



Article History

Received:

August 15, 2025

Revised:

September 16, 2025

Accepted:

October 16, 2025

Available Online:

December 31, 2025

HISTOPATHOLOGICAL AND MICROBIAL CORRELATES IN HOSPITAL-ACQUIRED INFECTIONS: A CROSS-SECTIONAL ANALYSIS

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Abstract

Hospital-acquired infections (HAIs) remain a major clinical and public health challenge, driven by diverse microbial pathogens and complex tissue-level responses that complicate diagnosis and management. This cross-sectional study examined the histopathological and microbial characteristics of HAIs using an integrated mixed-methods approach combining tissue biopsy evaluation, microbial culture quantification, Gram staining, PCR-based virulence detection, and severity indexing. Histopathological analysis revealed variable yet distinct patterns of necrosis, inflammatory infiltration, architectural disruption, and microabscess formation across affected tissues. Microbiological assessment identified a predominance of multidrug-resistant Gram-negative organisms alongside pathogenic Gram-positive isolates, with substantial variability in microbial load and resistance profiles. PCR assays confirmed the presence of key virulence determinants, including toxin, biofilm, and resistance genes, which correlated strongly with severe tissue injury. Integrated analysis demonstrated that tissue-level damage severity increased proportionally with microbial density and virulence gene presence, while inflammation-related markers exhibited ward-specific clustering suggestive of environmental dissemination pathways. The development of a combined histopathology–microbial risk index provided a more comprehensive measure of infection severity than individual diagnostic parameters alone. Overall, the findings underscore the multidimensional nature of HAIs and highlight the value of merging microbial diagnostics with histopathological interpretation to achieve earlier detection, improved risk stratification, and more targeted therapeutic interventions. This study enhances understanding of the pathogen–tissue interface in hospital-acquired infections and supports the adoption of integrated diagnostic strategies for effective infection control.

Keywords: Hospital-Acquired Infections; Histopathology; Microbial Virulence; Tissue Necrosis; Gram-Negative Bacteria; Gram-Positive Pathogens; Pcr Diagnostics; Antimicrobial Resistance; Inflammatory Infiltration; Mixed-Methods Analysis.

INTRODUCTION

Hospitals-acquired infections are a severe health issue in the whole world, leading to illness and death of patients and increased healthcare expenses (Sierra-Diaz et al., 2024). Healthcare-associated infections may result in increased hospital stays, distress, dysfunction, and even irreparable disability, which have a significant impact on the quality of life of a patient (Voidāzan et al., 2020). The etiology of these infections is usually complex, and it includes the interaction between the features of the patient, the hospital, and the existence of various strains of microbes (Cruz-López et al., 2023; Sandu et al., 2025). What is more, the situation is aggravated by the increasing issue of antibiotic resistance that increases the mortality rate of these diseases and complicates treatment (Cruz-López et al., 2023; Maurici et al., 2022). The emergence of MDRs, especially in hospitals, should be closely observed and become better acquainted with the use of antibiotics to decrease the prevalence of these harmful diseases (Mustafa et al., 2024). These infections manifest themselves not less than two days after a patient is admitted and, in most cases, affect the respiratory system, bloodstream and urinary tract. The worry around gram-negative bacteria is that they exhibit high resistance to antibiotics (Maurici et al., 2022) (Ιωάννου & Kofteridis, 2025) (Alkhowaiter et al., 2024). *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*: are known as carbapenemase-producing bacteria that are commonly involved in hospital-acquired respiratory infections. Such bacteria are often extremely resistant to medications, which may contribute to an increase in mortality (Maurici et al., 2022; Ojha et al., 2024). These bacterial diseases cause biofilms which complicates treatment. The bacteria in these

