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Risk Factors Leading to Extubation Failure in a Pediatric Intensive Care Unit: A Descriptive Study from a Tertiary Care Hospital in Pakistan

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ABSTRACT

Extubation failure (EF), defined as the need for reintubation within 72 hours of planned removal of mechanical ventilation, is a serious complication in pediatric intensive care units, yet local data from low- and middle-income countries are limited. **Objectives:** To describe clinical risk factors for EF among ventilated children in a tertiary Pediatric Intensive Care Unit (PICU) in Pakistan. **Methods:** This research conducted a six-month descriptive cross-sectional study in the PICU of Civil Hospital Karachi, enrolling all children under 12 years who received invasive mechanical ventilation for >12 hours and subsequently required reintubation within 72 hours of planned extubation. Demographic variables and predefined risk factors (hemodynamic instability, gas-exchange failure, airway obstruction, acute respiratory disease, chronic neurologic disease, malnutrition, poor cough reflex, and exposure to sedatives, inotropes, and steroids) were recorded on a standardized, validated proforma and analyzed using SPSS-23 with chi-square tests ($p \leq 0.05$). **Results:** Among 133 EF episodes, the most frequent risk factors were hemodynamic instability (24.8%), inotrope and steroid use (24.8% each), upper airway obstruction and hypoxemic respiratory failure (15% each), and poor cough reflex (15%), with several patients exhibiting multiple overlapping risk factors. Upper airway obstruction and poor cough reflex were more common in males, whereas cyanotic congenital heart disease and chronic neurologic conditions occurred exclusively in children >5 years of age. **Conclusions:** EF in this setting is multifactorial, dominated by hemodynamic instability, gas-exchange impairment, and airway-protective deficits; structured, age- and sex-aware extubation-readiness assessment focused on these risks may help reduce reintubation in resource-limited PICUs.

INTRODUCTION

In the pediatric intensive care unit (PICU), mechanical ventilation is a fundamental treatment aspect, and a high percentage of patients need high-level care involving intravenous ventilation [1, 2]. Ventilator liberation generally incorporates day-to-day preparedness examination and in numerous units impromptu breathing trials preceding removing the ventilator [1, 3]. The process of extubation remains, however, a high-stakes transition where the reintubation within 48-72 hours is always associated with an extended period of ventilation, increased use of resources, and ventilator-associated events, as well as extended stay in the PICU [4, 5]. Extubation failure (EF) rates are reported to be dependent on practice and case-mix, but are commonly between low single digits and one-fifth of those with intubation [1, 6]. Various bedside factors contaminate EF risk in children, such as an upper-airway compromise, hemodynamic instability or vasoactive support, impaired oxygenation or ventilation, prolonged exposures to ventilation, and neurologic dysfunction [4, 5]. Fluid overload, myocardial disease, and residual airway edema can also further decrease post extubation reserve in susceptible patients

