Comparison of pSOFA with PRISM III and PIM 2 as Predictors of Outcome in a Tertiary Care Pediatric ICU: A Prospective Cross-sectional Study

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Abstract

Aims and background: Severity scores are used to predict the outcome of children admitted to the intensive care unit. A descriptive score such as the pediatric sequential organ failure assessment (pSOFA) may be useful for prediction of outcome. This study was planned to compare the pSOFA score with these well-studied scores for prediction of mortality.

Materials and methods: This prospective cross-sectional study was conducted at the pediatric intensive care units (PICU) of a tertiary care hospital. Children aged from 1 month to 12 years were enrolled sequentially. The pediatric index of mortality (PIM 2) score was calculated within 1 hour, and pediatric risk of mortality (PRISM) III and pSOFA scores were calculated within 24 hours of PICU admission. The pediatric sequential organ failure assessment score was recalculated after 72 hours. The primary outcome variable was hospital mortality, and secondary outcome variables were duration of PICU stay, need for mechanical ventilation, and occurrence of acute kidney injury (AKI). Appropriate statistical tests were used.

Results: About 151 children with median (IQR) age of 36 (6, 84) months were enrolled. Mechanical ventilation was required in 87 (57.6%) children. Mortality was 21.2% at 28 days. The median (IQR) predicted mortality using PRISM III and PIM 2 score were 3.4 (1.5%, 11%) and 8.2 (3.1%, 16.6%) respectively. Area under ROC for prediction of mortality was highest for pSOFA 72 with a cut-off of 6.5 having sensitivity of 83.3% and specificity of 76.9%.

Conclusion: The pSOFA score calculated at admission and at 72 hours had a better predictive ability for the PICU mortality compared to PRISM III and PIM 2 score.

Keywords: Acute kidney injury, Calibration, Mechanical ventilation, Pediatric logistic organ dysfunction, Sequential organ failure assessment score, Severity score.

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Highlights

Pediatric risk of mortality (PRISM) III and pediatric index of mortality (PIM 2) showed good calibration with actual mortality. Pediatric risk of mortality III, pediatric modification of sequential organ failure assessment (pSOFA) 0 and pediatric modification of sequential organ failure assessment (pSOFA) 72 scores were significantly higher among the non survivors. Area under ROC for prediction of mortality was highest for pSOFA72.

Introduction

Pediatric intensive care units (PICU) are indispensable for the stabilization and management of critically ill children. Estimation of disease severity and mortality prediction is an important component of PICU care. Such estimation is usually done with the help of severity scores. Prognostic scores are those that provide the assessment of mortality risk at the time of admission to the PICU (e.g., PRISM, PIM) and descriptive scores provide the organ function assessment during the stay (e.g., pediatric logistic organ dysfunction score (PELOD), pediatric multiple organ dysfunction assessment score (PEMOD), logistic organ dysfunction score (LODS), and sequential organ failure assessment (SOFA).[1] Pediatric risk of mortality III and PIM scores have been evaluated and have shown good predictive ability for PICU mortality.[2–5] Study from rural India showed good discrimination in the PELOD-2 score for PICU mortality.[6] The sepsis-3 task force has recommended the use of the SOFA score for mortality prediction and management of patients with sepsis.[7] A recent study by Gogia et al. showed that higher PELOD and SOFA scores were associated with increased mortality and increased duration of stay; the positive and negative predictive ability of the SOFA score at 72 hours was similar to the PELOD score.[8] However, these definitions, and SOFA score are not applicable to the pediatric population. A pediatric modification of the SOFA (pSOFA) score was developed by Matics et al. and was

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found to have good predictive ability for the mortality, similar to the PELOD and PRISM III scores.[9] Many studies have evaluated PRISM III and PIM 2 scores for mortality prediction, but there is a paucity of studies comparing mortality prediction using the pSOFA score, especially in our country. This study was aimed at assessing the predictive ability of the pSOFA score in comparison with PRISM III and PIM 2 for the outcome of critically ill children in the PICU at a tertiary care hospital.

Materials and Methods

This was a prospective cross-sectional study conducted at a 12-bed Pediatric intensive care unit at a tertiary care hospital between March 2020 and December 2021. The primary objective of the study was to assess the predictive ability of PRISM III, PIM 2 and pSOFA (at admission, at 72 hours and delta SOFA) for ICU mortality at 28 days. The secondary objective was to assess the correlation of PRISM III, PIM 2 and pSOFA (at admission, at 72 hours and delta SOFA) with the duration of mechanical ventilation, and the duration of the PICU stay.

