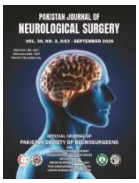

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Original Research

Surgical Site Infection After Craniotomy: Incidence, Microbiology, and Modifiable Risk Factors in a Retrospective Cohort of 350 Craniotomy Procedures

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ABSTRACT

Objective: To determine the incidence, microbiological profile, and modifiable perioperative risk factors of 30-day surgical site infection (SSI) after craniotomy.

Materials and Methods: This retrospective cohort study at Khyber Teaching Hospital, Peshawar, included 350 adult craniotomy procedures performed from January 2022 through December 2025; each procedure was one observation. The primary outcome was 30-day SSI, classified as superficial incisional, deep incisional, or organ/space infection. An exploratory multivariable logistic regression model estimated adjusted odds ratios (aORs) and 95% confidence intervals (CIs).

Results: SSI occurred after 25 of 350 procedures (7.1%): 10 organ/space, 10 superficial incisional, and five deep incisional infections. Cultures were positive in 21 cases (84.0%), of which five (23.8%) were polymicrobial. Recorded primary pathogens were methicillin-sensitive Staphylococcus aureus (n=5), coagulase-negative staphylococci (n=5), Cutibacterium acnes (n=4), Streptococcus species (n=3), Enterobacterales (n=3), and methicillin-resistant S. aureus (n=1). SSI occurred after 13 of 244 procedures (5.3%) with compliant prophylaxis timing, seven of 86 (8.1%) with noncompliant timing, and five of 20 (25.0%) with no prophylaxis. Absence of perioperative prophylaxis was associated with higher adjusted SSI odds (aOR 7.30; 95% CI 2.18-24.45; p=0.001), although based on only 20 procedures without prophylaxis.

Conclusion: Thirty-day SSI occurred after 7.1% of craniotomy procedures. Absence of perioperative prophylaxis was associated with higher adjusted odds of SSI, but the estimate arose from a small unexposed subgroup and should be interpreted cautiously.

Keywords: Craniotomy; Surgical Wound Infection; Antibiotic Prophylaxis; Risk Factors; Retrospective Studies; Cerebrospinal Fluid Leak.

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INTRODUCTION

Post-craniotomy surgical site infection (SSI) is an uncommon but clinically important complication of cranial neurosurgery. Cranial surgery has procedure-specific infection risks because it involves scalp incision, bone flap handling, dural opening, possible exposure to cerebrospinal fluid (CSF), and, in selected cases, the use of implants or CSF diversion devices. Although the reported incidence is usually low, post-craniotomy SSI may result in meningitis, ventriculitis, bone flap osteomyelitis, intracranial abscess, repeat surgery, prolonged antimicrobial treatment, readmission, and increased resource use.[1,2]

Previous studies have shown that the frequency and risk profile of SSI after craniotomy vary across clinical settings. Jiménez-Martínez et al, conducted a prospective cohort study of adult craniotomy patients at Bellvitge University Hospital, Barcelona, Spain, and highlighted the importance of identifying procedure-related and patient-related predictors of SSI after craniotomy. [1] Abu Hamdeh and Lytsy evaluated surgical site infections in standard neurosurgical procedures and reported that neurosurgical SSI was associated with clinical impact and potentially preventable perioperative risk factors.[2] Fang et al., in a systematic review and meta-analysis, identified several factors associated with neurosurgical site infection after craniotomy, including CSF leak, CSF drainage, repeated operation, longer operative duration, venous sinus entry, and higher American Society of Anesthesiologists score.[3] Campioli et al., in a four-year experience from a tertiary-care referral centre, reported that post-craniotomy SSI was more frequent in emergency procedures and dirty wound classification, and also discussed the role of perioperative antibiotic prophylaxis selection.[4]

The microbiological profile of post-craniotomy SSI is important because it guides empirical treatment and supports infection-prevention planning. Most reported infections are related to skin flora, particularly Staphylococcus aureus, coagulase-negative staphylococci, and Cutibacterium acnes. Gram-negative and polymicrobial infections may also occur, especially in patients with prolonged hospital exposure, contaminated wounds, CSF leakage, or device-related infection pathways. Culture-negative infections remain clinically relevant because they may reflect previous antibiotic exposure, low-burden organisms, delayed sampling, or limitations in microbiological recovery.[1,4,5]

