International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Literature Review: Emphysematous Pyelonephritis and Your Pathophysiological Mechanisms

Diego Bezerra Soares[1], Isabela Reis Manzoli[2], Gabriele Pereira dos Reis[3], Lohraine Talia Domingues[4], Enzo Henrique Oliveira Zanatta[5], Rodolfo Pereira Bezerra[6], Matheus Heitor Souza Tecchio[7], Igor Antônio de Macêdo Almeida[8], Rosângela Silva Heinzen[9], Khadyja Vythoria W. de O. Fares[10], Sabrina Teixeira Callegari[11], Matheus Platini de Souza[12], Thaís Rockenbach Gaona Lenzi[13]

Centro Universitário UNIFACIMED Cacoal-RO

Abstract: ***Introduction*: Emphysematous pyelonephritis is a rare and potentially fatal infectious disease caused in 80% of the cases by the bacteria Escherichia coli and Klebsiella sp. which mainly affects the renal parenchyma, collecting system and perirenal tissue. Furthermore, this pathology can be characterized as an aggressive bacterial invasion leading to important systemic changes, accumulation of air in the upper regions of the urinary tract and even tissue necrosis. *Objective*: Due to the high morbidity and mortality of this disease, the objective of this work is to characterize the pathophysiological mechanisms and promote a clinical approach to emphysematous pyelonephritis. *Methodology*: The research consists of a retrospective literature review, with the objective of elucidating the aspects involved in the pathogenicity of emphysematous pyelonephritis. For that, the Pubmed, Medline and SciELO databases were used. *Results*: From this study, it was possible to observe that bacteria, when invading the upper urinary tract, begin to trigger a metabolic process of glucose fermentation with production of carbon dioxide and other gases, implying the presence of air in the renal parenchyma causing strong compression of the structures. Blood pressure and impairment of functions, which may trigger necrosis. *Conclusion*: In summary, this study is important for a pathophysiological approach to emphysematous pyelonephritis and adequate clinical investigation aiming at a more accurate and early diagnosis, therefore, an optimization of the therapeutic plan as well as a better quality of life for the patient.***

Keywords: Urinary Tract Infection, Pathophysiological Mechanisms, Emphysematous Pyelonephritis

1. Introduction

Since ancient times, with the development of medicine and the advent of clinical observation of patients in an approach centered on anamnesis as well as physical examination, nephrology has always aroused human curiosity and instigated science to understand its pathophysiological mechanisms as well as its clinical aspects. incessantly seeking the cure of those diseases. The first to identify impairments in the urinary tract were the Egyptians in their process of mummification of corpses around 8000 BC, it was only in 3200 and 1200 BC that the first writings about nephrology appeared, with lithotomy surgery initially described around 600 BC . Centuries later, in the period of the Roman Empire, the need for an updated medical treatment for urinary pathologies was recognized and some publications appeared with descriptions of plants and empirical knowledge used to achieve this objective. In the Renaissance period, with the technical-scientific development, the splendor of science and the beginning of the modern age in the 18th century, the first anatomical and histopathological descriptions were made thanks to the development of microscopy and the work of great scientists such as the Belgian Andreas Versalius who contributed in the dissection of cadavers used to elucidate anatomical and pathophysiological aspects of the human body, mainly in the definition of fundamental structures to understand the works of modern nephrology.

Since then, with the advent of technology, new techniques and innovative treatments have been improved that allow understanding and treating the mechanisms of nephrological diseases. In this context, it is known that emphysematous pyelonephritis is one of the main diseases of the urinary tract with high morbidity and mortality and many diagnostic difficulties caused by its rapid evolution as well as its complex pathophysiological aspects. The first case of this disease was described in 1898 thanks to the work of researchers Kelly and MacCallum in the description of a situation of pneumaturia. It was only in 1962, with studies and clinical trials by Schultz and Klorfein, that the term “emphysematous pyelonephritis” was officially introduced and used by them to define this disease. Emphysematous pyelonephritis is a rare and potentially fatal infectious disease with an overall mortality rate of up to 43%, caused 80% of the time by the bacteria Escherichia coli and Klebsiella sp. that mainly affect the renal parenchyma, collecting system and perirenal tissue. Furthermore, this pathology can be characterized as an aggressive bacterial invasion leading to important systemic changes, accumulation of air in the upper regions of the urinary tract and even tissue necrosis. Between 60% and 70% of cases are related to diabetes mellitus with uncontrolled glycemia, this comorbidity results in the production of gases in the renal parenchyma that affect organic hemostasis.