Patients in the age group of 1 month to 12 years admitted to the PICU were included in the study. Readmissions were counted as separate admissions. Children with a length of stay less than 24 hours, those in whom adequate sampling could not be performed to calculate the scores, or those who could not be included due to refusal of consent, were excluded from the study. The primary outcome was hospital all-cause mortality (hospital mortality). We also defined the secondary outcomes as duration of hospital stay, requirement and duration of ventilation, and development of acute kidney injury (AKI) as per the kidney disease improving global outcome (KDIGO) classification.

After taking written informed consent from the primary caregiver, demographic details, anthropometry, diagnosis at admission, date of admission, date of discharge, outcome, duration of mechanical ventilation, development of AKI and length of stay, were recorded on the pro forma sheet for the study. Pediatric risk of mortality III score was calculated using the following parameters-systolic blood pressure (SBP), heart rate, temperature, mental status, pupillary response, acidosis, pH, pCO_2, total CO_2, PaO_2, glucose, potassium, creatinine, blood urea nitrogen (BUN), total leukocyte count, platelet count, prothrombin time (PT), and partial thromboplastin time (PTT).[10] We used pSOFA score developed by Matics et al. using PaO_2/FiO_2 ratio, platelet counts, serum bilirubin, Glasgow coma scale and age-based values of serum creatinine and mean airway pressure.[9] Pediatric risk of mortality III and pSOFA0 score were calculated within 24 hours of admission. Pediatric sequential organ failure assessment score was again calculated at 72 hours using latest clinical and lab data (pSOFA72). Delta pSOFA was recorded as the difference of absolute value of pSOFA0 and pSOFA72. Predicted mortality as per PRISM III score was calculated using regression equation for the derived score. Pediatric index of mortality 2 score provided the estimated mortality using a regression equation that was calculated within 1 hour of PICU admission. All the scores were calculated using online calculators. Patients were followed up till outcome (discharge/death), and duration of the PICU stay and mechanical ventilation were recorded. The data was entered in the password-protected database for future analysis.

The study was started after IEC approval vide F.1/IEC/MAMC/(72/07/2019/No.24), Dated: 18.02.2020 and CTRI registration vide: CTRI/2020/04/024433 dated 20.03.2020.

Sample Size

In the present study, hospital mortality served as the primary outcome. Taking the difference in proportion of mortality predicted by PRISM III and PIM 2 as 17% (*p*),[3] and expected PICU admission in 1 year at our center as 450 (*N*) (Total PICU admission in the last 1 year - 420), with a precision of 5% (*d*), and a 90% confidence interval, using the equation $n = [DEFF*Np\,(1–p)]/[(d^2/Z^2_{1-\alpha/2}*(N–1) + p*(1–p)]$, sample size calculated was 145.

Statistical Analysis

The mean and standard deviation were calculated for normally distributed data, and the median and interquartile range were calculated for non-normally distributed data. Chi-square/Fischer exact tests were applied for the comparison of categorical variables. Student *t*-test was used for comparison of categorical and descriptive variables with a normal distribution, and for non-normally distributed data, a Mann–Whitney *U*-test was performed. For comparison, of more than 2 groups, ANOVA or Kruskal–Wallis tests were used. Pearson and Spearman correlation coefficients were used for assessing the correlation between continuous variables.

Observed and expected mortality were compared. Calibration between estimated and actual mortality was done using the Hosmer–Lemeshow goodness of fit tests. The receiver operating characteristic curve was used to estimate the capacity of the model to discriminate between discharge and mortality, predict of ventilation requirement, and develop of AKI.

Results

During the period, the COVID crisis emerged, hence the period between 20-March-2020 and 20-February-2021 was excluded from the study, since the admitted patients were not representative of normal PICU admissions, and also the unit was working as a hybrid ICU, hence, recruitment was stopped during this period. The study recruitment was done from 20-February-2021 to 19-December-2021.

During this period, a total of 104,168 admissions took place in the hospital, of these 10,549 patients were pediatric admissions and 513 of them required PICU admission. About 141 patients refused consent, 13 were discharged against medical advice, 56 patients had a stay of less than 24 hours, and 152 patients could not be included due to a lack of adequate sampling or data (Fig. 1).