Effective perioperative antibiotic prophylaxis depends not only on administration but also on appropriate agent selection, administration within the recommended pre-incision window, and redosing when indicated during prolonged procedures. Noncompliance may arise from emergency scheduling, workflow failures, or incomplete documentation. Assessment of prophylaxis should therefore account for other procedure-related factors, including CSF leakage, drains, implants, and operative duration.[3-5]

Although post-craniotomy SSI is well described internationally, published evidence from tertiary neurosurgical centres in Pakistan remains limited. Differences in patient mix, surgical workload, antimicrobial use, infection-prevention practices, and post-discharge surveillance may limit the applicability of international estimates. Local data are therefore needed to inform hospital-level prevention and provide context-specific evidence for neurosurgical infection control.

MATERIALS AND METHODS

Study Design and Setting

This retrospective cohort study was conducted at the Department of Neurosurgery, Khyber Teaching Hospital, Medical Teaching Institution (MTI), Peshawar, Pakistan. The analytic cohort comprised 350 adult craniotomy procedures performed between January 4, 2022, and December 24, 2025. Each de-identified record represented one eligible craniotomy procedure, and no study identifier was

repeated; the unit of analysis and all outcome denominators were procedure-based. Consecutive eligible procedures during the study period were included using a non-probability sampling approach.

Inclusion Criteria

Adult patients aged 18 years or above who underwent craniotomy at Khyber Teaching Hospital MTI during the study period were included. Both elective and emergency craniotomy procedures were considered eligible if the medical record contained sufficient demographic, operative, perioperative antibiotic, microbiological, and postoperative follow-up information to determine 30-day surgical site infection status.

Exclusion Criteria

Patients were excluded if they were younger than 18 years, underwent a neurosurgical procedure other than craniotomy, or had incomplete medical records that prevented verification of the primary outcome. Procedures with documented active cranial infection at the time of surgery were also excluded to avoid misclassification of pre-existing infection as postoperative surgical site infection. Cases without adequate 30-day postoperative follow-up information were not included in the final analysis.

Operational Definitions

The primary outcome was 30-day surgical site infection (SSI), defined as any postoperative infection related to the craniotomy site occurring within 30 days of surgery. SSI was recorded as a binary outcome and further classified as superficial incisional, deep incisional, or organ/space infection. Superficial incisional SSI referred to infection involving the skin or subcutaneous tissue of the incision. Deep incisional SSI was defined as infection involving deeper soft tissues, including fascia or muscle layers. Organ/space SSI referred to infection involving intracranial, meningeal, ventricular, bone flap, or other operated spaces related to the craniotomy procedure. Cerebrospinal fluid (CSF) leak was defined as documented intraoperative or postoperative CSF leakage in the operative record, inpatient record, or follow-up documentation. Any CSF diversion drain referred to the use of an external ventricular drain or lumbar drain.

Antibiotic prophylaxis quality was recorded as a derived variable with three categories. Compliant timing was defined as administration of non-vancomycin prophylactic antibiotics within 0–60 minutes before incision or vancomycin-containing regimens within 60–120 minutes before incision. Noncompliant timing was defined as prophylaxis administered outside these timing windows. No prophylaxis was defined as the absence of perioperative prophylactic antibiotic administration.

Data Collection Procedure and Instrument

Data were collected using a structured extraction sheet. Sources included medical records, admission notes, operative and anaesthesia records, antibiotic administration records, microbiology reports, discharge summaries, readmission records, and follow-up documentation. Variables included demographic, clinical, operative, CSF-related, device-related, prophylaxis, microbiological, treatment, readmission, and mortality data. Microbiology fields recorded culture positivity, one primary pathogen per culture-positive SSI, and a separate indicator of polymicrobial growth; additional co-isolates in polymicrobial cases were not enumerated in the analytical dataset. Patient identifiers were removed before analysis, and confidentiality was maintained.

