Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

Analysis of molecular mechanisms of resistance and the systemic inflammatory response induced by carbapenemase-producing Klebsiella pneumoniae (KPC) and their hematological repercussions

Análise dos mecanismos moleculares de resistência e da resposta inflamatória sistêmica induzida por Klebsiella pneumoniae produtora de carbapenemase (KPC) e suas repercussões hematológicas

Análisis de los mecanismos moleculares de resistencia y de la respuesta inflamatoria sistémica inducida por Klebsiella pneumoniae productora de carbapenemasa (KPC) y sus repercusiones hematológicas

Gabrielly Salomão Barreto Rodrigues – Centro Universitário Instituto de Ensino Superior de Brasília – IESB
Thais Santana de Oliveira

Scientific project submitted as a partial requirement for the Bachelor's degree in Biomedicine at Centro Universitário Instituto de Ensino Superior de Brasília – IESB. Supervisor: Prof. Thais Santana de Oliveira, MSc. Brasília, DF, 2026.

Abstract:
INTRODUCTION: Infections caused by multidrug-resistant microorganisms are a major public health problem. In this context, Klebsiella pneumoniae, a member of the enterobacteria family, is particularly relevant. One of its resistance mechanisms is the production of the KPC carbapenemase enzyme. This study therefore aims to analyze the interaction between the microorganism and the immune system, emphasizing the molecular mechanisms involved in bacterial resistance, the inflammatory response and their hematological repercussions. METHODOLOGY: An integrative literature review was conducted through structured searches of the PubMed database, including only articles published from 2021 to 2026. RESULTS: The bacterium demonstrated considerable adaptability in its resistance mechanisms, including enzyme modification, porin alteration and recombination of genetic elements. The inflammatory response involved increased levels of pro-inflammatory cytokines. The hematological changes described were directly related to the severity of the condition. FINAL CONSIDERATIONS: This analysis demonstrates the importance of integrating knowledge across the areas addressed and the need for further studies of this kind to improve understanding of the subject.

Keywords: Klebsiella pneumoniae. KPC. Carbapenemase. Infection. Inflammatory response. Molecular mechanisms. Hematological changes.

Resumo:
INTRODUÇÃO: O desenvolvimento de infecções causadas por microrganismos multirresistentes configura-se como um grande problema de saúde pública. Nesse contexto, destaca-se a Klebsiella pneumoniae que faz parte da família das enterobactérias. Entre os mecanismos de resistência da K. pneumoniae, destaca-se a produção da enzima carbapenemase KPC. Dessa maneira, o presente estudo tem como objetivo a análise da interação do microrganismo e o sistema imune, com ênfase nos mecanismos moleculares envolvidos na resistência bacteriana, na resposta inflamatória e em suas repercussões hematológicas. METODOLOGIA: Foi realizada uma revisão integrativa de literatura por meio de buscas estruturadas na base de dados PubMed, considerando somente artigos publicados no período de 2021 a 2026. RESULTADOS: A bactéria mostrou-se bastante dinâmica em relação a resistência, sendo capaz de modificar a enzima, alterar as porinas e recombinar elementos

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

genéticos. Na resposta inflamatória, observou-se o aumento de citocinas pró-inflamatórias. Quanto às alterações hematológicas descritas mostraram-se diretamente relacionadas a gravidade da condição. CONSIDERAÇÕES FINAIS: Com essa análise é possível perceber a importância da integração de conhecimentos sobre os eixos abordados e que há a necessidade de mais trabalhos desse tipo para melhorar a compreensão do tema.

Palavras-chave: Klebsiella pneumoniae. KPC. Carbapenemase. Infecção. Resposta inflamatória. Mecanismos moleculares. Alterações hematológicas.

