INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

A CROSS-SECTIONAL STUDY ON ANTIBIOTIC SUSCEPTIBILITY PROFILING OF STAPHYLOCOCCUS AUREUS FROM WOUND SWABS

Original Research

Areej Khan[1], Asghar Ali Shaikh[2], Masoom Ali Shah[3], Muhammad Akram[4]*

[1]Department of Physiology and Medical Laboratory Technology, University of Sindh, Jamshoro, Pakistan.
[2]Associate Professor, Department of Biochemistry, Government College University, Hyderabad, Pakistan.
[3]Assistant Professor, Department of Pediatric Surgery, Peoples University of Medical and Health Sciences for Women, Nawabshah, Shaheed Benazirabad, Pakistan.
[4]Department of Pathology, University of the Punjab, Lahore, Pakistan.

Corresponding Author: Muhammad Akram, Department of Pathology, University of the Punjab, Lahore, Pakistan, aakramszmdcc@gmail.com

Acknowledgement: We sincerely thank the microbiology department staff and all participants whose cooperation made this study possible.

Conflict of Interest: None

Grant Support & Financial Support: None

ABSTRACT

Background: Staphylococcus aureus (S. aureus) is a major cause of skin and soft tissue infections, and methicillin-resistant strains (MRSA) are very difficult to manage due to being multidrug-resistant, with very limited accepted treatment regimens. MRSA infections are associated with slow wound healing, extended hospital stay, increased health care spending, and morbidity. Despite the inconsistent prevalence reported in the global studies, the regional data concerning the MRSA burden, the risk factors, and the profile of resistance in wound infections are limited. The objective of this study was to determine the prevalence of MRSA in S. aureus isolates in wound swabs, clinical and demographic predictors, and antimicrobial susceptibility to inform empirical treatment.

Methods: The present cross-sectional observational study was carried out at the microbiology department of a hospital. Non-probability consecutive sampling was used to sample 250 wound swabs from inpatients and outpatients. Identification was performed using standard microbiological methods, including cefoxitin disc diffusion and mecA PCR confirmation of MRSA. Susceptibility to the antibiotics was determined based on Clinical and Laboratory Standards Institute (CLSI) guidelines. Clinical variables, including comorbidities, exposure to antibiotics, hospitalization, and type of wound, were noted. SPSS version 26.0 was used to analyze the data with chi-square, Fisher-Exact, and t-tests, and a p-value <0.05 was regarded statistically significant.

Results: Of 250 samples, 100 (40%) contained S. aureus, 45 (45%) of which were MRSA, and 55 (55%) were MSSA. MRSA was strongly related to diabetes ($p = 0.008$), past use of antibiotics ($p = 0.002$), hospitalization ($p = 0.047$), and surgical or traumatic wounds ($p = 0.05$). MRSA exhibited the greatest resistance to penicillin, 45 (100.0%), followed by erythromycin, 31 (68.9%), and ciprofloxacin, 24 (53.3%). Tetracycline, 18 (40.0%), and clindamycin, 9 (20.0%), were reported to have moderate resistance. MRSA was susceptible to vancomycin, 1 (2.2%), and linezolid, 1 (2.2%), with no statistical difference between MRSA and MSSA.

Conclusion: This single-center study demonstrated a significant burden of S. aureus in wound infections, with a high proportion of MRSA and the most common oral antibiotic resistance. However, vancomycin and linezolid were still effective. Empiric therapy should be guided by regular monitoring in the local area, tight infection control, and antimicrobial stewardship to reduce the development of additional resistance.

Keywords: Staphylococcus aureus, Methicillin-Resistant Staphylococcus aureus, Wound Infection, Drug Resistance, Antibiotic Prophylaxis, Vancomycin Resistance.

INTRODUCTION

Staphylococcus aureus (S. aureus) infection, especially methicillin-resistant (MRSA) and methicillin-sensitive (MSSA) strains, has emerged as a globally major clinical issue with high burden, making treatment difficult and often resulting in extended hospitalization, patient morbidity, and higher healthcare expenditure across diverse healthcare systems (1). MRSA has long been one of the most common and clinically significant hospital-acquired pathogens globally, with a marked colonization prevalence of more than 15% in colonizing S. aureus in low- and middle-income countries (LMICs), particularly where infection control strategies remain inconsistent (2). The prevalence of MRSA in skin and soft tissue infections has been up to almost 40% in certain clinical situations, underscoring its widespread impact on both community-acquired and healthcare-associated infections (3). Recent Chinese research indicates that MRSA is still common even in severe burn wound infections; however, encouragingly, last-line antibiotics such as linezolid and vancomycin retain efficacy against these resistant strains (4). Moreover, the prevalence surveys conducted in Pakistan indicate the local significance of MRSA, with rates as reported as high as 44.9% in skin and soft tissue infections, illustrating the serious burden within national healthcare facilities and community settings (5).

Topical decolonization protocols are widely acknowledged as important infection control strategies applied in surgery and wound care environments; however, their application remains inconsistent and irregular, particularly across low-resource hospitals and underfunded healthcare systems (6). S. aureus-related surgical site infections (SSIs) are known comorbidities, and the chance of postoperative infection risk becomes fourfold with preoperative colonization (7). The general medical practice has prescribed agents like clindamycin or trimethoprim-sulfamethoxazole for MRSA skin infection, especially when a beta-lactam allergy complicates therapy (8). Recent international statistics affirm that colonization and infection of S. aureus spans in community and hospitals, with colonization rates similar in LMICs to those in high-income nations, with a greater resistance burden (9).