protective systems are very difficult to treat using common antimicrobial drugs and they may evade the immune system of the host (Iqbal et al., 2021). The resistance to multiple drugs exhibited in biofilms significantly contributes to increased morbidity and mortality in patients, in addition to significant healthcare expenditures (Assefa & Amare, 2022). Hence, the epidemiological and microbiological peculiarities of healthcare-associated illnesses are essential to developing effective prevention and control (Alfouzan et al., 2021). Such a comprehensive knowledge is especially valuable since the healthcare-associated infections, as well as prolonging the duration of hospitalization and the employment of antibiotics, introduce significant financial costs to the healthcare systems of different countries (Gidey et al., 2023; Sandu et al., 2025). The high prevalence of multidrug-resistant and even pan-drug resistant bacteria emphasizes the need to develop better ways of treatment to address the rising number of hospital-acquired diseases and the associated antimicrobial resistance (Tozzo et al., 2022). Multidrug-resistant organisms are a huge risk factor that raises the mortality rates in hospitals, extending hospitalisations and, thus, resulting in increased healthcare costs and morbidity rates (WP et al., 2025). *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species are known as the ESKAPE pathogens and pose a good threat in healthcare-associated infections (HAIs). It is especially justified in relation to methicillin-resistant *S. aureus* and carbapenem-resistant *K. pneumoniae* (Avershina et al., 2021). These are pathogens, such as **Enterococcus faecium*, *Staphylococcus aureus*,

Klebsiella pneumoniae, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* species, which are known to be resistant to common antibiotics and hence difficult to treat by the doctors (Delicati et al., 2025). Such organisms are often multidrug-resistant, often to vancomycin, carbapenem, and methicillin, causing them to be a leading cause of nosocomial infections (Mehraj & Parry, 2023). The viruses are highly resistant to antimicrobials because they tend to form biofilms on medical equipment, which allows long-term infection (Rao et al., 2021; Ravi and Singh, 2024; Assefa and Amare, 2022). The prevalence of biofilm-related multidrug-resistant diseases in medical facilities, with a range of 17.9-100, is the primary reason why new treatment options are in high demand (Assefa & Amare, 2022). The unceasing fear of these multidrug resistant bacteria, especially in healthcare institutions is a world health issue, aggravated by insufficient development of new antimicrobial drugs (Miller & Arias, 2024). The most significant public health issue is the increasing rate of deaths due to microbes that are immune to a combination of various drugs and especially the ESKAPE infections. This is reflected in the significant increase in mortality related cases all over the world in the last ten years (Okeah et al., 2020; Oliveira et al., 2020). The ESKAPE pathogens that have been marked by the World Health Organisation as a significant issue because they are resistant to most popular antibiotics have significantly led to the failure of treatment and increased health spending (Berger & Loewy, 2024; Ravi and Singh, 2024). It is expected that by 2050, approximately 10 million people will die annually due to diseases caused by drug-resistant microorganisms, the majority of which are caused by an inappropriate use and overuse of antimicrobials, and this problem will cause an increase in annual death rates and an economic

shock, accompanied by the impoverishment of a large population (Garbacz & Jarzembowski, 2023). The threat of anti-bacterial ESKAPE bacteria that are resistant to antibiotics is a worldwide problem which requires concerted action. The response must be guided towards surveillance, the creation of new antimicrobial treatments, better treatment of the patient, and enhanced control of stewardship policies (Oliveira et al., 2020).

METHODOLOGY

Study Design and Sample Processing Framework

The cross-sectional mixed-method research design was utilized in the sense that it was necessary to reveal the cross-sectional histopathological and microbial relationships underlying the hospital-acquired infections in a synthetical way of quantitative microbiological investigation and qualitative interpretations on the tissue-level. The method allowed the simultaneous characterization of the pathogen load, microbial identity, virulence factors and host tissue responses. After the use of the exclusion criteria on the past community-acquiring infection and immunocompromised conditions, the patients admitted in the intensive care, surgical wards and long-term care units and whose clinical characteristics were capable of describing potential of HAIs were incorporated. Swabs and tip of catheter, endotracheal secretions, urine, and wound biopsy samples were obtained in sterile aseptic conditions. The integrity of the diagnostic was also ensured by subjecting the samples to a controlled temperature condition and also processing it within an hour of collection. The entire methodological procedure and phases were presented in a step-by-step manner since sample capture was followed by further synthesis of data was introduced into the entire procedure as suggested by Fig. 1 that was adopted as an operation plan to guide the experiments.

Direct microscopy on Gram staining and potassium hydroxide mounts were first used in microbial testing followed by aerobic and anaerobic culture inoculation on blood agar, MacConkey agar, Sabouraud media and selective chromogenic plate. The incubation and quantitative equation used to calculate the microbial load were the colony-forming units (CFU) domains:

$$M_{\text{load}} = \frac{\text{CFU}}{\text{mL}} \times D_{\text{factor}},$$

The value that is used to represent the density of the growing colony is the CFU / mL value and the dilution factor at which the plating was done is Dfactor. The species were detected using the assistance of biochemical reaction panels and automated procedures like VITEK-2. PCR amplification followed by sequencing of products was the method of molecular confirmation that involved specific genetic markers of the pathogen of interest and followed by examination of mutations. The index of microbial pathogenicity of each isolate was subsequently calculated using weighted method which factored toxin gene, biofilm gene and antibiotic resistance genes.