Resumen:
INTRODUCCIÓN: El desarrollo de infecciones causadas por microorganismos multirresistentes se configura como un gran problema de salud pública. En ese contexto, se destaca la Klebsiella pneumoniae que forma parte de la familia de las enterobacterias. Entre los mecanismos de resistencia de la K. pneumoniae, se destaca la producción de la enzima carbapenemasa KPC. De esa manera, el presente estudio tiene como objetivo el análisis de la interacción del microorganismo y el sistema inmune, con énfasis en los mecanismos moleculares implicados en la resistencia bacteriana, en la respuesta inflamatoria y en sus repercusiones hematológicas. METODOLOGÍA: Fue realizada una revisión integradora de literatura por medio de búsquedas estructuradas en la base de datos PubMed, considerando solamente artículos publicados en el período de 2021 a 2026. RESULTADOS: La bacteria se mostró bastante dinámica en relación a la resistencia, siendo capaz de modificar la enzima, alterar las porinas y recombinar elementos genéticos. En la respuesta inflamatoria, se observó el aumento de citocinas proinflamatorias. En cuanto a las alteraciones hematológicas descritas se mostraron directamente relacionadas a la gravedad de la condición. CONSIDERACIONES FINALES: Con este análisis es posible percibir la importancia de la integración de conocimientos sobre los ejes abordados y que hay la necesidad de más trabajos de ese tipo para mejorar la comprensión del tema.

Palabras clave: Klebsiella pneumoniae. KPC. Carbapenemasa. Infección. Respuesta inflamatoria. Mecanismos moleculares. Alteraciones hematológicas.

1 Introduction

The development of infections caused by multidrug-resistant microorganisms is a major public health problem, being strongly associated with hospital environments. In this context, Klebsiella pneumoniae, a gram-negative, encapsulated, facultative anaerobic bacterium with the shape of a bacillus, belonging to the Enterobacteria family, is highlighted and characterized as an opportunistic bacterium. This species has the ability to colonize the mucous membranes and gastrointestinal tract of humans, leading to infections mainly in hospitalized patients, immunocompromised or submitted to invasive procedures. Among the resistance mechanisms of K. pneumoniae, we highlight the production of the enzyme carbapenemase KPC, a b-lactamase-like enzyme encoded by the blaKPC gene present in plasmids, capable of hydrolyzing b-lactam antibiotics (Jin et al., 2025)

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

K. pneumoniae infection starts with pathogen recognition by dendritic cells and macrophages through Toll-like receptors (TLRs). In sequence, signaling pathways are triggered from adaptor proteins such as MyD88 and TRIF, activating NFkB and MAPK family proteins. Process in which it directly impacts the expression of pro-inflammatory genes and the production of cytokines, such as TNF-a, IL-1B and IL-6, and chemokines, such as IL-8, thus recruiting inflammatory cells. In more severe cases, especially those caused by KPC-producing strains, there may be an inflammatory storm related to endothelial dysfunction, coagulation activation and hematologic changes (Chen et al., 2024; Liang et al., 2022).

These hematological manifestations are progressive and begin with leukocytosis and neutrophilia. With the evolution of the condition, platelet activation and microthrombus formation can lead to thrombocytopenia as a result of platelet consumption. Changes in coagulation and endothelial dysfunction may also occur, which facilitate the development of a prothrombotic state. Subsequently, hematopoiesis is compromised by reducing platelet production, while intensified action of sialidases causes greater destruction. In more severe cases, phagocytosis of blood cells may occur, contributing to the development of anemia and leukopenia due to persistent inflammation (Chen et al., 2024; Wang et al., 2023).

Therefore, infections caused by K. pneumoniae symbolize a major clinical problem due to virulence mechanisms and their ability to remain in the host organism even before the immune response. In addition, the bacterium shows not only to protect itself, but also directly interfere with the immune response, modulating signaling pathways and cellular mechanisms in the inflammatory process and elimination of the pathogen, favoring worsening of the clinical condition (Sá-Pessoa et al., 2025). Thus, the present study aimed to analyze the interaction between the microorganism and the immune system, with emphasis on the molecular mechanisms involved in bacterial resistance, inflammatory response and its hematologic repercussions, essential aspects for understanding the pathophysiological process caused by the bacterium and for improving diagnostic strategies, prevention and clinical management of affected patients.