Data Analysis Technique

Data were entered in Microsoft Excel and independently reanalysed for this revision using

Python 3.12.13 (pandas 2.2.3, NumPy 2.3.5, and SciPy 1.17.0). Continuous variables were reported as mean with standard deviation or median with interquartile range, as appropriate. Categorical variables were reported as frequencies and percentages. Continuous variables were compared using the Mann-Whitney U test; categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. The exploratory multivariable logistic regression model included age, diabetes mellitus, operative duration per hour, any CSF leak, implant use, any CSF diversion drain, and two indicator terms for prophylaxis quality, with compliant timing as the reference category. No automated variable-selection procedure was used. Because the model estimated eight predictor coefficients from only 25 SSI events, adjusted estimates were considered exploratory and were interpreted using aORs and 95% CIs rather than p-values alone. Discrimination was assessed using ROC-AUC, calibration using the Hosmer-Lemeshow test, and multicollinearity using variance inflation factors. A two-sided p-value <0.05 was considered statistically significant.

Ethical Approval

Ethical approval was obtained from the Institutional Research and Ethical Review Board, Khyber Teaching Hospital, Peshawar, Pakistan (Approval/Reference No. 154/DME/KTH, dated March 12, 2026). All data were handled anonymously and confidentially.

RESULTS

Cohort Characteristics

Among the 350 craniotomy procedure records, the mean age was 48.1 +/- 15.4 years, and the mean body mass index (BMI) was 27.1 +/- 4.2 kg/m2. Diabetes mellitus was documented in 75 records (21.4%). Intraoperative CSF leak occurred in 24 procedures (6.9%), and postoperative CSF leak occurred in 18 procedures (5.1%). An external ventricular or lumbar drain was used in 77 procedures (22.0%), and an implant was used in 120 procedures (34.3%). Immunosuppression or chronic steroid exposure was documented in 70 records (20.0%). Perioperative prophylaxis was administered in 330 procedures (94.3%): 244 had compliant timing, 86 had noncompliant timing, and 20 received no prophylaxis. Median operative duration was 172 minutes (interquartile range, 116-218 minutes).

Table 1 compares selected clinical and perioperative characteristics by 30-day SSI status. Perioperative prophylaxis was less frequent among procedures followed by SSI than among those without SSI (80.0% vs 95.4%; Fisher's exact p=0.009). Implant use occurred in 9 of 25 SSI procedures (36.0%) and 111 of 325 procedures without SSI (34.2%; p=0.830). None of the other displayed comparisons reached statistical significance.

Table 1: *Selected cohort and procedure characteristics by 30-day SSI status Values are median (interquartile range) or n/N (%). The unit of analysis was the craniotomy procedure.*

Variable	No SSI (n=325)	SSI (n=25)	p-value
Age (years)	49 (38–59)	44 (30–54)	0.178
BMI (kg/m^2)	26.9 (24.2–30.1)	28.0 (25.8–30.7)	0.142
Diabetes mellitus	67/325 (20.6%)	8/25 (32.0%)	0.205
Operative duration (min)	172 (116–218)	170 (132–211)	0.956
Intraoperative CSF leak	20/325 (6.2%)	4/25 (16.0%)	0.081
Postoperative CSF leak	17/325 (5.2%)	1/25 (4.0%)	1.000
Any drain, EVD or lumbar	70/325 (21.5%)	7/25 (28.0%)	0.456
Implant used	111/325 (34.2%)	9/25 (36.0%)	0.830
Perioperative prophylaxis given	310/325 (95.4%)	20/25 (80.0%)	0.009

Incidence and SSI Subtype Distribution

Thirty-day SSI occurred after 25 of 350 craniotomy procedures, giving an incidence of 7.1%. Among the 25 SSI cases, organ/space infection occurred in 10 (40.0%), superficial incisional infection in 10 (40.0%), and

deep incisional infection in five (20.0%).

Microbiology

The microbiological findings are summarized in Table 2. Cultures were positive in 21 of 25 SSI cases (84.0%), and five of the 21 culture-positive cases were polymicrobial (23.8%; 20.0% of all SSI cases). Table 2 reports one recorded primary pathogen per culture-positive case; these primary-pathogen counts sum to 21 and do not represent total isolate counts. MSSA and CoNS were the most frequent recorded primary pathogens, followed by Cutibacterium acnes; MRSA was recorded as the primary pathogen in one case.