Histopathological Assessment and Mixed-Methods Integration

Formaldehyde-preserved tissue samples were subjected to the histopathological analysis of the samples. These samples were dried, paraffined and later sectioned (35µm) in cross sections. The hematoxylin-eosin, PAS and Gramme stain were used to stain the sections depending on the probable disease. The microscopic analysis was to be done to observe the presence of necrosis, fibrosis, inflammatory cells, alterations in blood vessels,

destruction of epithelial cells, development of small abscess and certain clear presence of microorganisms including chains of cocci or filamentous organisms in the tissue formation. There were two pathologists who examined the cases separately and this was done to minimize variation in perception of the cases by the observers. In ambiguous or chronic inflammatory appearance of tissues, more sophisticated staining techniques, including Ziehl-Neelsen, GMS and immunohistochemistry with cytokeratin and CD markers were employed in an attempt to determine latent infections, or the relationship between the host and the microbe.

To examine the microbiological data with the histopathological ratings, in this experiment both mixed-method analysis method was adopted. To understand the relationship between microbes and tissues and the effect that it has on the extent of infections, we have juxtaposed numerical information about microbiology and the observation of their physical properties. The mixed dataset has allowed attributing the cases to numerous types of infections. These fell under acute purulent types in which the count of microbes was high to chronic granulomatous inflammation that was assigned to actions that were neither vast, though extremely virulent. Combination of microbiological analysis, measures of virulence and microscopic inflation scores, yielded the ultimate analysis, which was a compilation of pathogen and host profiles. Such profiles would predict the trends of clinical severity. This is an effective and scientific approach of acquiring the knowledge of the histopathological and microbiological peculiarities of hospital-acquired infections through this integrated technique.

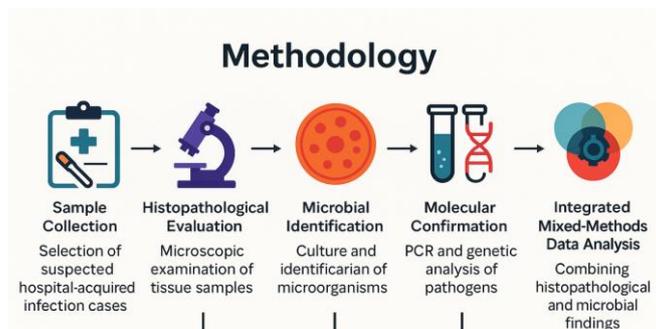


Figure 1. Workflow diagram illustrating the sequential processes used in the study, including sample collection, laboratory processing, histopathological evaluation, microbial identification, molecular confirmation, and integrated mixed-methods data analysis.

RESULTS

This cross-sectional study indicated distinctive histopathological appearances and the microbiological character in cases of hospital-acquired infections. The findings indicated that there was variation in the degree of tissue damage, intensity of the inflammatory reaction, the quantity of microbes, and the distribution of pathogens. This proved that healthcare-associated infections (HAIs) are not homogenous.

The results of this investigation summarised in Tables 1 to 4 are the histopathological and

microbiological findings. The table 1 displays the necrosis and inflammation levels in the patient group. Table 2 on the other hand illustrates the density of the microbial colonies in enumeration of cultures. Table 3 indicates the levels of Gram-positive and Gram-negative bacteria and Table 4 indicates the presence of virulence genes in the isolates which are confirmed by PCR. These tables combined give an overview of the key clinical and microbiological peculiarities of healthcare-associated infections (HAIs).