2 Methodology

This study is an integrative literature review that was developed through structured searches conducted in the National Library of Medicine (PubMed) database, without language restriction, considering only articles published between 2021 and 2026. This consultation was conducted in the database on 15/09/2026, the search was conducted using the following

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

descriptors: “Klebsiella pneumoniae”, “KPC”, “carbapenemase”, “infection”, “inflammatory response”, “molecular mechanisms” and “hematological changes”, combined by Boolean operators “AND” and “OR”, being selected by the theme of the study, contemplating etiological agent, pathophysiology and associated hematologic alterations. Only original studies and relevant reviews were considered.

The inclusion criteria established for the selection of articles were: studies on Klebsiella pneumoniae; works that discussed the inflammatory response, molecular mechanisms and hematological changes; publications within the time frame and articles available in full. Articles that are outside the established period were excluded; studies that did not relate the proposed themes; excessively specific works that did not present results applicable to the general context of this group; studies with strictly clinical approach; duplicate articles; and articles under embargo. The chosen studies were submitted to a previous reading, through the analysis of titles, abstracts and keywords, in order to verify whether they fit the objectives of the study.

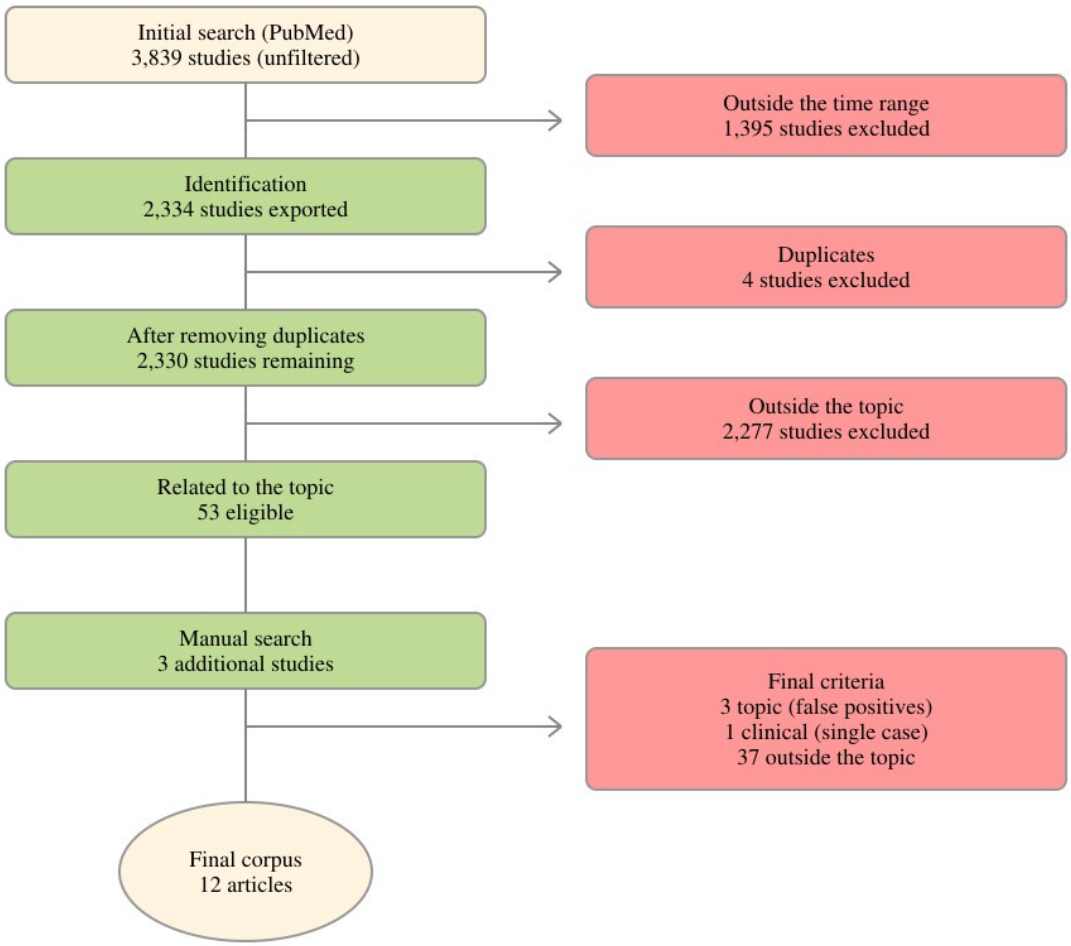
3 Results

By means of a structured search in the PubMed database, 3,839 papers were initially found. After reading the titles and abstracts, and applying the inclusion and exclusion criteria described in the methodology, 12 articles were selected to compose the corpus of the analysis. The stages of identification, screening, eligibility and inclusion are presented in the flowchart of Figure 1.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

Figure 1: Flowchart of choice of articles according to Prisma, 2026.