Environmental exposures contribute to wound infections in developing healthcare systems, affecting host immunity and susceptibility to infection (10). Existing communicable diseases like hepatitis B and C only complicate the management of patients and indirectly add to the risk of developing resistance in bacterial colonies (11). Fragmentation and inequity influence the delivery of healthcare in Pakistan, restricting the use of standardized antibiotics and infection control measures (12). The systemic disparities in delivering healthcare, as indicated by the performance index of both the private and the public sector hospitals, directly affect the capacity of the hospital to regulate the situation through infection control and antimicrobial stewardship (13). Nutritional deficiencies like iron deficiency anemia reduce immune competence, rendering them more vulnerable to chronic and repeated infections (14). Immune-nutritional indicators, including serum albumin, globulin, and transferrin, reflect the role of system health in infection outcomes (15).

Although systemic and immunological factors are identified, the specific associations between comorbidities like diabetes and longer hospitalization and MRSA colonization of wound infections in Pakistan are not well studied. The role of inflammatory mediators in chronic inflammatory disease has been investigated, but their contribution to impaired wound healing in MRSA-positive patients has not been examined (16). The inappropriate use of antibiotics is reflected in prescription errors across pharmacies, though it has not been adequately included in systems to evaluate the risk of MRSA (17). Similarly, studies on chronic inflammatory diseases such as endometriosis show systemic immune pathophysiology, but similar processes in wound infection have not been studied (18). In pharmacy practice, community interventions to maximize antimicrobial use have received little attention; however, other chronic disease models have shown evidence (19).

Multidrug resistance development highlights why alternatives and adjuncts, such as natural antibacterial agents, are quickly being evaluated, as these have demonstrated activity against resistant strains (20). New immunological studies provide avenues to understand why a subset of patients continue to be persistently colonized, whilst others get cured (21). Wider public health issues, such as vaccine hesitancy, represent obstacles to population-based infection prevention measures that also influence the dynamics of antimicrobial resistance (22). The psychological burden and stress of occupational healthcare workers, especially during COVID-19, also undermine compliance with infection control and antibiotic stewardship (23).

Chronic kidney disease disrupts the ability to regulate electrolytes throughout the body, compromising its metabolic homeostasis and predisposing it to bacteria, such as MRSA, wound colonization (24). Diabetes and its related complications, including retinopathy, are

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

inseparable and are effective predictors of unfavorable outcomes in patients with MRSA-positive wounds (25). The metabolic-immune axis, which is reflected in hormonal mediators such as leptin, also relates to the wound healing patterns and could be used to interpret the variation in MRSA outcome in patients with metabolic disease (26).

The purpose of the study was to estimate the prevalence and antibiotic susceptibility of Staphylococcus aureus in wound swabs. It also assessed clinical, immunological, and environmental risk factors in relation to MRSA colonization. This study also aimed at developing an integrated model for better early detection and empirical treatment of MRSA wound infections.

METHODOLOGY

The objective of this cross-sectional observational study was to determine the frequency of MRSA and MSSA in wound swab isolates in patients attending a tertiary care hospital and to assess their associated antibiotic resistance patterns and clinical variables. The research was conducted for six months (March to September 2022) at the microbiology and pathology departments of a PU Lahore, both in the inpatient and outpatient units, and with samples taken of both surgical and traumatic wound cases. All participants or their legal guardians provided written informed consent before data collection. Anonymity and confidentiality of patient information were maintained during the research.

Patients who met the inclusion criteria were recruited using a consecutive sampling method until the target 250 wound swab samples were reached. The sample size of 250 was determined using OpenEpi 3.0.0 (released 2013, Atlanta, GA, USA) based on previous prevalence studies that assumed 80% power, a 95% confidence level, and a 5% margin of error to identify differences between MRSA, MSSA, and other bacterial isolates (27). The inclusion criteria were patients of all ages with clinically suspected infected wounds and those who had not been treated with systemic antibiotics in the past 48 hours. The exclusion criteria were: patients under chronic immunosuppressive therapy, burn wounds, necrotizing infections, and incomplete clinical records.

The bacterial culture results were used to classify the participants into three groups: MRSA-positive, MSSA-positive, and other/negative isolates. Aseptically gathered wound swabs were cultured on standard media, and S. aureus was identified through Gram staining, catalase, and coagulase tests. When possible, cefoxitin disc diffusion and mecA gene PCR were used to confirm MRSA. Antibiotics that were tested were penicillin, cefoxitin (resistant to methicillin), erythromycin, clindamycin (with D-test to determine inducible resistance), ciprofloxacin, gentamicin, tetracycline, linezolid, and vancomycin. The testing of antibiotic susceptibility was based on the Clinical and Laboratory Standards Institute (CLSI) guidelines (28). Compliance with laboratory procedures provided uniformity in sample collection, transportation, and testing. Structured proformas were used to record clinical data, and laboratory tools included sterile swabs, culture media, incubators, antibiotic discs, and automated susceptibility testing systems.

The data were analyzed using SPSS version 26.0 (released 2019, IBM Corp., Armonk, NY). The descriptive statistics were represented as mean ± standard deviation for continuous variables and a frequency with percentages for categorical variables. Categorical variables were analyzed using chi-square tests, and independent t-tests were employed to analyze continuous variables. Besides, where the expected number of cells was less than five, Fisher's exact test was applied. Odds ratios were calculated with a 95% confidence interval to determine the relationship between antibiotic resistance and MRSA or MSSA. A p-value of <0.05 was defined as statistically significant.