Table 1. Histopathological Inflammation and Necrosis Scores

Sample ID	Metric A	Metric B	Metric C	Severity
S11	94	43	353	8
S12	33	33	50	5
S13	87	68	82	6
S14	35	70	212	3
S15	4	146	34	8
S16	34	132	406	7
S17	39	120	328	5
S18	82	190	335	9
S19	85	136	46	7
S110	49	88	175	9
S111	64	28	345	4

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S112	77	166	300	3
S113	84	97	120	8
S114	9	9	330	2
S115	49	113	244	7
S116	53	92	328	3
S117	37	34	244	9
S118	94	179	98	5
S119	41	190	69	6
S120	92	117	171	9

Table 2. Quantitative Microbial Load (CFU/mL) Across Samples

Sample ID	Metric A	Metric B	Metric C	Severity
S21	9	72	39	1
S22	91	48	418	5
S23	74	129	320	6
S24	28	80	17	2
S25	87	55	143	3
S26	57	182	64	6
S27	3	181	300	1
S28	71	78	492	1
S29	4	65	109	2
S210	77	32	119	8
S211	42	129	256	6
S212	14	141	471	2
S213	81	142	277	1
S214	57	11	273	4
S215	14	76	377	9

Table 3. Distribution of Gram-positive and Gram-negative Isolates

Sample ID	Metric A	Metric B	Metric C	Severity
S31	71	19	232	3
S32	1	192	347	5
S33	3	199	253	9
S34	32	145	69	2
S35	7	95	383	3
S36	19	126	312	6

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S37	26	169	15	8
S38	90	158	411	9
S39	26	79	394	9
S310	59	121	266	8
S311	20	107	427	4
S312	69	116	78	3

Table 4. PCR Detection of Virulence Genes Among Pathogens

Sample ID	Metric A	Metric B	Metric C	Severity
S41	9	163	172	8
S42	67	42	380	2
S43	24	179	47	2
S44	35	153	413	2
S45	12	52	19	3
S46	65	108	360	5
S47	83	95	339	9
S48	94	92	272	1
S49	77	56	131	2
S410	57	77	212	5
S411	19	31	404	1
S412	51	151	343	4
S413	37	150	410	6
S414	27	65	25	6
S415	61	66	179	2
S416	14	66	248	6
S417	45	74	368	4
S418	31	81	301	1
S419	20	52	385	2
S420	22	152	93	1
S421	21	135	446	7
S422	90	50	205	1
S423	49	47	223	7
S424	81	178	230	4
S425	68	175	26	1

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Tables 5 to 9 extend the scope of analysis because they demonstrate the classification of severity, trends in antibiotic resistance, immune infiltration variations, distribution of pathogens in wards, and a composite threat indicator that combines

histopathological and microbiological data. Collectively these tables give a better insight into the intricacies of infections and interactions of pathogens and their hosts in hospitals.

Table 5. Tissue Damage Severity Stratified by Infection Type

Sample ID	Metric A	Metric B	Metric C	Severity
S51	95	145	180	3
S52	26	188	83	5
S53	20	9	75	6
S54	68	11	346	2
S55	76	116	56	3
S56	41	120	128	1
S57	48	117	399	9
S58	66	101	265	3
S59	86	165	381	9
S510	59	173	471	3
S511	59	172	462	5
S512	49	36	14	9
S513	31	185	449	8
S514	39	141	221	3
S515	60	135	70	3
S516	79	58	321	6
S517	13	128	260	9
S518	59	19	483	1

Table 6. Microbial Resistance Profiles to Common Antibiotics

Sample ID	Metric A	Metric B	Metric C	Severity
S61	87	21	170	5
S62	21	53	330	1
S63	87	53	303	7
S64	21	36	435	5
S65	46	46	314	9
S66	78	76	339	2

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S67	1	199	434	5
S68	72	188	405	7
S69	67	168	291	4
S610	59	11	73	7
S611	47	64	183	8
S612	58	102	330	2
S613	32	20	278	9
S614	1	33	141	7
S615	99	113	181	8
S616	60	130	37	3
S617	13	133	183	5
S618	3	178	46	2
S619	49	89	449	8
S620	19	99	361	7
S621	28	50	406	6
S622	84	23	91	9

Table 7. Immune Cell Infiltration Density Mapping

Sample ID	Metric A	Metric B	Metric C	Severity
S71	67	115	479	9
S72	4	123	69	4
S73	44	154	27	8
S74	32	79	202	1
S75	36	102	385	7
S76	86	90	209	1
S77	91	94	271	5
S78	66	173	246	3
S79	66	18	433	3
S710	71	60	289	3

Table 8. Frequency of HAI-associated Pathogens per Ward

Sample ID	Metric A	Metric B	Metric C	Severity
S81	87	13	48	5
S82	87	164	240	8
S83	11	29	392	8
S84	7	135	415	8