Furthermore, the main symptoms are similar to those of acute pyelonephritis, consisting of the classic triad of fever, vomiting, and flank or lumbar pain. It is evident that its evolution, however, is much more serious if compared to common pyelonephritis, with its mortality rate reaching 70%, which is why it is considered a urological emergency. In addition, it tends to progress to renal failure and sepsis, mortality increases considerably if adequate treatment is not provided in a timely manner. This disease is more prevalent in women, with a ratio of 6:1, because the urethra of women is shorter than that of men and closer to the anus, which increases the incidence of urinary tract infections and,

consequently, the emergence of urinary tract infections. emphysematous pyelonephritis. Bilateral involvement of the kidneys is rare between 5 and 6%, the left kidney is the most affected with 67% compared to the right, which has 23%.

2. Methodology

This work was prepared from a retrospective literature review in the Med, SciELO and Medline databases. The keywords used were "Urinary Tract Infection", "Physiopathological Mechanisms", "Emphysematous Pyelonephritis" and their corresponding words in English "Urinary Tract Infection", "Pathophysiological Mechanisms" and "Emphysematous Pyelonephritis". Exclusion criteria were: articles that did not correlate the theme of emphysematous pyelonephritis as well as articles that were not between the period from 2001 to 2022.

A total of 845 articles were found, adding up all the databases. After reading the titles of the articles, it was noted that some of them did not meet the inclusion criteria of this study. Thus, it was possible to remove 105 duplicate articles and select 740 articles to read the abstract. Of these 708 were removed based on the analysis of the abstract as they were not consistent with the purpose of elucidating the pathophysiological mechanisms as well as emphysematous pyelonephritis, resulting in 32 full texts included in this literature review. The selection criteria were studies that compulsorily had the following inclusion criteria: Studies published in English and Portuguese; Systematic reviews, case reports and clinical studies; Characterization and pathophysiological mechanisms of emphysematous pyelonephritis and Articles published between 2001 and 2022.

3. Discussion

From the research carried out, it was observed that the condition of emphysematous pyelonephritis arises due to the interaction between infectious-metabolic processes presented during bacterial colonization of the urinary tract. These mechanisms of action are triggered mainly in adjacent tissues, perirenal parenchyma and in the nephron collecting system, where there is an environment conducive to the presence of invading bacteria that, through pathogenicity aspects, develop their anaerobic metabolic processes such as glucoses fermentation, resulting in an intense production of carbon dioxide and other toxic substrates, deregulating tissue hemostasis.

In this context, the air generated by the accumulation of carbon dioxide in the renal parenchyma can interact with the renal tissues, triggering intrinsic and extrinsic problems such as the strong compression of blood structures, impairment of functions, enzymatic imbalance, metabolic acidosis, which can, therefore, trigger a condition of cell necrosis. This pathophysiological mechanism can be explained by the persistent urinary infection in line with the metabolic decompensation of substrates present in the bloodstream, such as glucose in a clinical situation of hyperglycemia that serves as a bacterial gradient factor for the proliferation of pathogens and their anaerobic metabolism fermenter responsible for the accumulation of gases, mainly carbon dioxide that, when produced, can expand rapidly, increase its concentration and cause damage to kidney tissues, both intrinsically and systemic. In addition, decreased tissue perfusion, altered host immune mechanisms, and obstructive uropathy are important factors in the development of emphysematous pyelonephritis. Thus, it is understood that the probability of this infection occurring increases in patients with diabetes mellitus due to the high concentration of glucose in the tissues and the decrease in the immune response, due to leukocyte inhibition.