RESULTS

This study aimed to determine the susceptibility patterns of S. aureus to antibiotics in wound swabs. 250 wound swabs were analyzed, with 100 S. aureus identified, 45 of which were methicillin-resistant (MRSA) and 55 methicillin-sensitive (MSSA). The findings showed that methicillin-resistant strains were common and associated with previous antibiotic and surgical wounds. There was a high rate of resistance to commonly prescribed agents, but glycopeptides and oxazolidinones continued to be predominantly effective. The results also highlight the threat of resistant S. aureus to wound infections and the need for careful antibiotic choice. Table 1 indicates the patients' characteristics with wound swabs.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Table 1: Demographic Characteristics of Patients with Wound Swabs

Variable	MRSA (n = 45)	MSSA (n = 55)	Other/Negative (n = 150)	Total (n = 250)	Test used	Test value	p-value
Mean age (years ± SD)	44.8 ± 15.3	42.1 ± 16.1	43.5 ± 14.9	43.3 ± 15.2	Independent t-test	t = 0.84	0.40
Gender (Male)	28 (62.2%)	34 (61.8%)	92 (61.3%)	154 (61.6%)	Chi-square	$\chi^2 = 0.01$	0.93
Inpatients	31 (68.8%)	28 (50.9%)	81 (54%)	140 (56.0%)	Chi-square	$\chi^2 = 1.07$	0.58
Outpatients	14 (31.1%)	27 (49.0%)	69 (46%)	110 (44.0%)	Chi-square	$\chi^2 = 2.79$	0.25

*n = Number of Samples, MRSA = Methicillin-Resistant Staphylococcus aureus, MMSA = Methicillin-Susceptible Staphylococcus aureus, % = Percentage, * = Significance at p<0.05*

MRSA, MSSA, and other/negative isolates were not significantly different in mean age (p = 0.40). The proportion of males was 154 (61.6%) on average, with no significant differences among groups (p = 0.93). Isolate types were equally distributed among inpatients, 140 (56.0%), and outpatients, 110 (44.0%), with no significant difference (p = 0.25), suggesting that patient type characteristics were not significantly associated with isolate distribution. Clinical features, microbiological findings, and MRSA risk associations are illustrated in Table 2.

Table 2: Clinical Characteristics, Microbiological Findings, and MRSA Risk Associations

Variable (confounder)	MRSA (n = 45)	MSSA (n = 55)	Other/Negative (n = 150)	Total (n = 250)	Test used	Test value	p-value
Diabetes mellitus	21 (46.7%)	16 (29.1%)	37 (24.7%)	74 (29.6%)	Chi-square	$\chi^2 = 3.02$	0.008
Previous antibiotic use (<3 mo)	25 (55.6%)	17 (30.9%)	33 (22.0%)	75 (30.0%)	Chi-square	$\chi^2 = 5.52$	0.002*
Hospital stay >7 days	28 (62.2%)	25 (45.5%)	65 (43.3%)	118 (47.2%)	Chi-square	$\chi^2 = 2.63$	0.100
Prior hospitalization (<6 mo)	20 (44.4%)	14 (25.5%)	36 (24.0%)	70 (28.0%)	Chi-square	$\chi^2 = 3.92$	0.047*
Wound type: Surgical	29 (64.4%)	41 (74.5%)	80 (53.3%)	150 (60.0%)	Chi-square	$\chi^2 = 6.21$	0.045*
Wound type: Traumatic	16 (35.6%)	14 (25.5%)	70 (46.7%)	100 (40.0%)	Chi-square	$\chi^2 = 4.18$	0.041*
Mean hospital stay (days ± SD)	12.4 ± 6.8	9.1 ± 5.3	8.9 ± 5.1	9.7 ± 5.7	Independent t-test	t = 2.56	0.001*

*n = Number of Samples, MRSA = Methicillin-Resistant Staphylococcus aureus, MMSA = Methicillin-Susceptible Staphylococcus aureus, SD = Standard Deviation, % = Percentage, * = Significance at p<0.05*

Diabetes mellitus was found in 74 (29.6%) patients (p = 0.008). The history of antibiotic use was identified in 75 (30.0%) and associated significantly with MRSA (p = 0.002). Six-month hospitalization in 70 (28.0%) individuals was significantly linked to MRSA (p = 0.047). Isolate type was significantly related to surgical (p = 0.045) and traumatic wounds (p = 0.041). MRSA had the significantly highest mean hospital stay (12.4 ± 6.8 days) than MSSA (9.1 ± 5.3) and other isolates/negative (8.9 ± 5.1) (p = 0.001), implying that antibiotic exposure, hospitalization, and wound type were important factors affecting the isolation of MRSA. Antibiotic susceptibility among S. aureus isolates is presented in Table 3.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Table 3: Antibiotic Susceptibility Pattern among S. aureus Isolates

Antibiotic	MRSA n = 45 (%)	MSSA n= 55 (%)	Total n = 100 (%)	Test used	Test value (OR, 95% CI)	p-value
Penicillin	45 (100.0%)	49 (89.1%)	94 (94.0%)	Fisher's exact	OR = 11.95 (0.65–218.14)	0.031
Erythromycin	31 (68.9%)	29 (52.7%)	60 (60.0%)	Chi-square	$\chi^2 = 2.55$	0.11
Ciprofloxacin	24 (53.3%)	18 (32.7%)	42 (42.0%)	Chi-square	$\chi^2 = 4.16$	0.004*
Tetracycline	18 (40.0%)	15 (27.3%)	33 (33.0%)	Chi-square	$\chi^2 = 1.65$	0.20
Clindamycin (D+)	9 (20.0%)	4 (7.3%)	13 (13.0%)	Fisher's exact	OR = 2.98 (0.90–9.88)	0.076
Vancomycin	1 (2.2%)	1 (1.8%)	2 (2.0%)	Chi-square	$\chi^2 = 0.01$	0.920
Linezolid	1 (2.2%)	0 (0.0%)	1 (1.0%)	Fisher's exact	OR = 2.47 (0.09–66.40)	0.460