About 151 children with a median (IQR) age of 36 (6, 84) months were recruited, of them, 52 (34.4%) were infants. Median (IQR) duration of the PICU stay was 11 (6, 22) days, and median (IQR) gap between admission to the PICU transfer was 18 (4.5, 48) hours. Mechanical ventilation was required in 87 (57.6%) children for a median (IQR) duration of 12 (4, 20) days. The most common diagnoses (*N*, %) were sepsis (37, 24.5%) followed by pneumonia (28, 18.5%), central nervous system infections and injury (22, 14.6%) and congestive cardiac failure (15, 9.9%). At 28 days, 119 patients were alive with a mortality rate of 21.2% (Tables 1 and 2). Overall, 35 (23.2%) children died by the end of the study.

Mortality

The Median (IQR) PRISM III, pSOFA0 and pSOFA 72 scores were 7 (3, 13), 5 (3, 8) and 4 (2, 7), respectively (Table 2). Median (IQR) predicted mortality using PRISM III and PIM 2 scores were 3.4 (1.5, 11%) and 8.2 (3.1, 16.6%), respectively, which was lower than actual mortality. Hosmer–Lemeshow goodness of fit test showed good calibration of both PRISM III and PIM 2 (Table 3). Median PRISM III, pSOFA 0 and pSOFA 72 scores were significantly higher among the non survivors.

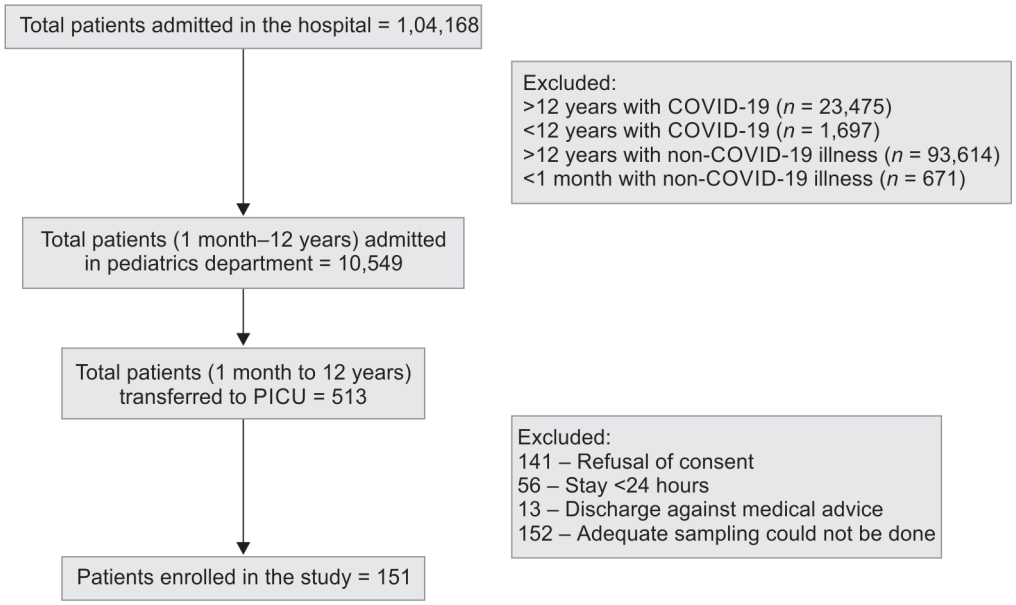

Fig. 1: Study flowchart

*COVID, corona virus disease; PICU, pediatric intensive care unit

Table 1: Demographic and clinical characteristics of the study population

Age (months)	36 (6, 84)
<1year	
1–5 years	
>5 years	
Weight (kg)	10 (5, 18)
Height (cm)	87 (63, 118)
BMI (kg/m^2)	13.5 ± 2.7[#]
Diagnosis *N* (%)[##]	
Sepsis	37 (24.5)
Pneumonia	28 (18.5)
TBI/AES/TBM	22 (14.6)
CHF	15 (9.9)
Poisoning	11 (7.3)
Asthma	10 (6.6)
Postoperative	9 (5.9)
Acute liver failure	8 (5.3)
Hypertensive emergency	4 (2.6)
Dengue	4 (2.6)
Diabetes ketoacidosis	2 (1.3)
Guillain Barre syndrome	1 (0.7)

[##]values in *N* (%); all the other values are median (IQR); AES, acute encephalitic syndrome; BMI, body mass index; CHF, congestive heart failure; TBI, traumatic brain injury; TBM, tubercular meningitis; [#], value in Mean (SD)