Source: Elaborated by the author (2026)

Among the 12 articles chosen for analysis, aspects related to carbapenemase-producing K. pneumoniae (KPC) infection were examined, focusing on the molecular mechanisms associated with systemic inflammatory response and its hematologic repercussions. Studies address different manifestations related to host organism response to infection, including changes in leukocytes and platelets, among others. The information of the articles that were part of the results or scope of the study as title, authors, year of publication, objectives and main results will be listed in Chart 1.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

Chart 1: Summary of the Studies chosen to compose this literature review, 2026.

TITLE	AUTHORS	YEAR	OBJECTIVES	RESULTS
Induction of innate immune responses by KPC-producing Klebsiella pneumoniae of the pandemic sequence type 258-clade I.	Balaska A, et al.	2021	Test how this pandemic strain of KPC-Kp interacts with components of innate host immunity (human serum and macrophages), evaluating phagocytosis activation and cytokine production.	The strain is still recognized by the innate immune system, causing bactericidal activity of serum and production of inflammatory cytokines (IL-1β, TNF-α, IL-6) by macrophages, despite their antibiotic resistance.
Thrombocytopenia in Klebsiella pneumoniae liver abscess: a retrospective study on its correlation with disease severity and potential causes.	Chen L, et al.	2024	To investigate the correlation between thrombocytopenia and disease severity in 361 patients with hepatic abscess by K. pneumoniae, seeking possible causes (peripheral consumption vs. medullary production).	Platelet loss was associated with greater clinical severity of the abscess; the study does not confirm whether the isolates were KPC producers.
Klebsiella pneumoniae carbapenemase variants: the new threat to global public health.	Ding L, et al.	2023	To review the clinical, epidemiological and susceptibility characteristics of variants of the enzyme KPC, in addition to the detection methods available.	More than 150 variants of KPC have been described worldwide, most only in recent years; these variants reduce the efficacy of ceftazidime-avibactam, and there are no formal guidelines for treating infections caused by them.
Genome sequencing unveils blaKPC-2-harboring plasmids as drivers of enhanced resistance and virulence in nosocomial Klebsiella pneumoniae.	Han X, et al.	2024	To elucidate the evolution of hospital K. pneumoniae with KPC-2 plasmids and their transmission between patients and the environment, from 237 strains in an ICU.	They found a high frequency of multiple copies of the KPC-2 gene; an unpublished hybrid plasmid conferred at the same time more virulence and less sensitivity to ceftazidime-avibactam.
Clinical outcomes and plasmid-associated features in KPC-producing Klebsiella pneumoniae bacteraemia.	Hsieh YC, et al.	2026	To investigate the association between capsular types and plasmid factors with mortality in patients with CKP bacteremia (402 patients, two medical centers, 2017– 2021).	KPC was a significant predictor of mortality specifically in K64 capsule strains, but not in K47, showing that the capsular type modulates the clinical impact of carbapenemase.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