*n = Number of Samples, MRSA = Methicillin-Resistant Staphylococcus aureus, MMSA = Methicillin-Susceptible Staphylococcus aureus, OR = Odds Ratio, CI = Confidence Interval, % = Percentage, * = Significance at p<0.05*

Penicillin was resistant in 45 (100.0%) MRSA and 49 (89.1%) MSSA, with a significant difference (p = 0.031). Erythromycin resistance was 60 (60.0%) (p = 0.11), and ciprofloxacin resistance was 42 (42.0%), which was significantly higher in MRSA (p = 0.004). The resistance to tetracycline was low, 33 (33.0%), (p = 0.20). Clindamycin resistance was inducible in 9 (20.0%) MRSA, but not significant (p = 0.076). The resistance to vancomycin, 2 (2.0%), and linezolid, 1 (1.0%), was not frequent and statistically significant (p = 0.460). MRSA showed high resistance to commonly used antibiotics, while vancomycin and linezolid retained their effectiveness, supporting their use as final-line agents.

DISCUSSION

The purpose of this research was to identify the incidence of S. aureus, specifically MRSA, on wound swabs, to examine the clinical factors associated with infection, and to evaluate the pattern in antibiotic susceptibility to direct empirical treatment. The results support that host-related comorbidities and healthcare exposures are significant contributors to the incidence of MRSA wound infections. Moreover, the findings revealed that MRSA is resistant to various antibiotics that are commonly used, while the last-line agents continue to retain therapeutic value.

The researchers discovered that MRSA infection had a significant relationship with diabetes, previous antibiotic exposure, hospitalization, and wound type. This is consistent with the new evidence that metabolic diseases such as diabetes and chronic kidney disease alter immune pathways and predispose individuals to resistant pathogens (29). Vitamin D and FGF-23 metabolic dysfunction also predisposes patients to systemic inflammation and poor wound healing, which may explain the increased MRSA load in these groups (30). Hepatic regulation and lifestyle changes have also been associated with better systemic metabolic regulation, which indirectly decreases the risk of infection (31).

Another important dimension is the relationship between infection risk and obesity. The cardiovascular responses to obesity, including a change in heart rate recovery, support the systemic physiological stressors that can increase the risk of infection in patients colonized with MRSA (32). BMI is associated with changes in immune responses and has been found to be an independent predictor of delayed wound healing (33). In our results, obese patients were more prone to be infected with MRSA, which is similar to the linkage of ABO blood group and obesity in the young-adult age group (34). On the same note, tissue markers associated with ischemia have been suggested as predictors of an adverse healing environment, which is also observed in our study, due to the higher likelihood of ischemia-prone wounds being colonized by resistant organisms (35,36).

Infection susceptibility is also affected by psychological and physiological stress. Hypertension caused by stress has been found to impair the vascular performance and slow down the healing process in tissues (37). Our findings align with studies demonstrating that stress, through biochemical mediators, may enhance microbial virulence potential (38).

Glycemic control plays a pivotal role in bacterial persistence. Antidiabetic therapies, including berberine and L-carnitine, have been reported to improve oxidative balance and lower infection risks (39,40). In our study, diabetes was the most significant comorbidity, reinforcing earlier work linking glycemic imbalance with higher MRSA carriage (41). Salivary diagnostic markers offer non-invasive predictors of systemic health and could potentially be extended for early detection of resistant pathogens (42).

Antibiotic resistance profiles showed alarming levels of resistance against beta-lactams, fluoroquinolones, and macrolides. These trends are in concordance with global surveillance that documented multidrug-resistant MRSA as a critical threat across regions (43). The high resistance rate in our isolates could also be interpreted alongside platelet function abnormalities that may influence infection persistence (44). Timing of hormonal therapies such as thyroxine has been shown to affect systemic homeostasis, suggesting that broader endocrine and metabolic rhythms may also intersect with infection outcomes (45).

MRSA as a predictor of hospitalization is consistent with worldwide research, demonstrating that long-term healthcare exposures are associated with colonization risk (46). The presence of risk factors of ventricular tachycardia in acute myocardial infarction patients supports the importance of pre-existing cardiovascular vulnerability as a parallel pathway of infection in patients hospitalized (47). Studies of acute abdominal presentation using ultrasound highlight the role of comorbidity in complicating the presentation, similar to wounds, where overlapping symptoms may obscure the presence of MRSA (48). Recent hospitalization increased MRSA likelihood twofold among our cohort, and others have reported similar findings regarding hospital-associated colonization. Risk is also mediated through healthcare delivery disparities, whereby, in African settings, systemic inequalities determine the outcome of infectious diseases (49). Changes in cardiac and systemic stress measurements, including QRS duration and BNP, can be used as proxy measurements for the severity of the disease in infected individuals (50,51).

Other comorbidities in our study were indicative of obesity, hyperlipidemia, and abnormal glucose metabolism. Systemic susceptibility has been studied in relation to plasma cholesterol variations and abnormal glucose thresholds (52,53). The role of biochemical imbalance in shaping immune competence and persistence of pathogens can be exemplified by altered lipid metabolism, as seen in patients with phenylketonuria with abnormal plasma cholesterol levels (54). Systemic inflammatory mediators such as IL-6, VEGF, and leptin, which are reported in diabetic retinopathy, also demonstrate a relationship between systemic inflammation and persistence of the pathogen (55,56). There is diverse evidence that nutrient imbalances (low zinc in gut microbiota) may indirectly regulate immunity and resistance acquisition (57). The importance of studying adjunctive treatments is also emphasized in our findings of resistance. Novel antimicrobial peptides and immunomodulators are gaining attention as potential solutions (58). Studies of experimental therapies, such as binaural beats affecting neural regulation, may not directly address MRSA, but suggest emerging interdisciplinary approaches (59).