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[4, 5]. Sedative and analgesic needs can dampen the respiratory drive and slow readiness measures, making it harder to decide on weaning and obscure clinical indicators of fatigue [1, 3]. The nutritional deficit is less likely to be examined in extubation studies, but undernourishment among children is linked to an increased requirement for a mechanical ventilator and increased ventilator time, which would possibly aggravate the respiratory muscle performance and immune resistance [7]. Most units offer post-extubation noninvasive respiratory support (NRS) like high-flow nasal cannula, CPAP, or bilevel modalities to reduce risk, though their access and consistent use differ, especially in resource-constrained units [8, 9]. The recent multicenter database studies add to the fact that EF is prevalent and multifactorial, and airways and non-airways mechanisms are implicated in it [4, 5]. The surveys also exhibit discrepancies in extubation-readiness testing and portray operational obstacles that can delay prompt extubation [3]. The field of postextubation NRS has increased evidence that is randomized and comparative, with large pragmatic studies and network meta-analyses, but findings are context-dependent [8, 9]. By and large, modern syntheses emphasize heterogeneity of the populations and lack of information in non-high-income settings [6, 9]. Data on low- and middle-income PICUs is limited, particularly on the relative role of easily quantifiable clinical issues among children who actually fail extubation. The present research so characterizes feasible clinical risk factors implicating EF in a Pakistani PICU in a way that aids the appropriation of extubation preparedness evaluation and follow-up planning onto contextual ground. Although increased awareness of extubation failure as a complex phenomenon in the PICU has changed, new findings have highlighted the presence of gaps in standardized preparedness criteria and the impact of heterogeneous clinical forewarnings on the result of extubations. Modern evidence indicates that the frequency of extubation fail has not decreased, but still falls within non-negligible margins in a heterogeneous cohort of patients and that patient-specific influencing factors, including younger age, extended mechanical ventilation, pre-existing respiratory comorbidity, and post-extubation airway obstruction are persistently linked with an increased incidence of reintubation, which underscores the necessity of refined stratification and predictive methods when such cases get into practice [10-12]. Specific prediction tools that were created on a special subpopulation, including pediatric cardiac patients, have demonstrated encouraging discrimination abilities through the use of clinical past and physiologic variables, additionally indicating the possible advantages of organized risk scoring units to aid in timing extubation and post-extubation decision-making [13]. Systematic syntheses also indicate that there remains consistent heterogeneity in readiness testing techniques and that there is a need to achieve consensus on the best evaluation parameters to enhance prognostic accuracy [14]. Besides, evidence of overlap and distinct risk factor phenotypes within context-specific studies based on tertiary care centers (including low- and middle-income settings) suggests an even greater complexity, given that the relationships vary based on the demographic, ventilatory, and respiratory support variables associated with extubation outcomes [15, 16]. Altogether, these results emphasize both the advances and the persistent issues in the reduction of the extubation failure with the help of the individual evaluation and assistance paradigms, as well as emphasize the absence of solid data in resource-limited PICUs, and the urgency of acquiring localized evidence in support of the contextualized weaning plans and extubation preparedness models [14-16].

This study aimed to focus on profiling easily measurable clinical risk factors among children with EF in a resource-limited Pakistani Pediatric Intensive Care Unit (PICU) to help refine locally appropriate extubation-readiness assessment and follow-up.

METHODS

A descriptive cross-sectional study was conducted at the Department of Pediatrics in the Pediatric Intensive Care Unit (PICU), Civil Hospital Karachi, from 22 September 2021 to 22 March 2022 after approval by the College of Physicians and Surgeons Pakistan Research Evaluation Unit (IREB No. CPSP/REU/PED-2019-183-5108). The study evaluated the clinical risk factors associated with extubation failure (EF) in children receiving invasive mechanical ventilation. Written informed consent was obtained from parents or legal guardians of all participants, with assent from older children where appropriate, and confidentiality of patient data was strictly maintained. A non-probability consecutive sample of 133 children aged <12 years who were admitted to the PICU, intubated and mechanically ventilated for >12 hours, and planned for extubation was enrolled. Sample size was calculated using Open Epi version 3.01, assuming a 9.5% EF risk, 95% confidence interval, and 5% precision. EF was defined as the need for reintubation within 72 hours of a planned extubation attempt; each extubation failure episode was counted once in the analysis. Data were collected prospectively on a structured proforma. Hemodynamic instability was defined as age-specific hypotension or requirement for fluid boluses and/or vasoactive support persisting within 24 hours of extubation, based on Pediatric Advanced Life Support thresholds. Upper airway obstruction was diagnosed clinically by the presence of

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stridor, increased work of breathing, or need for nebulized epinephrine or steroids within 48 hours of extubation. Hypoxemic respiratory failure was defined as PaO2 <60 mmHg on arterial blood gas with normal or low PaCO2, and hypercapnic respiratory failure as PaCO2 >50 mmHg with accompanying respiratory acidosis. Acute respiratory disease (e.g., asthma, bronchitis, pneumonia) and pulmonary hypertension were documented according to standard WHO/CDC case definitions and echocardiographic reports, respectively. Cyanotic congenital heart disease was confirmed by cardiology records and prior echocardiography. Chronic neurologic conditions (e.g., cerebral palsy, neuromuscular disease, epileptic encephalopathy) were recorded from prior diagnoses and neuroimaging where available. Nutritional status was classified using WHO growth standards; children with weight-for-age or weight-for-height z-scores <−2 SD were labeled malnourished. Cough reflex was judged as poor when the bedside clinician documented absent or weak cough with suctioning or inability to clear secretions despite stimulation before extubation. Exposure to sedatives (benzodiazepines, opioids), inotropes, and systemic corticosteroids was recorded as present when these drugs were administered for ≥24 hours in the 48 hours preceding extubation. Duration of mechanical ventilation was calculated from intubation to first extubation attempt and categorized as ≤72 hours or >72 hours for stratified analyses. All variables were captured using a standardized proforma adapted from published extubation-readiness checklists and refined after review by three senior pediatric intensivists to ensure content validity. Data entry was double-checked against medical records for accuracy. Statistical analysis was performed using SPSS version 23.0; categorical variables were summarized as frequencies and percentages, and associations between risk factors and age, sex, and ventilation duration were explored using chi-square tests with p≤0.05 considered significant. Because only patients with extubation failure were enrolled and no comparison group of successfully extubated children was available, multivariable logistic regression to identify independent predictors of EF could not be performed in this dataset.