TITLE	AUTHORS	YEAR	OBJECTIVES	RESULTS
Global emergence of Carbapenem-resistant Hypervirulent Klebsiella pneumoniae driven by an IncFII(K34) KPC-2 plasmid	Jiang J, et al.	2025	To investigate, on a global scale, the role of a specific type of plasmid (KPC-2 carrier) in the dissemination of strains that combine resistance to carbapenems and hypervirulence.	This specific plasmid appears repeatedly in different countries as the vehicle behind the formation of these "double dangerous" strains, indicating an international dissemination pattern coordinated by this genetic structure.
Clinical and Molecular Characteristics of Patients with Bloodstream Infections Caused by KPC and NDM Co-Producing Carbapenem-Resistant Klebsiella pneumoniae	Li J, et al.	2024	Comparing clinical and molecular characteristics of 231 patients with CKP bacteremia, separating those who had strains only with KPC from those who had strains with KPC and NDM together.	Patients infected with co-producer strains of KPC and NDM had a higher mortality rate than those infected with only KPC strains, confirmed by complete genomic sequencing.
CpxR promotes the carbapenem antibiotic resistance of Klebsiella pneumoniae by directly regulating the expression and the dissemination of blaKPC on the IncFII conjugative plasmid.	Liu Z, et al.	2023	Identify which bacterial regulatory system controls the activation of the KPC gene by testing the knockout of 24 candidate regulatory systems.	The CpxR protein binds directly to the KPC gene, increasing its activation, and also accelerates the transfer of resistance plasmid between strains, revealing a new regulatory mechanism behind the dissemination of resistance.
Clonal dissemination and plasmid plasticity of KPC-3-producing Klebsiella pneumoniae ST512 during a hospital outbreak in Spain.	Riesgo-Magaña M, et al.	2026	To describe the first outbreak of K. pneumoniae ST512 KPC-3 producer in a hospital in Zaragoza, characterizing clinical, microbiological and genomic aspects.	130 isolates from 33 patients (2022–2024); most cases were detected by active surveillance, and the comparison with almost a thousand international genomes revealed the phylogeographic position of this lineage.
Genomic characterization of ceftazidime/avibactam-resistant KPC-producing Klebsiella pneumoniae in bloodstream infections indicates OmpK35 and OmpK36 as pivotal key players in resistance mechanisms.	Vaiana C, et al.	2026	Genetically isolated characterization of ceftazidime/avibactam resistant KPC-Kp in bloodstream infections.	All isolates had OmpK35 truncated porin, with or without mutations in OmpK36; two new variants of the enzyme KPC were identified, and most patients already had intestinal colonization by bacteria.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

TITLE	AUTHORS	YEAR	OBJECTIVES	RESULTS
In-depth characterization of Klebsiella pneumoniae carbapenemase (KPC)-encoding plasmids points at transposon-related transmission of resistance genes Autores: van Almsick VF, et al.	van Almsick VF, et al.	2025	To investigate how resistance via KPC is transmitted within a hospital, analyzing the bacterial isolate to the level of plasmid and transposon.	In an outbreak of 7 patients in a German hospital, two different genetic clusters shared the same group of transposons, suggesting that it is transposon, not the entire plasmid, the main vehicle for spreading resistance.
Transposition of insertion sequence element from KPC plasmid enhances intracellular survival of Klebsiella pneumoniae.	Xie Y, et al.	2025	Investigating as a mobile genetic element of the KPC plasmid affects the bacteria' ability to survive within host cells.	When this element "jumps" to another part of the genome, the bacterium survives better within epithelial cells and macrophages, linking an event of the plasmid resistance to a direct virulence gain.

Source: Elaborated by the author (2026)

4 Discussion

The carbapenemase-producing K. pneumoniae (KPC) raises major concerns and is considered one of the largest public health problems worldwide. This bacterium has the ability to develop different resistance mechanisms, such as those that allow them to escape the action of antibiotics. Among them, the production of the enzyme KPC stands out, which acts in the degradation of certain antimicrobials favoring dissemination (Li et al., 2024). Given this scenario, seeking to understand how it resists and how it acts in the organism, the selected and analyzed studies allowed discussing its molecular mechanisms, inflammatory response and hematological repercussions.

To understand the molecular mechanisms of resistance, it is necessary to contextualize two terms. First, the porins that are proteins that form channels in the external membrane of the bacteria, in which changes have the ability to modify membrane permeability (Vaiana et al., 2026). And secondly, plasmids, which are a type of mobile DNA that brings together genetic elements that can shift or change positions. The gene responsible for the KPC is usually in plasmids, which facilitates transmission to different offspring or bacteria (Han et al., 2024).

In the work of Ding et al., (2023) it is observed the increasing variants of the enzyme KPC, which reached 145 records accumulated in 2023, where the authors concluded that variants represent a great threat and defend the monitoring of sensitivity. In general, they

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

appeared in treatment with ceftazidime-avibactam, and the cases analyzed had a failure percentage of 38.9%. The study also showed the transmission of variants among patients and changes to which, usually leave the bacteria resistant to antibiotics and makes therapeutic management difficult, although the bacterium can regain sensitivity to carbapenems.