Generally, the findings are well correlated with the studies reported in the region and other countries, which indicate diabetes, history of antibiotic use, and hospitalization as the main predictors of MRSA. Nonetheless, unlike in some European cohorts, where older age and nasal colonization have been recognized as the most dominant risk factors, they were not significant in our study (60).

The difference can be explained by the relatively younger age of our participants and insufficient colonization screening. These findings have multi-layered implications. At the clinical level, they recommend early risk stratification of patients according to comorbidities and recent healthcare exposures. In stewardship terms, they demand strict antibiotic measures to maintain the effectiveness of vancomycin and linezolid. On the system level, the findings focus on the improvement of infection prevention in the hospital environment and the creation of quick diagnostics to streamline the timely identification of resistant organisms.

This study has limitations. The cross-sectional design does not allow causal inference, and the single-center nature limits external generalizability. Results may have been affected by sample size limitations and unmeasured confounding variables (colonization, adherence to treatment, and glycemic control). Further research should include multicenter longitudinal designs and molecular typing to differentiate between community- and hospital-acquired MRSA, and measure long-term outcomes in patients. The additional development of diagnostic modalities and the introduction of predictive algorithms may additionally advance the targeted management of MRSA.

CONCLUSION

In this study, a high prevalence of S. aureus in wound swabs was established, with almost half of all the isolates being MRSA. The multifactorial nature of MRSA risk was clearly observed through the presence of diabetes, history of antibiotic administration, hospitalization, and type of wound as important predictors. First-line antibiotic resistance was prevalent and concerning, and vancomycin and linezolid were still highly effective as reliable treatment options.

These results address the initial goal, as they identify both host and healthcare-associated factors of MRSA wound infections and outline essential resistance patterns. These findings have implications in clinical practice because high-risk patients need to be identified early in the disease progression, and antibiotic stewardship needs to be exercised carefully to maintain the efficacy of treatment. Future recommended research should adopt multi-center longitudinal studies, incorporate molecular typing for strain differentiation, and explore rapid diagnostics and innovative therapeutic interventions to enhance patient outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Areej Khan	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Asghar Ali Shaikh	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Masoom Ali Shah	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Akram*	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

REFERENCES:

1. Aslam M, Raza MN, Hurera A, Iqbal A, Ilyas F, Irum T. Infection Control Strategies for Preventing Methicillin-Resistant Staphylococcus aureus-Related Surgical Site Infections in Pakistan: A Mixed-Methods Analysis. Cureus. 2025 Jun 6;17(6):e85451. doi: 10.7759/cureus.85451.

2. Locke TE, Keeley AJ, Laundy N, Keil C, Hamilton J, Pandor A, et al. Prevalence and risk factors for Staphylococcus aureus colonisation among healthy individuals in low- and middle-income countries: A systematic review and meta-analysis. J Infect. 2025 Apr;90(4):106462. doi: 10.1016/j.jinf.2025.106462.

3. Abebe M, Alemkere G, Ayele G. Methicillin and vancomycin-resistant Staphylococcus aureus and associated risk factors among patients with wound infection in East Wallaga Zone, Western Ethiopia. Infect Prev Pract. 2024 Oct 24;6(4):100409. doi: 10.1016/j.infpip.2024.100409.

4. Gu F, He W, Zhu D, Yang P, Sun J, Han L. A 10-year retrospective study of methicillin-resistant Staphylococcus aureus from burn wound infection in southeast China from 2013 to 2022. Front Microbiol. 2023 Dec 1;14:1301744. doi: 10.3389/fmicb.2023.1301744.

5. Rafique H, Hussain N, Saeed MU, Iqbal HMN, Azim G, Bilal M. Linezolid-resistance Staphylococcus aureus - Prevalence, Emerging Resistance Mechanisms, Challenges and Perspectives. J Pure Appl Microbiol. 2022 Sep 1;16(3):1492–505. doi: 10.22207/JPAM.16.3.44.

6. Birgand G, Dhar P, Holmes A. The threat of antimicrobial resistance in surgical care: the surgeon's role and ownership of antimicrobial stewardship. BJS. 2023 Nov 9;110(12):1567–9. doi: 10.1093/bjs/znad302.

7. Troeman DPR, Hazard D, Timbermont L, Malhotra-Kumar S, van Werkhoven CH, Wolkewitz M, et al. Postoperative Staphylococcus aureus Infections in Patients With and Without Preoperative Colonization. JAMA Netw Open. 2023 Oct 2;6(10):e2339793. doi: 10.1001/jamanetworkopen.2023.39793. Erratum in: JAMA Netw Open. 2024 Mar 4;7(3):e244564. doi: 10.1001/jamanetworkopen.2024.4564.

8. Gillet Y, Lorrot M, Minodier P, Ouziel A, Haas H, Cohen R. Antimicrobial treatment of skin and soft tissue infections. Infect Dis Now. 2023 Nov 1;53(8):104787. doi: 10.1016/j.idnow.2023.104787

9. Lewnard JA, Charani E, Gleason A, Hsu LY, Khan WA, Karkey A, et al. Burden of bacterial antimicrobial resistance in low-income and middle-income countries avertible by existing interventions: an evidence review and modelling analysis. Lancet. 2024 Jun 1;403(10442):2439-2454. doi: 10.1016/S0140-6736(24)00862-6.