Table 2: *Microbiological findings among 30-day SSI cases (n=25).*

Finding	Value
Culture-positive SSI	21/25 (84.0%)
Culture-negative SSI	4/25 (16.0%)
Polymicrobial SSI	5/25 (20.0%); 5/21 (23.8%) of culture-positive SSI
Primary pathogen - MSSA	5/21 (23.8%)
Primary pathogen - CoNS	5/21 (23.8%)
Primary pathogen - Cutibacterium acnes	4/21 (19.0%)
Primary pathogen - Streptococcus species	3/21 (14.3%)
Primary pathogen - Enterobacterales	3/21 (14.3%)
Primary pathogen - MRSA	1/21 (4.8%)

Note: Primary-pathogen counts represent one recorded primary organism for each culture-positive SSI and sum to 21; they are not total isolate counts. Five cases were flagged as polymicrobial, but additional co-isolates were not captured in the analytical dataset.

Antibiotic Prophylaxis Quality and SSI Rates

SSI occurred after 13 of 244 procedures (5.3%) with compliant prophylaxis timing, seven of 86 (8.1%) with noncompliant timing, and five of 20 (25.0%) with no perioperative prophylaxis.

Table 3*: Exploratory multivariable logistic regression predicting 30-day SSI (n=350) based on 25 SSI events; reference category for prophylaxis quality was compliant timing.*

Predictor	aOR	95% CI	p-value
Age, per one year	0.98	0.96–1.01	0.227
Diabetes mellitus	1.89	0.74–4.84	0.182
Any CSF leak, intraoperative or postoperative	2.25	0.75–6.76	0.148
Implant used	0.98	0.39–2.44	0.959
Any drain, EVD or lumbar	1.58	0.60–4.11	0.353
Operative duration, per hour	1.00	0.69–1.44	0.988
Timing noncompliant versus compliant	1.60	0.59–4.35	0.358
No prophylaxis versus compliant timing	7.30	2.18–24.45	0.001

Treatment Patterns and Clinical Outcomes

Among the 25 SSI cases, treatment included bone flap removal with antibiotics in seven cases, minor incision and drainage with antibiotics in four cases, bedside wound care with antibiotics in four cases, operating-room incision and drainage with bone flap retention in three cases, drainage through EVD or lumbar route with antibiotics in three cases, antibiotics alone in two cases, operating-room washout with antibiotics in one case, and operating-room incision and drainage with antibiotics in one case.

Thirty-day readmission occurred after 37 of 350 procedures (10.6%). Readmission followed 17 of 25 SSI procedures (68.0%) and 20 of 325 procedures without SSI (6.2%). Thirty-day mortality occurred after two procedures (0.6%), neither of which was followed by SSI.

Multivariable Logistic Regression

Table 3 presents the exploratory multivariable logistic regression model for 30-day SSI. After adjustment for the clinically selected variables, absence of perioperative prophylaxis was associated with higher SSI odds than compliant

timing (aOR 7.30; 95% CI 2.18-24.45; p=0.001). Timing noncompliance had a higher point estimate than compliant timing, but its CI included the null. Other predictors also had wide CIs and were not statistically significant.

The model showed modest discrimination (ROC-AUC 0.676) and acceptable calibration on the Hosmer-Lemeshow test (chi-square=11.61, df=8, p=0.170). Variance inflation factors were <1.1 for all predictors. In Figure 1, absence of prophylaxis had the largest adjusted point estimate, accompanied by a wide confidence interval.