A work that contradicts this article is that of Vaiana et al., (2026), because they record that 11 of the 16 isolates resistant to ceftazidime-avibactam were also resistant to meropenem. This indicates that the recovery of sensitivity to carbapenems does not always occur and depend on the antibiotic and variant. The authors also point out that changes in porins, channels of the membrane of bacteria through which antimicrobials are absorbed, constitute the main resistance factor, thus suggesting a more punctual contrast.

Other important points of the study by Vaiana et al., (2026) are the presence of at least one non-functional porin in all isolates observed in the retrospective study. For the authors, changes in porins, more than the variant of KPC alone, would be the possible central factor of resistance, based on genomic association. Thus, the study mainly emphasizes porins, unlike Ding and Liu, which show enzymes. Still compared to Liu, we have a difference seen in resistance to meropenem, since Vaiana et al., (2026) record resistance to this antimicrobial.

Still in this scenario, the study by Riesgo-Magaña et al., (2026) also contributes to understanding some molecular mechanisms of resistance by documenting an outbreak of K. pneumoniae, in which a clone proved to have plasticity in the plasmid, with changes in this structure responsible for resistance. Thus, the authors concluded that the clone persisted due to clonal dissemination, selective pressure and plasticity of mobile genetic material. Corroborating, then, Ding et al (2023), which describes the same scenario and, in contrast, Vaiana et al., (2026), as they reinforce that central factor would be porins, proteins present in bacterial channels, whose alteration may hinder the entry of antibiotics.

Hsieh et al., (2026) conclude on how the clinical impact of KPC depends on the capsular type and plasmid of a specific type, especially in the K64 strain. These factors facilitate the joint dissemination of resistance and possible markers of virulence. The authors treat this as exploratory, and clinical severity remains a determining factor of mortality. On the other hand, the article by Riesgo-Magaña et al., (2026) suggests that, without hypervirulent genes, the success of the clone in focus in the study, ST512, is attributed to colonization and survival of the bacteria, they do not discuss mortality, highlighting only a difference in the explanation proposed by the authors.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

Under another approach, Van Almsick et al. (2025) observed different events, in which two bacterial isolates with distinct genetics presented the blaKPC-3 gene, responsible for KPC production. The analysis did not indicate the transfer of plasmids between the two isolates, as they presented significant genetic differences. Nevertheless, the evaluation performed identified in all plasmids a region identical to transposon, which carries the blaKPC-3 gene and was present in different strains. Now Hsieh et al., (2026) already highlights plasmid as a dissemination pathway, because the strains studied presented a conjugation system.

In contrast, we have the study by Jiang., et al., (2025) who saw conjugative plasmid as an influencer of dissemination, through a genetic material analysis of bacteria from Chinese hospitals and databases, while Van Almsick et al., (2025) found no transfer of plasmid between two clones by means of transposons. In addition, the isolates remained with hypervirulence in animals models used for research and assays with neutrophils. Another very relevant aspect addressed concerns hematologic changes, when describing a thrombocytopenia in the hepatic abscess, and this alteration may be directly related to Chen et al. 2024, which describes thrombocytopenia.

In agreement with some previous findings, the study by Xie et al., (2025) highlights the relevance of insertion sequences (short pieces of DNA that jump from place to place) linked to the KPC plasmid in the adaptation of bacteria, besides its antibiotic resistance function. This shows that these elements act as an auxiliary adaptation mechanism, and that resistant strains that carry virulence plasmids may undergo changes in the capsule and mucoviscosity through genomic plasticity. However, the study by Jiang et al., (2025) has a factor that contradicts this finding, because in Xie it was observed that capsule loss attenuated virulence without antibiotic, while in Jiang reduced mucoviscosity maintained hypervirulence, given the tests performed to assess whether bacteria remained virulent, including resistance to neutrophil death.