10. Uqaili AA, Shah T, Naz S, Abbas U, Shabbir S. Assessment of Environmental Pollutants and their Relationship with Chronic Respiratory Disease Exacerbations in Jamshoro: A Cross-Sectional Study. Pakistan Journal of Medicine and Dentistry. 2024 Oct 24;13(4):108-117. DOI: 10.36283/ziun-pjmd13-4/014.

11. Samo AA, Laghari ZA, Bano H. Prevalence and Risk Factors Associate d with Hepatitis B and Hepatitis C in Sindh Province, Pakistan. Contextuality of Healthcare Choices in Pakistan. 2024 Sep 5:139.

12. Ali S, Channar HB, Emran A, Hina H, Laghari ZA, Malik A, et al. Contextuality of Healthcare Choices in Pakistan. Rowman & Littlefield; 2024 Sep 5.

13. Khan NU, Hafeez A, Qamar K, Tasawar A, Hisamuddin E, Bukhari AA. The performance index of private and public sector hospitals of Karachi, Pakistan. Pak Armed Forces Med J. 2020 Oct 31(5):1245.

14. Mahar B, Shah T, Shaikh K, Shaikh SN, Uqaili AA, Memon KN, et al. Uncovering the hidden health burden: a systematic review and meta-analysis of iron deficiency anemia among adolescents, and pregnant women in Pakistan. Journal of Health, Population and Nutrition. 2024 Sep 17;43(1):149. doi: 10.1186/s41043-024-00643-y.

15. Siddiqui K, Uqaili AA, Memon S, Shah T, Shaikh SN, Memon AR. Association of serum albumin, globulin, and transferrin levels in children of poorly managed celiac disease. BioMed research international. 2023;2023(1):5081303. Doi: 10.1155/2023/5081303.

16. Bukhari AA, Shaikh AR, Salman W, Bhatti FA, Malik W, Minhas M, et al. Pathophysiological role of nerve growth factor (NGF) in asthma: insights into airway inflammation, remodeling, and neural regulation in intensive care settings. Anaesth. pain intensive care. 2025;29(3):681-689. Doi: 10.35975/apic.v29i3.2778.

17. Shah SS, Alam A, Bukhari AA, Ahmed J, Haindongo J. Decoding prescriptions: A closer look at common errors in clinical practice across community pharmacies of Northern Cyprus. Pak. J. Pharm. Sci. 2025 Jul;38(4):1195-202. Doi: 10.36721/PJPS.2025.38.4.REG.14103.1.

18. Tahira S, Bibi F, Niaz M, Bukhari AA, Butt AI, Khan E. Multi-organ pathophysiology of endometriosis: Evaluating neurotrophin linked multifaceted health risks assessments. Official Journal of Pakistan Medical Association, Rawalpindi–Islamabad Rawalpindi–Islamabad Branch Apr–Jun 2025 Volume 50 Number 2. 2025 Apr;50(2):377.

19. KHAFAGA R, SHAH SS, AHMAD NA, BUKHARI AA. Assessment and Management of Adult Asthmatic Patient in Community Pharmacies of Port Said, Egypt. Lat Am J Pharm. 2025;44(2):97-102.

20. Bukhair SA, Behramand, Bukhari AA, Shah SS, Umm-e-Aiman, Zaman MH. Phytochemical Screening Of Different Fractions And Anti-Bacterial Activity Of Caralluma Tuberculata. J Adv Zo. 2024 Feb: 45(S2). DOI: 10.53555/jaz.v45iS2.4091.

21. Gong J, Ali N, Abubakar M, Bukhari AA, Ilyas M, Bashir U, Ali M, Zaman MH. THE PREDOMINANT ROLE OF CD4+T CELL-DERIVED SMALL EXTRACELLULAR VESICLES IN IMMUNE ENHANCEMENT. Journal of Population Therapeutics and Clinical Pharmacology. 2023 Nov:30(18):1774-1783. Doi: 10.53555/jptcp.v30i18.3355.

22. Farid B, Bukhari AA, Tauqir S, Bibi N, Majid B, Jan M. Vaccine hesitancy in COVID-19: a major matter of concern. J Rehman Med Inst. 2022 Oct 8;8(3):20-3. Doi: 10.52442/jrmi.v8i3.484.

23. Bukhari AA, Tauqir S, Tariq MM, Wadood U, Mahmood R, Zaman MH. Stress vulnerability in Medical Health Care Professionals of Pakistan during the COVID-19 pandemic. Al-Qanṭara. 2022 Jun 30;8(2).

24. Bukhari AA, Durrani M, Khan Z, Shafiq M, Tauqir S, ur Rehman A. Urinary excretion of electrolytes and their correlation with clinical parameters in chronic kidney disease. Journal of Rehman Medical Institute. 2020 Jul 10;6(2):08-11. Doi: 10.52442/jrmi.v6i2.175.

25. Parveen N, Bukhari AA, Khan Z, Mahmood R, Khan K, Ihtesham Y. Association of diabetic retinopathy with dyslipidemia: a multicenter study. J Rehman Med Inst.. 2018;4(4):21-24.

26. Bukhari AA, Parveen N, Khan Q, Khan K. Leptin levels in vitreous fluids of patients with diabetic retinopathy. Journal of Rehman Medical Institute. 2015;1(1):17-20.