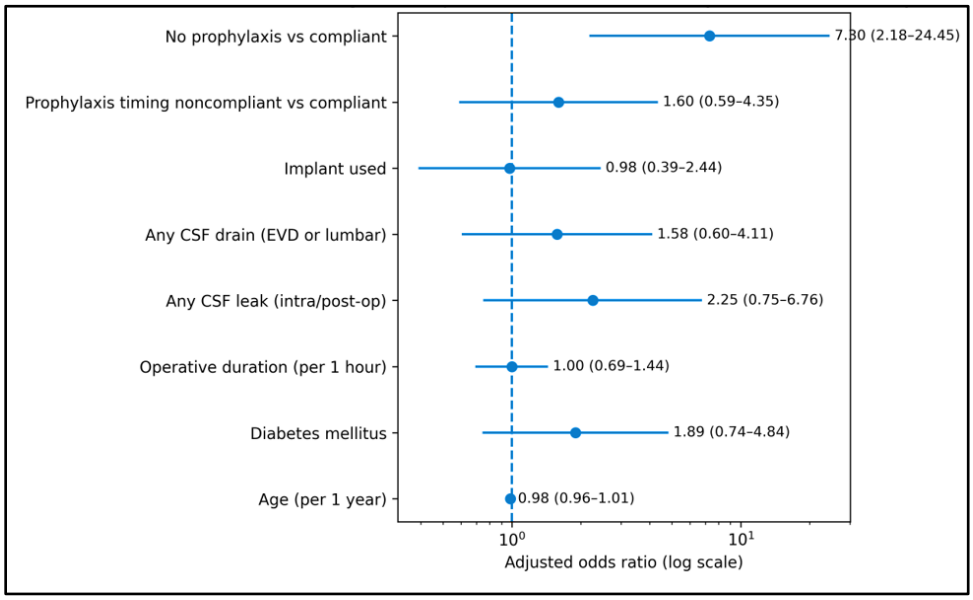

Figure 1: *Forest plot of adjusted odds ratios for 30-day SSI.*

DISCUSSION

In this retrospective cohort of 350 adult craniotomy procedures, the 30-day SSI incidence was 7.1%. Organ/space and superficial incisional infections each accounted for 40.0% of cases, while deep incisional infection accounted for 20.0%. This distribution shows that post-craniotomy SSI may involve both the incision and deeper cranial or intracranial spaces. Comparisons with other cohorts should account for differences in case mix, emergency workload, operative complexity, SSI definitions, surveillance periods, and post-discharge follow-up.[1-4]

Variation in reported SSI rates and predictors is also evident in cohorts examining post-craniotomy meningitis, craniotomy or craniectomy, elective neurosurgery, brain-tumour craniotomy, and readmission after nonemergent craniotomy.[6-10]

The findings are consistent with Jiménez-Martínez et al., who emphasized the importance of procedure-related and perioperative predictors in adult craniotomy patients. [1] Similarly, Abu Hamdeh and Lytsy reported that neurosurgical SSI carries important clinical impact and is influenced by operative and perioperative factors.[2] The present study also supports the risk-factor pattern reported by Fang et al, in their systematic review and meta-analysis, particularly the relevance of CSF-related factors, drains, operative complexity, and repeated surgical exposure.[3] However, some predictors that are commonly highlighted in earlier studies, such as CSF leak, drains, implant use, and operative duration, did not reach statistical significance in the current adjusted model. This difference is likely explained by the relatively small number of SSI events, heterogeneity in clinical indications, and wide confidence intervals rather than a definite absence of association.

Skin flora predominated among the recorded primary pathogens, particularly MSSA, CoNS, and Cutibacterium acnes, consistent with previous neurosurgical infection studies.[1,4,5] The organism distribution in Table 2 represents one primary pathogen for each of the 21 culture-positive cases, not all isolates. Five cases were flagged as polymicrobial, but the available analytical dataset

did not enumerate their additional co-isolates. Enterobacterales among the recorded primary pathogens and the presence of polymicrobial cases suggest a broader microbiological spectrum in some patients. The four culture-negative infections may reflect prior antimicrobial exposure, delayed or limited sampling, a low organism burden, or failure of culture recovery.

In the exploratory adjusted model, procedures without documented perioperative prophylaxis had the largest point estimate for SSI compared with procedures receiving prophylaxis at compliant timing. However, this estimate was based on only 20 procedures without prophylaxis, including five SSI events, and the 95% CI was wide.[2,18-24] Sparse data, residual confounding, emergency case mix, or incomplete documentation may have influenced the association; it should not be interpreted as proof of causality. Ensuring reliable prophylaxis delivery nevertheless remains a reasonable quality-improvement target.[3-5]

Timing noncompliance was not statistically associated with SSI, although its point estimate exceeded one. With only 25 SSI events, the study had limited precision for detecting modest associations. Differences in antibiotic agents, infusion duration, emergency scheduling, redosing, and documentation accuracy may also have influenced the estimate. These data therefore support continued monitoring of dosing and timing without establishing an independent effect of timing noncompliance.

The direction of association for CSF leak was positive in the adjusted model, but it was not statistically significant and had a wide confidence interval. This finding is clinically relevant as CSF leakage can allow the entry of microorganisms; it may also represent more complex surgery or poor wound closure. However, these results should be cautiously interpreted as the association was not statistically significant. Likewise, there were no strong independent relationships between drains and implants, and these factors could be influenced by indication-based confounding since devices are more likely to be used in more complicated cases. The present results, therefore, indicate that more local data are required before definitive conclusions on device-related and CSF-related risks can be drawn.