RESULTS

A total of 133 Pediatric patients admitted to the Pediatric Intensive Care Unit (PICU) at Civil Hospital Karachi who met the inclusion criteria were included in this study. The study summarizes the cohort's continuous variables: age (years), duration of mechanical ventilation (hours), and time between extubation and reintubation (hours), each reported as mean ± SD with minimum–maximum values. The mean age of the patients was 3.25 ± 4.49 years, with ages ranging from 1 month to 12 years. The average duration of mechanical ventilation was 96.72 ± 10.24 hours (range 85–107 hours), and the mean time from extubation to reintubation was 5.56 ± 3.24 hours. Table 1 provides descriptive statistics of the study population (Table 1).

Table 1: Descriptive Statistics (n=133)

Variables	Mean ± SD	Min-Max
Age (Years)	3.25 ± 4.49	1 – 12
Duration of Mechanical Ventilation (h)	96.72 ± 10.24	85 – 107
Time Between Extubation and Reintubation (h)	5.56 ± 3.24	2 – 9

Out of 133 patients, 78 (58.6%) were male, and 55 (41.4%) were female. A larger proportion of patients (66.17%, n = 88) were older than 5 years, while 45 (33.83%) were 5 years or younger (Figure 1).

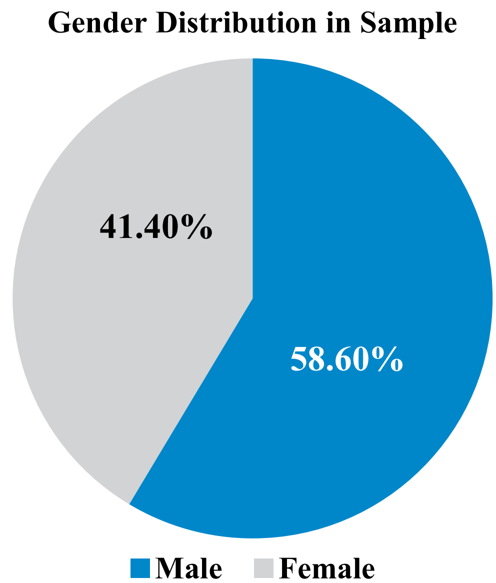

Figure 1: Gender Distribution in Sample

Findings list each predefined risk factor and its frequency (%): hemodynamic instability; inotrope use; steroid use; upper airway obstruction; hypoxemic respiratory failure; poor cough reflex; acute respiratory disease; hypercapnic respiratory failure; sedative use; cyanotic congenital heart disease; chronic neurologic condition; and malnutrition. In terms of clinical risk factors contributing to extubation failure (EF), the following frequencies were observed. Hemodynamic instability was noted in 33 (24.8%) of patients, while the use of inotropes and steroids before extubation was reported in 33 (24.8%) each. Upper airway obstruction and hypoxemic respiratory failure were present in 20 (15.0%) of the cases, and a poor cough reflex was recorded in 20 (15.0%) of the cases. Hypercapnic respiratory failure and acute respiratory disease each accounted for 14 (10.5%). Sedative use was recorded in 11 (8.3%). Cyanotic congenital heart disease was present in 7 (5.3%), chronic neurologic conditions in 7 (5.3%), and malnutrition, as defined by WHO standards, in 5 (3.8%) (Table 2).