Still on molecular mechanisms, the work of Han et al., (2024) demonstrated that the presence of KPC plasmid is not directly associated with virulence, as its effects may vary according to the genetic context and acquired virulence elements. The authors also show that the bacteria that acquired a hybrid plasmid reached greater virulence. On the other hand, we have the findings of Xie et al., (2025), where virulence plasmid imposed a cost to resistant strain, and an element of KPC plasmid decreased virulence (without antibiotic). Although the finding shows similarity with other aspects discussed, there is a limited comparison because virulence is measured in different experimental models.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

There are factors in the bacteria themselves that regulate the expression of the blaKPC gene, which may be associated with different levels of resistance to carbapenems, as seen in a strain of K. pneumoniae strain ST11 KPC producer in the work of Liu et al., (2023). In this study the bacteria itself regulates the activation of the resistance gene that is necessary for the transfer of plasmid, and the authors put this mechanism as common, because the regulator's binding site was in 57% of the promoters analyzed. Regarding the dissemination, while Liu et al., (2023) show the conjugation of the whole plasmid as an efficient and regulated pathway by bacteria, Van Almsick et al., (2025) did not show plasmid transfer between clones that shared a transposon.

Regarding the hematological alterations, Li et al. (2024) reported a lower platelet count and more neutrophils in patients who died. They also observed that patients infected by bacteria in which they had a second resistance enzyme died. The study by Chen et al., (2024) corroborates the fact that severity is associated with platelet decrease, but it provides different information to show that neutrophils did not present differences between groups, Li et al., (2024) shows a higher percentage of neutrophils in cases of death.

Chen et al., (2024) have found that, with care, we were able to approach hematological changes and their mechanisms, such as immunothrombosis, changes in platelet production and hemophagocytosis, even though it is not the main points of the study. Low platelets were associated with D-dimer and higher hepatic thrombophlebitis, thus suggesting a relation between coagulation activation and platelet consumption in systemic inflammatory response. These findings are close to the findings of Li et al., (2024), as previously addressed, especially regarding changes in platelet series and their impacts on clinical severity, although Chen et al. did not describe KPC nor show a relationship between mortality level and thrombocytopenia.

In the study by Balaska et al. (2021), the authors address a strain of K. pneumoniae that demonstrates to be sensitive to blood defense cells, being quickly phagocytized and able to cause an adequate inflammatory response, despite being resistant to antibiotics. In addition, this research cites the production of pro-inflammatory cytokines, indicating the participation of mechanisms related to the inflammasome, which contributes to the permanence of inflammation and can mediate hematologic changes as a result of these responses. On the other hand, the bacteria studied by Jiang et al. (2025) are aggressive and resistant to antibiotics, tolerant of cells in the human body defense system. This means that the isolated presence of the enzyme KPC does not cause bacteria to escape the immune response, forming a general comparison.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

From the analysis of the present studies, it was possible to perceive that K. pneumoniae KPC-producing is very complex, especially when it comes to the molecular mechanisms of resistance and response of the host organism. Although molecular mechanisms are widely investigated, there are still gaps in the interpretation of how these mechanisms relate to the inflammatory response and possibly with the hematologic changes that may come. This discussion process is important for the integration of findings on the three axes addressed.

5 Final considerations

The present integrative review study enabled a joint understanding of the molecular mechanisms of K. pneumoniae KPC-producing resistance, inflammatory response triggered and associated hematologic changes. This study showed the resistance of bacteria is a complex process that involves different mechanisms, such as changes in the production of enzymes, changes in porins and how the bacterium itself has the ability to reproduce the resistance gene, increasing propagation. In addition, it allowed the understanding of how the host organism reacts to infections considering cytokine mediation and its hematological impacts, which were directly related to severity.

In this context, it is clear the relevance of the integration of these aspects, because bacteria, resistance, inflammatory response and hematological changes are part of the same process, since the joint analysis of these factors provides a broader view of the infection and its repercussions on the host organism.

In Biomedicine, the study is relevant, especially because it highlights how understanding bacterial resistance and evaluation of laboratory findings are important, reinforcing the role of biomedical professionals in research and scientific production.

However, limitations were identified, particularly regarding the molecular mechanisms involved in the systemic inflammatory response and hematological changes, which represents a major obstacle to a deeper understanding of the subject.

