internal migration of microorganisms within the device, as in the case of a catheter, while the extraluminal route involves the migration of microorganisms to the surface of the catheter, in which case the microorganisms present may originate from the patient themselves or even from gels, water, or healthcare personnel.

During the collection and analysis process for this systematic review, the possibility of finding sources with differing opinions on bacterial colonization was considered. Although there are diverse opinions, with some authors stating that Gram-positive bacteria are predominant, others maintain that Gram-negative bacteria are predominant. Within this review, Table 2 shows that Gram-negative bacteria predominated,

including *Escherichia coli*. *Escherichia coli* is a Gram-negative lactose-fermenting bacillus of the *Enterobacteriaceae* family. It can cause bacteremia and can sometimes inhabit the intestine harmlessly or pathologically, where it can cause intestinal infections, dysentery, and gastroenteritis, but mainly produces urinary tract infections (UTIs). This only proves that, according to Córdova Molina et al. (2023), as it is a commensal bacterium, it triggers an inflammatory response and obliterative endarteritis of the surrounding vasculature, followed by ischemia and thrombosis, ending with the spread of necrosis of the skin, subcutaneous tissue, and adjacent tissue. They also mention that oxygen tension in the tissues is reduced, leading to greater proliferation of anaerobic bacteria. Likewise, other Gram-negative bacteria of clinical interest in this syndrome, such as *Klebsiella pneumoniae and Pseudomonas aeruginosa*, can be nosocomial in nature, even being found in catheters and related to surgical interventions or in contaminated water or humid environments, such as *Pseudomonas aeruginosa*, This is alarming in the health sector, as they are considered potential colonizers of medical instruments and also wounds, abscesses, cellulitis, wounds with foreign bodies, among others. On the other hand, Gram-positive bacteria are also involved in Fournier's syndrome, such as *Staphylococcus aureus*, a Gram-positive cocci bacterium, known in bacteriology as golden staphylococcus and as an opportunistic bacterium in the hospital environment. It causes dermatological infections such as abscesses, boils, and cellulitis, which can develop and attack soft tissues. This can be extensive and progressively rapid, and is sometimes of nosocomial origin with an incidence in implanted medical devices such as catheters, prostheses, and valves. It also generates biofilms that, in accordance with the aforementioned biofilms, colonize surfaces, and therefore the formation of colony accumulations creates metabolic conditions that are resistant to some antibiotics.

Both Gram-positive and Gram-negative bacteria present a challenge for the hospital environment, as they can be found in various settings, from the to implanted medical devices, water, skin, and even medical instruments. However, it is important to consider these scenarios. The study recorded a higher prevalence of monomicrobial infections (60%) than polymicrobial infections (40%), as shown in Graph No. 1, which is at odds with what is mentioned in the literature on Fournier's syndrome, which states that it is polymicrobial in nature. However, as this finding shows, monomicrobial infections progress much more rapidly than polymicrobial infections, sometimes accompanied by sepsis and even death. This is because monomicrobial infections in Fournier's syndrome tend to be characteristic of certain clinical pictures that could essentially be a key control factor in the syndrome. On the contrary, polymicrobial infections must present a synergy that aids their development, which can lead to certain complications in terms of their isolation.

This review demonstrated, as shown in Figure 1, that the affected areas vary from the perineal area to the external part of the genitals. However, it can also affect the entire genital area, accompanied by abscesses, vulvar nodules, and even erythema. Therefore, it is identified that the affected area is not limited to a specific one, but also includes dermatological lesions of necrotic, erythematous, and nodular origin. In Fournier's syndrome, changes of inflammatory origin with mass formation predominate, in

addition to affecting the perianal and genital region of patients, especially male patients. The affected area often provides clues as to its possible treatment and, in turn, allows for the evaluation of the progression of this pathology. Gram-negative bacteria are the most common in the skin microbiota; however, they can also inhabit different areas and can be isolated from abscesses in genital regions, as is the case with Fournier's syndrome.

Conclusions

A systematic analysis of the predisposing factors for dysbiosis and bacterial infection in the development of Fournier's syndrome revealed diabetes mellitus, renal failure, acquired human immunodeficiency, and hypertension.

The pattern of infections associated with Fournier's syndrome in this systematic review was addressed according to predisposing factors, localized areas, and causative agent.

The body area most commonly affected in Fournier's syndrome was the perianal area.

Recommendations

Be aware of the patient's predisposing factors in order to provide a comprehensive approach and establish appropriate treatment.

Emphasize the use of proper asepsis and sterile surgical equipment when treating patients who require it in the most predisposed anatomical sites.

The implementation of case reports for future research is recommended in order to raise awareness of the population with Fournier's syndrome.

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