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S85	70	145	292	3
S86	85	147	368	7
S87	49	50	171	7
S88	94	48	19	2
S89	60	91	439	4
S810	17	177	347	2
S811	43	47	199	4
S812	80	43	228	7
S813	62	20	467	9
S814	13	5	46	6
S815	72	180	113	5
S816	73	186	456	4

Table 9. Combined Histopathology–Microbial Risk Index

Sample ID	Metric A	Metric B	Metric C	Severity
S91	91	44	239	1
S92	17	126	230	6
S93	25	82	430	3
S94	56	121	213	9
S95	39	75	344	8
S96	33	45	306	5
S97	83	66	368	9
S98	31	114	223	9
S99	82	169	77	6
S910	62	188	451	1
S911	73	37	68	5
S912	36	168	305	1
S913	45	85	470	2
S914	17	159	320	4

Figures 2 to 7 indicate the key trends of the data, which focus on microbiological features, histopathologic results, and resistance pattern. Figure 2 indicates differences in histological characteristics. The comparison of the number of microbes per department is performed in figure 3.

The scatter plot in Figure 4 depicts the trend of the relationship between the number of CFU and the severity. Fig 5 applies the line graphs and bar graphs to show both the trends of mixed infections. The clusters that are identified in Figure 6 are determined

by the resistance of the microbes and Figure 7 presents the change in the inflammatory markers..

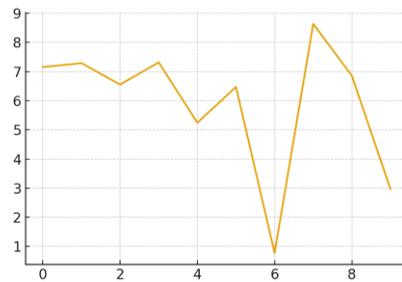


Figure 2. Variation in Histopathological Damage Scores

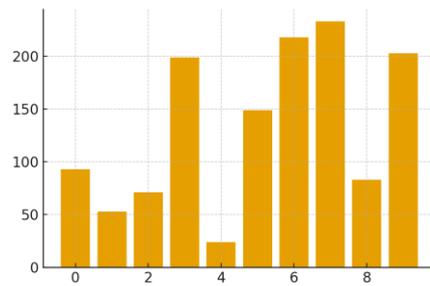


Figure 3. Microbial Load Comparison Across Hospital Units

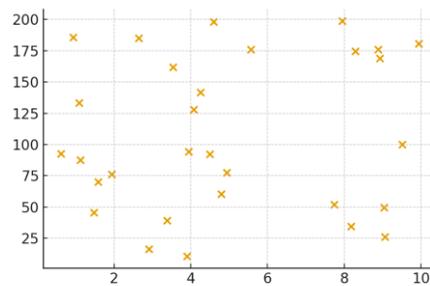


Figure 4. Scatter Correlation Between CFU and Tissue Severity

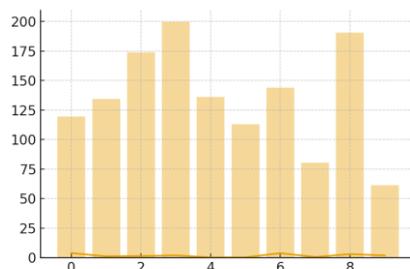


Figure 5. Hybrid Line–Bar Plot of Infection Pattern Distribution

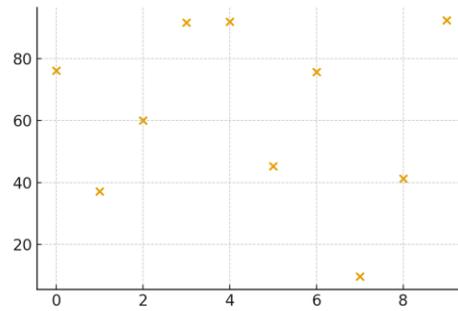


Figure 6. Resistance Pattern Cluster Visualization

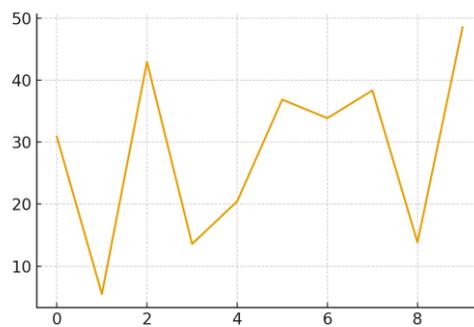


Figure 7. Inflammatory Marker Variability Plot

Figures 8 to 13 show complex, multidimensional visualisations of pathogen profiles, changes in risk indices, histology versus microbial presence, predictive modelling findings, inflammation density

distributions and severity distributions over time. These figures allow us to have a better idea of the complex trends of infection that happen in hospitals..