A high 30-day readmission rate for patients with SSI was a reflection of the clinical burden of this infection. In 68.0% of SSI cases, readmission was noted, while in only 6.2% of non-SSI patients, readmission was noted. This difference underscores the impact of post-craniotomy infection on patients and hospital resources. It also reinforces the importance of early surveillance of wound healing, early microbiological sampling, careful post-discharge supervision, and early management of suspected infection. In addition, the type of surveillance window that is used to assess SSI may influence the reported incidence of SSI following craniotomy, since incidence might differ between 30-day, 90-day, and longer follow-up surveillance. In this study, a 30-day outcome was chosen to ensure a well-defined and clinically relevant follow-up period.[11]

Practice implications: The findings support auditing whether prophylaxis was administered and documenting its timing before incision, while recognizing that this single-centre observational analysis cannot establish causality. Broader prevention efforts should also address CSF leak prevention, wound closure, device management, and post-discharge surveillance. These implications are consistent with general SSI guidance and craniotomy-specific prevention literature but do not constitute a formal clinical guideline.[12-17]

Standardized classification and documentation are also important in the reporting of post-craniotomy infection. There is a growing number of studies in the recent literature on bone flap infection, cranial neurosurgery infection algorithms, and post-craniotomy infection, which highlight the importance of having clear definitions, uniform surveillance techniques,

microbiological documentation, and management pathways.[18-20]

Limitations

This study has several limitations. First, its retrospective design permits residual confounding, incomplete documentation, and variation in surveillance. Second, only 25 SSI events were observed, limiting statistical power and producing imprecise estimates in the exploratory multivariable model, particularly for the 20 procedures without prophylaxis. Third, the microbiology dataset retained one primary pathogen per culture-positive case and a separate polymicrobial flag; additional co-isolates, susceptibility profiles, specimen sites, and sampling times were unavailable. Primary-pathogen counts therefore must not be interpreted as total isolate counts. Fourth, the single-centre setting limits generalizability. Despite these limitations, the study provides local data on SSI incidence, recorded microbiology, and potentially modifiable perioperative factors after craniotomy.

CONCLUSION

Thirty-day SSI occurred after 7.1% of craniotomy procedures. Organ/space and superficial incisional SSI were the most frequent subtypes, and the recorded primary pathogens were predominantly staphylococci and Cutibacterium acnes. Absence of documented perioperative prophylaxis was associated with higher adjusted odds of SSI, but the estimate was based on only 20 unexposed procedures and had a wide confidence interval. The association should be interpreted cautiously and confirmed in larger multicentre cohorts.

Additional Information

Ethical Declaration: The study was carried out after obtaining ethical approval from the Institutional Research and Ethical Review Board, Khyber Teaching Hospital, Peshawar, Pakistan (Approval/Reference No. 154/DME/KTH, dated 12 March 2026). All patient data were anonymised and kept confidential.

Disclosures: Authors report no conflicts of interest.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Data Availability Statement: For data sharing, interested researchers can contact the corresponding authors

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Artificial Intelligence Disclosure

During revision, ChatGPT (OpenAI) was used solely to assist with English-language editing, improvement of readability, and organization of responses to peer-review comments. The authors reviewed and verified the final text, numerical results, interpretations, and references and accept full responsibility for the content. The AI tool was not listed as an author.

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AUTHORS CONTRIBUTIONS

Role	Contributing Author(s)	Role	Contributing Author(s)
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Methodology	Muhammad Idris Khan; Aziz Ur Rehman	Writing – Original Draft/ Literature Review	Muhammad Idris Khan; Aziz Ur Rehman
Software	Not applicable	Writing - Review & Editing	All authors
Validation	Aziz Ur Rehman; Sajjad Ullah; Adnan Munir	Visualization	Muhammad Idris Khan; Aziz Ur Rehman
Formal analysis	Muhammad Idris Khan; Aziz Ur Rehman	Supervision	Adnan Munir
Investigation	Muhammad Idris Khan; Sajjad Ullah	Project administration	Aziz Ur Rehman; Adnan Munir
Resources	Sajjad Ullah; Adnan Munir	Any other (Misc.)	All authors - final approval and accountability