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Table 2: Frequency and Percentage of Clinical Risk Factors Associated with Extubation Failure (n=133)

Risk Factors	Frequency (%)
Hemodynamic Instability	33 (24.8%)
Inotrope Use	33 (24.8%)
Steroid Use	33 (24.8%)
Upper Airway Obstruction	20 (15.0%)
Hypoxemic Respiratory Failure	20 (15.0%)
Poor Cough Reflex	20 (15.0%)
Acute Respiratory Disease	14 (10.5%)
Hypercapnic Respiratory Failure	14 (10.5%)
Sedative Use	11 (8.3%)
Cyanotic Congenital Heart Disease	7 (5.3%)
Chronic Neurologic Condition	7 (5.3%)
Malnutrition	5 (3.8%)

Gender-based stratification revealed that 25.6% of male patients experienced upper airway obstruction, compared to 0% of female patients, indicating a statistically significant difference (p=0.01). Similarly, hemodynamic instability was more prevalent in male patients (33.3%) than in female patients (12.7%), with a significant p-value of 0.01. Cyanotic congenital heart disease was observed in 12.7% of female and none of the male patients, again reflecting statistical significance (p=0.01). Acute respiratory diseases did not show a significant gender-based difference (p=0.48). Among genders, malnutrition was slightly more common in male (5.1%) than female (1.8%), although this was not statistically significant (p=0.32). Cough reflex was judged as poor in 15% of patients, without significant variation across age groups (p=0.69) or ventilation duration (p=0.58), but with a highly significant gender difference—present in 25.6% of male and none of the female (p=0.01). Gender differences were significant in airway obstruction and cough reflex, though limited to EF cases (Figure 2).

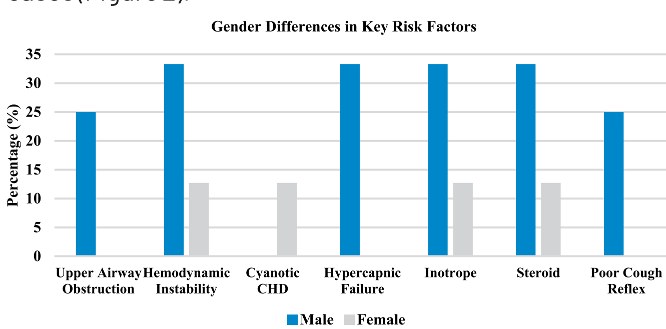

Figure 2: Gender Differences in Key Risk Factors

When stratified by age, hemodynamic instability was noted in 28.9% of children aged 5 years or younger and in 22.7% of those aged 5 years or older (p=0.43). Upper airway obstruction had a slightly higher frequency in older children (15.9%) compared to younger ones (13.3%), though this difference was not statistically significant (p=0.69). Interestingly, cyanotic congenital heart disease and chronic neurologic conditions were found exclusively in children older than 5 years (p=0.05 for both). Acute respiratory diseases were also significantly more frequent in older children (27.2%) than in younger children (0%), with a p-value of 0.01. CCHD and chronic neurologic conditions were more frequent in shorter MV durations (Table 3).

Table 3: Age/Durational Associations with Risk Factors (Statistically Significant)

Risk Factors	Group with Higher Prevalence	p-value
Cyanotic Congenital HD	Age > 5 Years	0.05
Acute Respiratory Disease	Age > 5 Years	0.01
Chronic Neurologic Condition	Age > 5 Years	0.05

Duration of mechanical ventilation (MV) was also stratified to assess its influence on EF risk factors. For upper airway obstruction, 16.3% of patients on mechanical ventilation (MV) for more than 72 hours developed this condition, compared to 12.8% of those on MV for 72 hours or less (p=0.58). Hemodynamic instability occurred in 22.1% of patients with mechanical ventilation (MV) lasting more than 72 hours and in 29.8% of those with MV lasting 72 hours or less (p=0.32). Cyanotic congenital heart disease was significantly more prevalent in patients ventilated for ≤72 hours (14.9%) compared to those in the >72 hours group (p=0.01). Hypercapnic respiratory failure showed a similar distribution across both MV duration groups (14.9% vs. 8.1%), with no significant difference (p=0.22). Hypoxemic respiratory failure was present in 12.8% of the ≤72 hours group and 16.3% in the >72 hours group (p=0.58). For inotropic use, 29.8% of patients ventilated ≤72 hours received inotropes, as opposed to 22.1% in the >72 hours group (p=0.32). Steroid use followed a similar pattern, showing no significant difference across ventilation durations (p=0.32). Sedative use also showed a non-significant trend, with 6.4% of the ≤72 hours group and 9.3% of the >72 hours group having been on sedatives (p=0.55). Malnutrition showed no significant association with age, gender, or mean vital sign duration. Among those ≤5 years, 2.2% were malnourished compared to 4.5% in older children (p=0.50) (Figure 3).