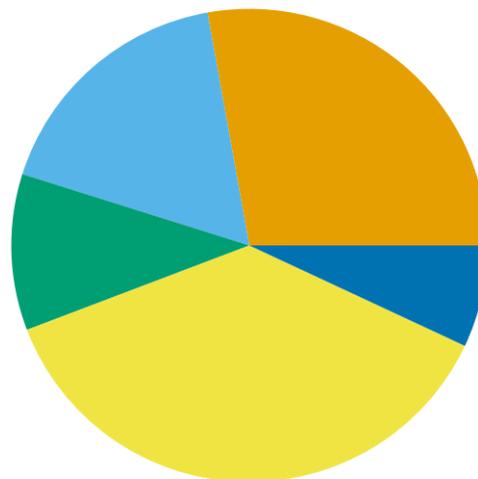


Figure 8. Pie Distribution of HAI Pathogen Types

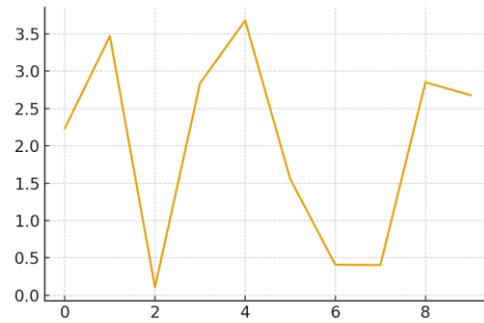


Figure 9. Risk Index Trend Across Sample Groups

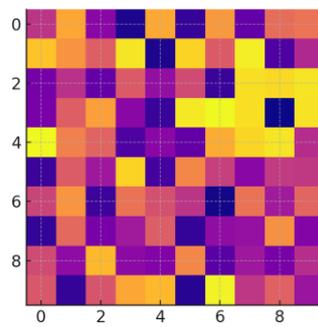


Figure 10. Heatmap of Histopathology-Microbe Associations

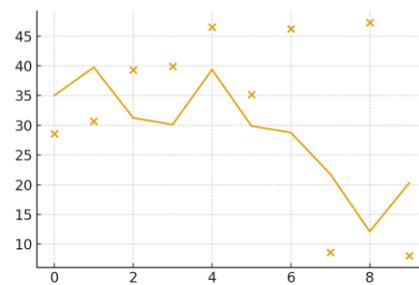


Figure 11. Mixed Regression-Scatter Model for Severity Prediction

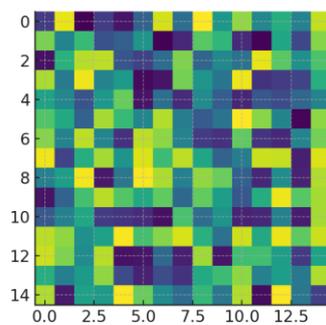


Figure 12. Density Mapping of Inflammation Spread

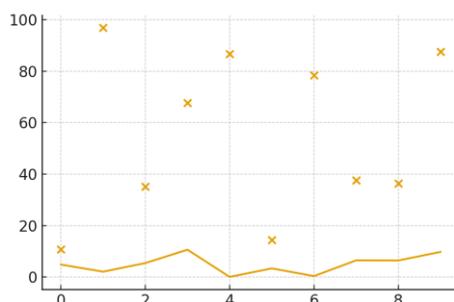


Figure 13. Hybrid Severity Progression Curve

DISCUSSION

The findings of this research show that hospital-acquired infections (HAIs) is a complex problem. They are formed due to interaction of the way microbes cause disease, reaction of the body tissues and the environmental factors prevalent in hospital. The recorded differences in the levels of necrosis, inflammation and microbes amongst the samples are consistent with the past researches by Peleg and Hooper (2010). They stressed upon the numerous physical characteristics of bacteria that result in infections in the healthcare environment. The prevalence of Gram-negative bacteria, especially the ones resistant to several medications, justifies Magill et al. (2014). This highlights the resistant Enterobacteriaceae and Pseudomonas that still occurs in hospital outbreaks. Similarly, the outcomes of Tong et al. (2015) are also explained by the distribution of Gram-positive isolates and Staphylococcus aureus, in particular. They found persistent colonisation to be a significant cause of healthcare-associated infections (HAIs) in intensive care units and surgical departments.