As for the diagnosis, the best way to diagnose emphysematous pyelonephritis is through imaging tests, abdominal computed tomography allows defining the extent of the emphysematous process, in addition to allowing classification according to severity, this test can define the possible treatments and prognosis for the disease. Thus, the gold standard is the classification proposed by Huang et al., which uses computed tomography of the abdomen and the location of radiological findings, dividing it into four classes: I- presence of gas confined to the collecting system; II - gas confined to the renal parenchyma, IIIA - when there is gas or abscess also in the perirenal space, IIIB - presence of gas or abscess in the pararenal space, IV - bilateral or single kidney.

Classification	Location on Tomography
I	Presence of gas confined to the collector system
II	Gas confined to the renal parenchyma
IIIA	When there is gas or abscess also in the perirenal space
IIIB	Presence of gas or abscess in the pararenal space
IV	Bilateral or single kidney

Figure 2.1: Classification of Huang et al.

Figure 2.2: Plain abdominal radiography: radiolucency and dense striated appearance in the topography of the left kidney. (SANTOS, Luciano Batista Silveira et al., 2010)

Furthermore, the treatment for emphysematous pyelonephritis consists of adequate support for the patient with glycemic control, a sepsis protocol, hydration, intravenous fluids administered at the appropriate time, early broad-spectrum antibiotic therapy, correction of acid-base balance and hydroelectrolyte disturbances. In cases of patients with sepsis and risk factors with a worsening of the prognostic-infection picture presenting characteristics of polymicrobial colonization, renal dysfunction, shock and disorientation, they should receive minimally invasive procedures to clear the urinary tract. In more extreme and severe cases, nephrectomy is a possibility to be used. Under this bias, Sarvpreet et al. (2011) propose a treatment choice based on the classification by Huang et al. Through the identification of tomographic findings in order to reduce mortality, since in many cases with indication of nephrectomy as the first option, mortality reached 50% of cases.

4. Conclusion

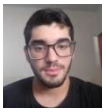
It is inferred, therefore, that emphysematous pyelonephritis is a rare comorbidity with a high mortality rate, being more prevalent in females and diabetics. The rarity of the disease can be one of the factors that make its diagnosis difficult, so it is essential to diagnose the disease early to improve the prognosis of patients and avoid invasive treatment. In addition, it is necessary to elucidate its mechanisms of action to understand its pathogenicity aspects in order to optimize the identification of the disease, the therapeutic choice and offer a better quality of life as well as an adequate clinical treatment aimed at the patient. Regarding patient management, percutaneous drainage associated with antibiotic therapy is a minimally invasive strategy with good results, however, in cases of fulminant emphysematous pyelonephritis with the presence of more than one risk factor, nephrectomy is the most indicated option. Historically, nephrectomy was the first treatment of choice, but with the advent of more modern imaging, successful renal preservation using a percutaneous drainage procedure has been allowed, however, each treatment is individualized according to the needs and needs of the patient. the severity of the patient.