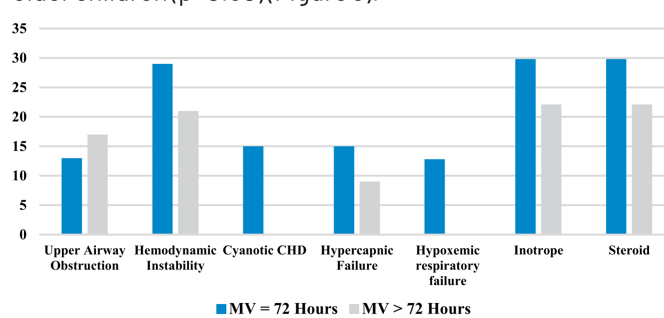

Figure 3: Comparison of Risk Factors by Duration of Mechanical Ventilation

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The most frequent extubation failure risks were blood pressure problems, steroid/inotrope use, and upper-airway obstruction.

DISCUSSION

Extubation failure (EF) was found to happen in a clinically significant proportion of mechanically ventilated children in this study, which is consistent with the conclusion that ventilator liberation is a high-stakes clinical event in the PICU [1]. The recent literature in the pediatric community has conceptualized EF as a result of the susceptibility of patients and alterable mechanisms like readiness assessment, sedation procedures, and post-extubation surveillance [2, 3]. Although the physiologic shift of positive-pressure ventilation to unassisted spontaneous ventilation is planned, such as during extubation, the physiologic step change may predispose to clinical deterioration and initiate the reintubation response. Our cohort showed higher illness severity as measured by markers that EF was correlated with. Children either on inotropes or being hemodynamically unstable at the time of removal were more prone to reintubation, which is reasonable to expect considering the fact that withdrawal of positive pressure may cause an increase in the work of breathing and venous return, as well as afterload, which places undue pressure on limited cardiovascular reserve. More recent multicenter databases with the Virtual Pediatric Systems registry also report that EF is comparably prevalent across diagnoses, and also that it correlates with increased ventilation duration and increased length of stay in the ICUs, which points to EF not being a solitary airway event but rather an indicator of an underlying complex physiologic vulnerability [4]. Practically, sustained vasoactive requirements should necessarily stimulate rethinking the timing of extubation, the optimization of perfusion, and upstream consideration concerning the monitoring and support of the post-extubation period. Obstruction of the upper airways (UAO) became one of the dominant proximate causes of failure in our patients. The existing data confirms the separation of airway and non-airway EF phenotypes as they might have varying antecedents, time frames, and prevention approaches. The proliferation of airway-predominant failures was dominant, and with identifiable risk factors and outcomes in a recent study that differentiated airway and non-airway EF, with justification of the relevance of proactive prevention of airway edema, management of secretions, and early escalation in the case of stridor or obstruction emerged [5]. Within our cohort, the correlation between steroid use and EF may be a result of clinician awareness of airway risk (or more extreme airway pathology), but not a causal relationship, and hence the emphasis on understanding treatment markers (eg, steroids) as risk indicators, in addition to any interventions. Accurate prediction of EF remains difficult. A recent systematic review and meta-analysis found substantial heterogeneity in extubation readiness tests and EF definitions, with no single pre-extubation index demonstrating consistently high diagnostic accuracy across settings [6]. Our results reinforce the pragmatic value of bedside indicators—particularly cough effectiveness and secretion burden—because inability to clear secretions can precipitate both airway and respiratory deterioration after tube removal. From a process perspective, these findings support a multimodal readiness approach that integrates clinical airway assessments, neurologic readiness, hemodynamic stability, and disease trajectory rather than reliance on any single index. Undernutrition was frequent and was associated with poorer outcomes in our study. This aligns with evidence that undernutrition at PICU admission is associated with deterioration in clinical outcomes, including increased need for and duration of mechanical ventilation [7]. Optimizing nutrition may therefore be an important supportive strategy to improve respiratory muscle function and recovery, particularly in children anticipated to require prolonged ventilation or repeated weaning attempts. Additionally, the observed association between congenital cardiac anomalies and EF in our sample may reflect reduced cardiopulmonary reserve and higher susceptibility to changes in intrathoracic pressure and preload/afterload conditions during the peri-extubation period. Post-extubation noninvasive respiratory support (NRS) may reduce respiratory-predominant failure in selected patients. In the FIRST-ABC step-down trial, high-flow nasal cannula (HFNC) was not inferior to CPAP for time to liberation from respiratory support after extubation in critically ill children [8]. Complementary evidence from a network meta-analysis in infants and young children suggests that CPAP, HFNC, and BiPAP may reduce EF compared with conventional oxygen therapy, with CPAP ranking most effective for EF prevention among the analyzed trials [9]. In practice, these data support an individualized post-extubation strategy: children with a high risk of respiratory decompensation may benefit from planned NRS, while those with predominant airway-obstruction risk require vigilant airway observation and rapid access to escalation pathways. Recent international guidance provides an increasingly standardized framework for pediatric ventilator liberation. The PALISI network executive summary of pediatric ventilator liberation clinical practice guidelines offers evidence-based recommendations spanning readiness assessment, spontaneous breathing trials, and post-extubation support for children ventilated