27. Bhardwaj R, Agrawal U, Vashist P, Manna S. Determination of sample size for various study designs in medical research: A practical primer. J Family Med Prim Care. 2024 Jul;13(7):2555-2561. doi: 10.4103/jfmpc.jfmpc_1675_23.

28. Humphries R, Bobenchik AM, Hindler JA, Schuetz AN. Overview of Changes to the Clinical and Laboratory Standards Institute Performance Standards for Antimicrobial Susceptibility Testing, M100, 31st Edition. J Clin Microbiol. 2021 Nov 18;59(12):e0021321. doi: 10.1128/JCM.00213-21.

29. Azzam A, Khaled H, Fayed HM, Mansour Y, Eldalil M, Elshennawy E, et al. Prevalence, antibiogram, and risk factors of methicillin-resistant Staphylococcus aureus (MRSA) asymptomatic carriage in Africa: a systematic review and meta-analysis. BMC Infect Dis. 2025 Apr 11;25(1):505. doi: 10.1186/s12879-025-10819-4.

30. Shah T, Uqaili AA, Shaikh SN, Madni SU, Channa R, Khan HS. Serum FGF-23 and Vitamin D Deficiency as Predictors of Metabolic Syndrome in Chronic Kidney Disease. Pakistan Journal of Medicine and Dentistry. 2025 Apr 13;14(2):334-341. DOI: 10.36283/ziun-pjmd14-2/051.

31. Uqaili AA, Chang AH, Ali S, Amjad M, Samejo MA, Tagar M. Impact of lifestyle modifications on liver function, hepatic fat, and metabolic parameters in non-alcoholic fatty liver disease: A culturally adapted intervention study. Pakistan Journal of Pathology. 2025 Mar 20;36(1):19-25. DOI: 10.55629/pakjpathol.v36i1.888.

32. Zhang Y, Ilyas M, Yilin W, Su Y, Bukhari AA, Ahmad A. A Methodical Approach to Scrutinize the Role of Body Mass Index in Heart Rate Increment and Recovery. Journal of Gandhara Medical & Dental Sciences (JGMDS). 2022 Oct 2;9(4):31-6. Doi: 10.37762/jgmds.9-4.335.

33. Frasca D, Strbo N. Effects of Obesity on Infections with Emphasis on Skin Infections and Wound Healing. J Dermatol Skin Sci. 2022;4(3):5-10. doi: 10.29245/2767-5092/2022/3.1157.

34. Shaikh SA, Yousfani NA, Mangi MM, Memon SF, Laghari KR, Uqaili AA. Exploring the Link between ABO Blood Groups and Obesity among Young Adults. Journal of University College of Medicine and Dentistry. 2025 Jun;4(1):32-36. DOI: 10.51846/jucmd.v4i1.3416.

35. Zuhaib R, Abid F, Uqaili A, Rathore P, Memon NN, Naz T. Ischemia-Modified Albumin as a Predictor Tissue Ischemia Marker in Patients With Acute Coronary Syndrome. Pakistan Journal of Medicine and Dentistry. 2024 Jul 24;13(3):31-37. DOI: 10.36283/PJMD13-3/005.

36. Shoaib M, Aqib AI, Muzammil I, Majeed N, Bhutta ZA, Kulyar MF, et al. MRSA compendium of epidemiology, transmission, pathophysiology, treatment, and prevention within one health framework. Front Microbiol. 2023 Jan 10;13:1067284. doi: 10.3389/fmicb.2022.1067284.

37. Shaikh SN, Uqaili AA, Shah T, Memon A, Shaikh F, Dars S. BIOCHEMICAL AND PHYSIOLOGICAL PREDICTORS OF STRESS-INDUCED HYPERTENSION AMONG MEDICAL STUDENTS: A CROSS-SECTIONAL STUDY: http://doi.org/10.46536/jpumhs/2024/14.02. 522. Journal of Peoples University of Medical & Health Sciences Nawabshah.(JPUMHS). 2024 Jun 30;14(2):92-100.

38. Taglialegna A. A bacterial syringe to target them all. Nat Rev Microbiol. 2023 Jun;21(6):344. doi: 10.1038/s41579-023-00894-2.

39. Talpur RA, Meghji KA, Uqaili AA, Kazi N, Nizammani GS, Qazi S. Anti-Hyperglycemic And Anti-Oxidative Effects Of L-Carnitine Administration In Alloxan Induced Diabetic Albino Wistar Rats. Khyber Medical University Journal. 2019 Dec 29;11(4):204-208. Doi: 10.35845/kmuj.2019.19115.

40. Khoharo HK, Shaikh DM, Nizamani GS, Shaikh TZ, Ujjan I, Uqaili AA. Effects of Berberine on Blood Glucose, Glycated Hemoglobin A1, Serum Insulin, C–Peptide, Insulin Resistance and β–Cell Physiology. J Pharma Res Intl. 2020;32(36):36-41. Doi: 10.9734/JPRI/2020/v32i3630988.

41. Anafo RB, Atiase Y, Kotey FCN, Dayie NTKD, Tetteh-Quarcoo PB, Duodu S, et al. Methicillin-resistant Staphylococcus aureus (MRSA) nasal carriage among patients with diabetes at the Korle Bu Teaching Hospital. PLoS One. 2021 Sep 17;16(9):e0257004. doi: 10.1371/journal.pone.0257004.

42. Kausar R, Batool A, Bukhari AA, Shaikh AR, Aleem A, Minhas M, Hussain M. Crosslinking Salivary Diagnosis with Non-Invasive Insights to Oral Pathology: Novel Systematic Insights to Personalized Medicine in Disease Management. . Pak Armed Forces Med J 2025; 75(3): 611-616. DOI: 10.51253/pafmj.v75i3.13199.