References

[1] Mohsin N, Budruddin M, Lala S, Al-Taie S. Emphysematous pyelonephritis: a case report series of four patients with review of literature. Ren Fail. 2009;31:597-601.
[2] Derouiche A, Ouni A, Agrebi A, Slama A, Ben Slama MR, Chebil M. Management of emphysematous pyelonephritis based on a series of 21 cases. Prog Urol. 2008;18:102-7.
[3] Duque Fernández de Vega S, González Ortega FJ, Ruiz de Arévalo A, Narvona S, Tinaut J. Emphysematous pyelonephritis early diagnosed. Actas Urol Esp. 2008 ;32:473.
[4] Khaira A, Gupta A, Rana DS, Gupta A, Bhalla A, Khullar D. Retrospective analysis of clinical profile prognostic factors and outcomes of 19 patients of emphysematous pyelonephritis. Int Urol Nephrol. 2009;41:959-66.
[5] Eid YM, Salam MM. Diabetic ketoacidosis presenting with emphysematous pyelonephritis. J Diabetes Complications. 2010;24:214-6.
[6] Pontin AR, Barnes RD. Current management of emphysematous pyelonephritis. Nat Rev Urol. 2009;6:272-9.
[7] Kapoor R, Muruganandham K, Gulia AK, Singla M, Agrawal S, Mandhani A, et al. Predictive factors for mortality and need for nephrectomy in patients with emphysematous pyelonephritis. BJU Int. 2010;105:986-9.
[8] Fujita S, Watanabe J, Reed AI, Hemming AW, Solis D, Netzel TC, et al. Case of emphysematous pyelonephritis in a renal allograft. Clin Transplant. 2005;19:559-62.
[9] Schultz EH Jr, Klorfein EH. Emphysematous pyelonephritis. J Urol. 1962;87:762-6.
[10] Carvalho M, Goulão J, Monteiro C, Madeira A. Pielonefrite enfisematosa: revisão da literatura a propósito de um caso clínico. Acta Urológica. 2006; 23:75-80.
[11] Michaeli J, Mogle P, Perlberg S, Hemiman S, Caine M. Emphysematous *pyelonephritis*. J Urol. 1984; 131:203-8.
[12] Schaeffer AJ. Infections of the urinary tract. In: Walsh

PC, Retik AB, Vaughan ED, Wein AJ. Campbell's urology. Philadelphia: Elsevier Science; 2002. p.556-8.
[13] Tang HJ, Li CM, Yen YS, Wann SR, Lin HH, Lee SS, et al. Clinical characteristics of emphysematous *pyelonephritis*. J. Microbiol. Immunol. Infect 2001;34(2):125-30.
[14] Shetty S. Emphysematous *Pyelonephritis*. fev 2006. [Citado em 2010 jan. 04]. Disonivel em: w ww.emedicine.com/MED/topic3440.htm.
[15] D'Ippolito G, Abreu Jr L, Borri ML, Galvão Filho MM, Hartmann LGC, Wolosker AMB. Pielonefrite aguda: classificação, nomenclatura e diagnóstico por imagem. Rev Imagem. 2005;27:183-94.
[16] LI, Shengxian et al. Emphysematous pyelonephritis and cystitis: A case report and literature review. **Journal of International Medical Research**, v. 46, n. 7, p. 2954-2960, 2018.
[17] SCHUTZ, Eduardo Augusto et al. Emphysematous pyelonephritis caused by C. glabrata. Brazilian Journal of Nephrology, 2021.
[18] Michaeli J, Mogle P, Perlberg S, Hemiman S, Caine M. Emphysematous *pyelonephritis*. J Urol. 1984;131:203-8.
[19] Schaeffer AJ. Infections of the urinary tract. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ. Campbell's urology. Philadelphia: Elsevier Science; 2002. p.556-8.
[20] 20- Tang HJ, Li CM, Yen YS, Wann SR, Lin HH, Lee SS, et al. Clinical characteristics of emphysematous *pyelonephritis*. J. Microbiol. Immunol. Infect 2001;34(2):125-30.
[21] Shetty S. Emphysematous *Pyelonephritis*. fev 2006. [Citado em 2010 jan. 04]. Disonivel em: w ww.emedicine.com/MED/topic3440.htm.
[22] D'Ippolito G, Abreu Jr L, Borri ML, Galvão Filho MM, Hartmann LGC, Wolosker AMB. Pielonefrite aguda: classificação, nomenclatura e diagnóstico por imagem. Rev Imagem. 2005;27:183-94.
[23] Wan YL, Lo SK, Bullard MJ, Chang PL, Lee TY. Predictors of outcome in emphysematous *pyelonephritis*. J Urol. 1998;159(2):369-73.
[24] Huang JJ, Tseng CC. Emphysematous *pyelonephritis*: clinicoradiological classification, management, prognosis, and pathogenisis. Arch Inter Med. 2000;160(6):797-805.
[25] Rumack CM. Tratado de ultra-sonografia diagnóstica. 3ª ed. Rio de Janeiro: Elsevier; 2006.
[26] Carvalho M, Goulao J, Monteiro C, Madeira A. Pielonefrite enfisematosa-Revisão da literatura a propósito de um caso clínico. Acta Urol. 2006,23;4:75-80.
[27] Schaeffer *et al*. Predictors of outcome in emphysematous *pyelonephritis*: Editorial Comment. J Urol. 1998;159(2):373.
[28] Craig WD, Wagner BJ, Travis MD. *Pyelonephritis*: Radiologic-Pathologic Rev Radiograp. 2008 Jan-Feb;28(1):255-77; quiz 327-8.
[29] Baumgarten DA, Baumgartner BR. Imaging and radiologic management of upper urinary tract infections. Urol Clin North AM. 1997;24:545-69.
[30] Lee JKT. Tomografia computadorizada do corpo em correlação com ressonância magnética. 4ª ed. Rio de Janeiro: Guanabara Koogan; 2008.
[31] SANTOS, Luciano Batista Silveira et al. Pielonefrite enfisematosa: relato de dois casos e revisão da literatura. **Rev Med Minas Gerais**, v. 20, n. 3, p. 380-384, 2010.
[32] DE OLIVEIRA, Raphael Augusto Gomes et al. Pielonefrite enfisematosa. Relato de caso. **Revista da Sociedade Brasileira de**, v. 10, n. 4, p. 354-7, 2012.