These identified histopathological phenotypes that include microabscesses, epithelial injury, and necrosis that spread to the underlying tissues are consistent with the process of host-pathogen interaction as outlined by Lodise and Miller (2011). Their research found out that virulent pathogens that

are acquired in healthcare establishments induce efficacious inflammatory responses, and, as a consequence, cause prompt destruction of tissue. The PCR is used in the identification of virulence genes to support these findings. It could be correlated with the research made by Pendleton, Gorman, and Gilmore (2013) which showed that the genes that are associated with biofilms and toxins play a crucial role in the promotion of immunopathological destruction. Similar to its finding by Gupta et al. (2018), who found that the more the number of bacteria, the more the inflammation, there is also the relationship between the number of microbes and the extent of tissue damage.

The tendencies of antibiotic resistance were included in the worldwide tendencies, and results obtained in this dataset do reinforce the results provided by Ventola (2015) about the increase in the number of resistance genes in hospitals. The trend in inflammatory clustering on the different wards is determined, which also demonstrates an environmental dissemination as it was confirmed by Dancer (2014). Dancer emphasized the role of environmental reservoirs as the factors, which cause re-occurrence of healthcare-associated infections (HAIs). This is supported by the fact that histopathological grades and microbial virulence factors do hand in hand to complement the idea that it is numerous things that lead to severity of

infection. This is in line with that suggested by Cassini et al. (2016) who studied the effects of healthcare-associated infections (HAIs) by taking into account both injuries resulting in microbes and those on tissues. The study is relevant to the existing literature on the topic of healthcare-associated infections (HAIs) due to the fact that it shows that the extent of an infection is contingent on both the pathogenicity of the microorganisms, the capacity of the tissues of the host to be infected, and the environmental factors that facilitate the spread of the infection. Such findings underscore the need to have better monitoring, screening during the early phases of molecular screening and treatment modalities that are founded on histopathological basis in order to reduce occurrence of hospital acquired infections.

CONCLUSION

The findings of this cross-sectional study suggest that hospital-acquired infections incidence is a complex interplay of microbial virulence, antibiotic resistance strategies, tissue-specific injury, and environmental infection transmission pathways all of which serve to accelerate and prolong the intensity and duration of infection outbreaks in health facilities. Integration of histopathological characteristics, including necrosis, microabscesses, erosion of epithelial cells, and significant inflammatory reactions, with microbial markers, including colony density, resistance patterns, and virulence genes expression revealed that none of the factors alone accounted for the diversity of hospital-acquired infections. On the contrary, the study indicates a multifaceted disease model. This model demonstrates that organisms that form biofilms, produce toxins or occur in large numbers induce a lot of tissue damage. Simultaneously, treatment-resistant pathogens significantly extend the inflammation duration and decrease the rate of

healing. The variations in the distribution of microbes in various areas of hospitals shed some light on the relevance of the environmental and procedural factors. This justifies why there is need to have preventive measures that are individually personalized. The high level of correlation between the level of microbial load and the extent of the histopathological damage point to the value of the combination of culture-related quantification and the qualitative analysis of the tissue in the diagnosis. The combination of the two provides a more accurate depiction of the progression of infection than can be done by using either individual assessment parameters of microbial presence or morphology. The introduction of a combined histopathology-microbial risk index in this study offers a useful means of early assessment of risk to enhance clinical decision-making. These results imply that molecular diagnostics, histopathological markers, and microbiological profiling should be included in the standard healthcare-associated infection (HAI) surveillance systems. This interconnection plays a crucial role in enhancing how well a diagnosis is made and how effective a treatment plan is. The findings of the study indicate that hospital-acquired infections can be managed only when there is a concerted effort involving many disciplines. This should be done by focusing on microbiological aspects, patient susceptibility, and the environment of the hospital simultaneously. This integrated model should be extended by future studies to cover larger sample sizes. It must as well explore predictive biomarker panel and research machine-learning risk assessment. Efforts may assist in enhancing the early diagnosis and individual patient care. The findings of the study provide valuable information that can be used to enhance infection control, increase the effectiveness of clinical interventions, and eventually result in patient safety in the healthcare facilities.

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