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for more than 24 hours [17]. Complementing this, consensus-driven operational definitions have been published to harmonize what constitutes "respiratory support," "liberation," and "failed" attempts, which is essential for benchmarking and comparing EF outcomes across institutions [18]. Importantly, protocolization itself may improve liberation efficiency: a large pragmatic randomized trial found that implementing a sedation and ventilator liberation protocol produced a statistically significant reduction in time to first successful extubation compared with usual care (with uncertain clinical importance of the effect size) [19]. Together, these developments support moving from ad hoc decision-making toward reproducible, protocol-supported extubation practices—particularly for patients with identifiable high-risk features such as vasoactive requirements, UAO risk, or high secretion burden. Sedation, delirium, and mobility practices can influence extubation success through effects on respiratory drive, airway protective reflexes, and secretion management. The SCCM PANDEM guidelines emphasize structured approaches to pain and agitation management, delirium prevention/management, neuromuscular blockade, ICU environment, and early mobility for critically ill children [20]. Implementing these recommendations may indirectly support safer ventilator liberation by reducing oversedation and facilitating neuro-respiratory readiness at the time of extubation. Overall, these findings align with and extend existing EF literature by emphasizing readily observable clinical signs of hemodynamic stability, gas-exchange adequacy, airway patency, and cough effectiveness that can be systematically integrated into extubation-readiness protocols in resource-limited settings. Future research from this and similar PICUs should prospectively include both extubation successes and failures to permit robust multivariable modelling of independent predictors, as well as to validate pragmatic, age-tailored extubation bundles that incorporate the risk factors highlighted in this study. Future analyses: The frequent co-occurrence of hemodynamic instability, airway obstruction, and gas-exchange failure suggests overlapping EF phenotypes. A prospective all-extubations registry should apply multivariable logistic regression and, where feasible, clustering/latent-class methods to disentangle independent effects and delineate EF risk phenotypes.

CONCLUSIONS

Extubation failure in this resource-limited tertiary PICU was most frequently associated with hemodynamic instability, impaired gas exchange, airway obstruction, and poor cough reflex, often in combination. Targeted, age-aware extubation-readiness assessment focusing on these high-yield clinical risk factors, alongside systematic attention to chronic neurologic disease and malnutrition, may help reduce reintubation and improve outcomes in similar settings.

Authors Contribution

Conceptualization: IR
Methodology: IR
Formal analysis: NB
Writing and drafting: MA, FY, NUNM, SA, YY
Review and editing: IR, NB, MA, FY, NUNM, SA, YY

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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