Table 2: Outcome parameters of the study population

Outcome parameter	*Value*
Duration from admission to PICU transfer (days)	18 (4.5, 48)
Duration of PICU stay (days)	11 (6, 22)
Duration of HHHFNC (days)	4 (2, 5)
Duration of ventilation (days)	12 (4, 20)
Mortality at 28 days, *N* (%)	32 (21.3)[#]
Mortality at the end of the study, *N* (%)	35 (23.2)[#]
PRISM III	7 (3, 13)
pSOFA0	5 (3, 8)
pSOFA72	4 (2, 7)
Delta pSOFA	0.5 (0, 2)

[#]values in *N* (%); rest of the values are in median (IQR); PICU, pediatric intensive care unit; PRISM, pediatric risk of mortality; PIM, pediatric index of mortality; pSOFA, pediatric sequential organ failure assessment

Table 3: Calibration of PRISM III and PIM 2 scores for prediction of mortality

Parameter	*PRISM III*	*PIM 2*
Median (IQR) of mortality risk	3.4 (1.5, 11)	8.2 (3.1, 16.6)
Hosmer–Lemeshow test, c^2	4.8	4.7
Hosmer–Lemeshow test, *p*-value	0.77	0.78

PRISM, pediatric risk of mortality; PIM, pediatric index of mortality

A significantly higher number of non-survivors had developed AKI compared to the survivors (Table 4).

Secondary Outcomes

There was no significant correlation between the PRISM III score and the duration of PICU stay (r = 0.075, p-0.39), and mechanical ventilation (r = 0.018, p-0.86). There was no significant correlation between PIM 2 and duration of PICU stay and mechanical ventilation (r = –0.07, p-0.39 and r = –0.07, p-0.52, respectively). Similarly, there was no significant correlation of pSOFA 24 and pSOFA 72 scores and the duration of PICU stay (r =0.05, p = 0.54 and r = 0.03, p = 0.72, respectively) and mechanical ventilation (r = 0.06, p = 0.58 and r = –0.13, p = 0.24).

Area under the ROC for prediction of mortality was highest for pSOFA 72 with a cut-off of 6.5 and a sensitivity of 83.3%, and a specificity of 76.9% (Table 5, Fig. 2).

Table 4: Comparison of characteristics of survivors and non-survivors at 28 days

Parameter	*Survivors (119)*	*Non-survivors (32)*	*p-value*
Age (months)	24 (6, 84)	42 (8, 90)	0.14
Gender			
Male *N* (%)	72 (60.5)	20 (62.5)	0.82[##]
Female *N* (%)	47 (39.4)	12 (37.5)	
AKI *N* (%)	34 (28.5)	21 (65.6)	<0.001[##]
Duration from admission to PICU transfer (hours)	20 (4, 48)	17 (5.7, 24)	0.65
Duration of PICU stay (days)	12.5 (7, 26)	4 (3, 12)	<0.003
Duration of ventilation (days)	16 (7, 29)	4 (3, 13)	<0.00009
PRISM-III	7 (3, 12)	10 (8, 18)	<0.0002
Mortality risk (PRISM III) (%)	3.4 (1.5, 8.3)	6.2 (4, 25.1)	0.0005
Mortality risk (PIM 2) (%)	7.1 (2.9, 14.8)	16 (6, 31)	0.002
pSOFA0	5 (2, 7)	9 (6.5, 14)	<0.0001
pSOFA72	3.5 (1, 6)	10 (7, 14)	<0.0001

[##]Values in *N* (%); all other values are in median (IQR); AKI, acute kidney injury; PICU, pediatric intensive care unit; PRISM, pediatric risk of mortality; PIM, pediatric index of mortality; pSOFA, pediatric sequential organ failure assessment

Table 5: Performance of PRISM III, PIM 2 and pSOFA scores for prediction of mortality

Score	*AUROC*	*95% Confidence interval*	*Cut-off*	*Sensitivity*	*Specificity*
PRISM III	0.701	0.593–0.809	7.5	75%	57.3%
PIM 2	0.635	0.501–0.770	13.1	62.5%	70.1%
pSOFA-0	0.765	0.651–0.879	5.5	83.3%	59.8%
pSOFA 72	0.870	0.782–0.958	6.5	83.3%	76.9%
Delta pSOFA	0.805	0.714–0.897	–0.5	91.7%	55.6%

PRISM, pediatric risk of mortality; PIM, pediatric index of mortality; pSOFA, pediatric sequential organ failure assessment