Author Profile



Diego Bezerra Soares, Graduating in medicine at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED). Beginning of graduation in 2019. He was a member of the Interdisciplinary Academic League in Pediatrics (LACIP) of Unifacimed, holding the position of Director in the Scientific Initiation sector from November 2020 to October 2021. Member of the International Federation of Medical Students Association Brazil (IFMSA) Brasil Unifacimed), acting as Local Director of Medical Education (LOME-D). Institutional monitor in the field of Anatomy (2021.2 and 2022.1). Member of the home visit teaching extension project "Medicina em Cena. " Institutional monitor in the field of Semiology (2021.2 and 2022.1). Co-founder of the Academic League of Intensive Medicine and Palliative Care (LAMIP) and holds the position of director of Scientific Initiation. Institutional monitor in the subjects of Specific Skills IV and V (2022) and Associate of the Brazilian Society of Family and Community Medicine- SBMFC.

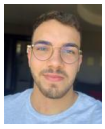
Isabela Reis Manzoli, Undergraduate course in medicine at the University Center (UNIFACIMED). Beginning of graduation in 2019. She was a member of the Interdisciplinary Academic League in Pediatrics (LACIP), holding the position of Vice-Director in the Scientific Initiation Sector from November 2020 to October 2021. She is co-founder and Vice-President of the Academic League of Intensive and Palliative Medicine (LAMIP). Member of the International Federation of Medical Students Association Brazil (IFMSA Brazil UNIFACIMED) acting as Local Director for sexual and Reproductive Health and Rights including HIV/AIDS. She monitors institutional in the subjects of Specific Skills IV and V. (2022).

Gabriele Pereira dos Reis, Graduation in progress in the Medicine course at the University Center for Biomedical Sciences of Cacoal (UNIFACIMED). Beginning of graduation in 2019. Currently monitors Semiology (2022.1) and co-founder of the Academic League of Intensive and Palliative Medicine (LAMIP), acting as Relationship and Marketing Director.

Lohraine Talia Domingues, medical student at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED). Beginning of graduation in 2019. She was a member and Deputy Director General of the Interdisciplinary Academic League in Pediatrics (LACIP) from November 2020 to October 2021.

Enzo Henrique Oliveira Zanatta, Graduating in Medicine at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED). Beginning of graduation in 2019. In 2019, he was a member of the Neuroscience Academic League (LANCI) of UNIFACIMED. He was part of the board of the League of Neurosciences (LANCI), from February 2020 to November 2021. Current member of the Academic League of Intensive and Palliative Medicine (LAMIP) of UNIFACIMED and member of the Medical Education Committee (SCOME) of the International Federation of Medical Students Association (IFMSA).