References

BALASKA, Asimina et al. Induction of innate immune responses by KPC-producing Klebsiella pneumoniae of the pandemic sequence type 258-clade I. Access Microbiology, v. 3, n. 11, p. 000275, 2021.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

CHEN, Lulu et al. Thrombocytopenia in Klebsiella pneumoniae liver abscess: a retrospective study on its correlation with disease severity and potential causes. Frontiers in Cellular and Infection Microbiology, v. 14, p. 1351607, 2024.

DING, Li et al. Klebsiella pneumoniae carbapenemase variants: the new threat to global public health. Clinical microbiology reviews , v. 36, n. 4, p. e00008-23, 2023.

HAN, Xinhong et al. Genome sequencing unveils bla KPC-2-harboring plasmids as drivers of enhanced resistance and virulence in nosocomial Klebsiella pneumoniae. MSystems, v. 9, n. 2, p. e00924-23, 2024.

HSIEH, Yu-Chia et al. Clinical outcomes and plasmid-associated features in KPC-producing Klebsiella pneumoniae bacteraemia. Tropical Medicine and Health, 2026.

JIANG, Jianping et al. Global emergence of carbapenem-resistant hypervirulent Klebsiella pneumoniae driven by an IncFIIK34 KPC-2 plasmid. EBioMedicine, v. 113, 2025.

JIN, Shan-Shan et al. A comprehensive overview of Klebsiella pneumoniae: resistance dynamics, clinical manifestations, and therapeutic options. Infection and Drug Resistance, p. 1611-1628, 2025.

LI, Jiayang et al. Clinical and molecular characteristics of patients with bloodstream infections caused by KPC and NDM co-producing carbapenem-resistant Klebsiella pneumoniae. Infection and Drug Resistance, p. 1685-1697, 2024.

LIANG, Zihan et al. Host defense against the infection of Klebsiella pneumoniae: New strategy to kill the bacterium in the era of antibiotics?. Frontiers in Cellular and Infection Microbiology, v. 12, p. 1050396, 2022.

LIU, Zhiyuan et al. CpxR promotes the carbapenem antibiotic resistance of Klebsiella pneumoniae by directly regulating the expression and the dissemination of bla KPC on the IncFII conjugative plasmid. Emerging microbes & infections, v. 12, n. 2, p. 2256427, 2023.

RIESGO-MAGAÑA, María et al. Clonal dissemination and plasmid plasticity of KPC-3–producing Klebsiella pneumoniae ST512 during a hospital outbreak in Spain. European Journal of Clinical Microbiology & Infectious Diseases, p. 1-14, 2026.

SÁ-PESSOA, Joana et al. Klebsiella pneumoniae emerging anti-immunology paradigms: from stealth to evasion. Trends in microbiology, v. 33, n. 5, p. 533-545, 2025.

VAIANA, Claudia et al. Genomic characterization of ceftazidime/avibactam-resistant KPC-producing Klebsiella pneumoniae in bloodstream infections indicates OmpK35 and OmpK36 as pivotal key players in resistance mechanisms. Frontiers in Microbiology, v. 17, p. 1840520, 2026.

VAN ALMSICK, Vincent F. et al. In-depth characterization of Klebsiella pneumoniae carbapenemase (KPC)-encoding plasmids points at transposon-related transmission of resistance genes. Frontiers in Cellular and Infection Microbiology, v. 15, p. 1542828, 2025.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.

Ano VII, v.1 2026 | submissão: 08/11/2026 | aceito: 15/11/2026 | publicação: 20/11/2026

WANG, Xueting et al. Pyroptosis, apoptosis, and autophagy are involved in infection induced by two clinical Klebsiella pneumoniae isolates with different virulence. Frontiers in Cellular and Infection Microbiology, v. 13, p. 1165609, 2023.

XIE, Yingzhou et al. Transposition of insertion sequence element from KPC plasmid enhances intracellular survival of Klebsiella pneumoniae. Ebiomedicine, v. 120, 2025.

Este é um artigo publicado em acesso aberto (Open Access) sob a licença CreativeCommons Attribution, que permite uso, distribuição e reprodução em qualquer meio, sem restrições desde que o trabalho original seja corretamente citado.