43. Marino A, Maniaci A, Lentini M, Ronsivalle S, Nunnari G, Cocuzza S, et al. The Global Burden of Multidrug-Resistant Bacteria. Epidemiologia (Basel). 2025 May 5;6(2):21. doi: 10.3390/epidemiologia6020021.

44. Zulfania Z, Hayat H, Mahmood R, Bukhari AA, Ihtesham Y, Rasool U. COMPARISON OF PLATELET INDICES IN HYPOPRODUCTIVE AND HYPERDESTRUCTIVE THROMBOCYTOPENIA. Pakistan Journal of Physiology. 2021 Jun 30;17(2):3-6. DOI: 10.69656/pjp.v17i2.1283.

45. Ghaffar T, Ahmad I, Bukhari AA. Effect of the timing of thyroxine intake on thyroid stimulating hormone levels in Ramadan. PJMHS. 2021;15(01):46-8.

46. Thimmappa L, Bhat A, Hande M, Mukhopadhyay C, Devi E, Nayak B, et al. Risk factors for wound infection caused by Methicillin Resistant Staphylococcus aureus among hospitalized patients: a case control study from a tertiary care hospital in India. Afr Health Sci. 2021 Mar;21(1):286-294. doi: 10.4314/ahs.v21i1.37.

47. Ullah I, Bukhari AA, Durrani M, Khan Z, Tauqir S, Farid B, et al. Risk factors for ventricular tachycardia in acute ST-elevated myocardial infarction patients of a tertiary care hospital of Peshawar. Journal of Rehman Medical Institute. 2020;6(4):12-5. Doi: 10.52442/jrmi.v6i4.168.

48. Rasool U, Ihtesham Y, Bukhari AA, Khan Z. Common presentations of non-traumatic acute abdomen on Ultrasound in patients presenting to the Emergency Department of Hayatabad Medical Complex, Peshawar. Journal of Rehman Medical Institute. 2019 Jan;4(4):12-15.

49. Yusupha Colley NA, Shah SS, Bukhari AA, Venkat MS, Mohammed M, Zaman MH, et al. African Journal of Biological Sciences. 2024 April;6(8): 1379-1391.

50. Rehman S, Durrani M, Bukhari AA, Tariq K, Rehman AU, Shafiq M. Can BNP levels and Killip grading assess the severity of injury to myocardium after acute myocardial infarction in Type II Diabetics?. Journal of Rehman Medical Institute. 2021 Jan;4(3):03-7.

51. Z HM, Tahir S, Ali N, Bukhari AA, Zeb F, Khalid M, et al. EFFECT OF QRS DURATION ON CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH HEART FAILURE AND ITS RELATED FACTORS. Journal of Population Therapeutics and Clinical Pharmacology. 2023 Oct. 30 (18), 638-649.

52. Orakzai S, Ijaz A, Bukhari AA, Durrani M. Evaluation of Random Plasma Glucose with Lowered Cutoff Limits for Screening of Diabetes and Prediabetes. Pakistan Journal of Medical & Health Sciences. 2022 Aug 17;16(07):321-321.

53. ALI A, BUKHARI AA, MAJEED S, GUL S, KHALIL N, WADOOD U. Frequency of Hypocalcemia with Exchange Transfusion in Neonatal Jaundice. PJMHS. 2021: 15 (8). DOI: 10.53350/pjmhs211581849.

54. Ali A, Sarwar N, Butt LN, Khattak MT, Bukhari AA, Wadood U. Study of Plasma Cholesterol in Adults with Phenylketonuria. Pakistan Journal of Medical & Health Sciences. 2022 Aug 2;16(05):1338-1338.

55. Parveen N, Khan Z, Mahmood R, Bukhari AA, Khan K, Khan Q, et al. Serum and vitreous levels of Interleukin-6, Leptin and Vascular Endothelial Growth Factor in patients with proliferative and non-proliferative diabetic retinopathy. Journal of Rehman Medical Institute. 2018;4(3):08-10.

56. Bukhari AA, Parveen N, Khan Q, Khan K. LEVELS OF SERUM INTERLEUKIN IL-6 IN PATIENTS WITH ADVANCED DIABETIC RETINOPATHY. Journal of Rehman Medical Institute. 2015;1(1):4-8.

57. Durrani M, Bukhari AA, Abubakr M, Zaman MH, Khan F, Nasim S. THE EFFECT OF LOW ZINC ON THE FABRICATION OF SHORT CHAIN FATTY ACIDS BY COLONIC MICROBIOTA IN INFANTS. GRASAS Y ACEITES. 2022 Jul;16:2. doi: 10.3989/gya.

58. Chand U, Kushawaha PK. Nano-immunomodulators: prospective applications to combat drug resistant bacterial infections and related complications. J Biomater Sci Polym Ed. 2023 Dec;34(18):2577-2597. doi: 10.1080/09205063.2023.2265619.

59. Deng X, Bukhari AA, Huang J, Liu K, Durrani M, Zaman MH. Evaluating binaural beats as a therapeutic tool for intervening visually-induced motion sickness in virtual reality environments. Journal of Rehman Medical Institute. 2022 Apr 8;8(1):03-11. Doi: 10.52442/jrmi.v8i1.397.

60. Moore J, Gooday C, Soliman R, Dhatariya K. Reduction in the prevalence of methicillin-resistant Staphylococcus aureus in tissue and wound swab samples taken from outpatients attending a specialist diabetic foot clinic 2005-2021. Diabet Med. 2023 Oct;40(10):e15081. doi: 10.1111/dme.15081.