Rodolfo Pereira Bezerra, Medical student at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED). Start of graduation in 2017.1. Monitor in the field of Human Anatomy in 2019. Member of the Academic League of Urgency, Emergency and Trauma (INTERVEM) in 2017. Member of the Academic League of Dermatology and Dermatologic Surgery (LADERC) in 2018. Member of the Academic League of Clinical Oncology and (LACON) in 2018. Vice President of the Academic League of Clinical and Surgical Oncology (LACON) in 2019. Member and Financial Director of IFMSA Cacoal in 2019. Co-founder and Financial Director of the Academic League of Intensive and Palliative Medicine (LAMIP) in 2022.



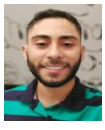
Matheus Heitor Souza Tecchio, Graduating in Medicine at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED), starting graduation in 2019. Member of the Academic League of Intensive Medicine and Palliative Care (LAMIP).

Igor Antônio de Macêdo Almeida, Graduating in Medicine at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED). Start of graduation in 2020. He is currently a member of the Academic League of Intensive Medicine and Palliative Care (LAMIP) and is also a member of the International Federation of Medical Student Associations (IFMSA) Brasil Unifacimed.

Rosângela Silva Heinzen, Medical student at the University Center of Biomedical Sciences of Cacoal (UNIFACIMED). Started graduation in 2019.2. In 2021, she was one of the founders of the project "My Blood, Your Blood", which sought to increase the collection of blood bags for the Foundation of Hematology and Hemotherapy of the state of Rondônia (Fhemeron). She is currently a member of the League of Palliative Care and Intensive Medicine (LAMIP) and works as a student monitor in the disciplines of Specific Skills IV and V, which addresses topics such as medication administration, gynecology, pediatrics and probes (2022.1).

Khadyja Vythoria W. de O. Fares, Graduating in Medicine at the Centro Universitário de Ciências Biomédicas de Cacoal (UNIFACIMED), starting graduation in 2020. Member of the Academic League of Intensive Medicine and Palliative Care (LAMIP).

Sabrina Texeira Callegari, Undergraduate student in Medicine at the University Center for Biomedical Sciences of Cacoal (UNIFACIMED). Beginning of graduation in 2018. She was a member of the Academic League of Oncology (LACON) of FACIMED from 2019 to 2021. Member of the International Federation of Medical Students Association Brazil (IFMSA Brasil Unifacimed), acting as Local Director of Medical Education (LOME- D).Member of the Academic League of Intensive Care and Palliative Care (LAMIP).



Matheus Platini de Souza, Graduating in Medicine at the University Center for Biomedical Sciences of Cacoal (UNIFACIMED) (2017-2022). He was a member of the academic league of General Surgery (LAC) of UNIFACIMED, holding the position of vice president (2019-2020). He was a member of the International Federation of Medical Students Association Brazil (IFMSA Brasil), serving as Regional Assistant of the National Exchange Team 2018-2019 management and National Coordinator of the Medical Education Program 2019-2020 management. He is an institutional monitor in the subjects of Anatomy (2018.1 and 2018.2), Semiology (2019.1 and 2019.2) and Surgical Technique (2020.1 to 2021.1). He has a professional technical course in Occupational Safety Technician by SENAI-Regional Department of Rondônia (2015).

Thaís Rockenbach Gaona Lenzi, Graduated in Medicine from the Faculty of Biomedical Sciences of Cacoal (2017). He is currently a physician on duty at the ICU of the Hospital dos Acidentados e Maternidade São Lucas. I studied medical residency in Internal Medicine at Hospital Regional de Cacoal, completed in February 2020. Postgraduate student in Palliative Care at Instituto Paliar - SP (2020-2021). Has experience in the field of Medicine, working mainly on the following subjects: rural worker, cryptococcosis, carcinogenesis, infectology and sjögrens syndrome.