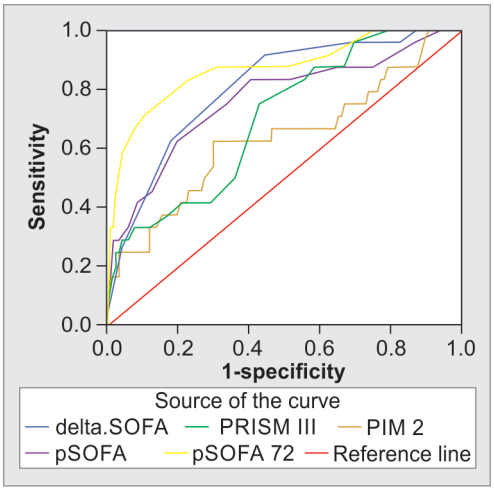

Fig. 2: Receiver operator curve for the prediction of mortality as per the severity scores

Discussion

In low-resource countries, resource allocation is a priority, and hence it is important that the sickest children are identified early in their course of stay, preferably at admission, or within the first 48–72 hours of stay, and they can be moved to a place with more intensive monitoring, with dedicated manpower, and where they can be escalated to higher modalities of respiratory and cardiovascular support, be it PICU or pediatric high dependency unit (PHDU). Hence, scoring systems that can predict an end point, in most cases the mortality scores, have been developed, since this has the most external validity, enabling resource allocation to these children early in their course of stay.

But practically there are other morbidities as AKI, and the requirement of additional respiratory support, be it ventilation or heated humidified high flow nasal cannulas (HHHFNC), which require the allocation of additional resources, and influence the decision to transfer these patients to dedicated areas such as PHDU or PICU, early in their course of stay.

Hence, a study was planned to assess whether the scoring systems developed in the west, PRISM III or PIM 2, can be a predictor of mortality in a resource-limited setting such as India. Since these systems were developed in the west, with different disease profiles and hence the original data on which they systems were developed would be more diverse than most hospitals across the India, where infectious diseases and septic shock are the predominant high-risk etiologies, as compared to severe combined immune deficiency, hypoplastic left heart syndrome, etc., which are the high-risk etiologies for these systems.[11]

Hence, intuitively, scoring systems that are based only on physiological parameters will be more practical in resource-limited settings, than those based on etiologies. Moreover, those scoring systems that are based on serial monitoring and evolution of physiology over the course of the stay, as SOFA at admission and 72 hours, may be more reliable.

Though the prediction scores as PIM 2 and PRISM III, have stood the test of time, many studies have evaluating predictiveness and most of them have shown good predictive ability for PRISM III and PIM 2.[2–4,12–22] Studies have also shown good calibration between predicted and actual mortality (Table 6).

However, in the present study, the pSOFA score showed a better discrimination for 28 day mortality compared to the PRISM III and PIM 2 scores, with the best discrimination seen with pSOFA72. Both pSOFA24, pSOFA72 and Delta pSOFA showed good sensitivity of 83.3, 83.3, and 91.7% respectively at a cut-off of 5.5, 6.5, and –0.5, respectively. The specificities at this cut-off were 59.8, 76.9, and 55.6%, respectively. Many studies have previously evaluated pSOFA for mortality prediction and showed good discriminating ability. This score was developed by Matics et al. in 2017 based on age-dependent parameters, and they showed that pSOFA on the day of admission performed better than PRISM III for predicting in hospital mortality (AUROC 0.94 vs 0.88) while it was similar to other descriptive scores like PELOD and PELOD-2.[9] Study from Pakistan showed better mortality discrimination and accuracy with pSOFA compared to PRISM III within 24 hours of admission (AUROC-0.81 for pSOFA vs 0.75 for PRISM III)`pSOFA score had sensitivity of 93.8% and specificity of 38.2% at a cut-off of 2.[23] Aulia et al. assessed pSOFA scores for detecting sepsis among 108 children and found that pSOFA scores of 8 or more had good discriminating ability (AUROC 0.939), which was similar to PELOD-2 score.[24] Kumbar and Chandrashekhara modified pSOFA score by adding lactate to

Table 6: Indian studies assessing the performance of PRISM III and PIM scores

		PRISM III			*PIM 2/3*		
Study	*Study subjects*	*AUROC*	*SMR*	*HL*	*AUROC*	*SMR*	*HL*
Mehta et al.[2] (Maharashtra)	400	0.920					
Kaur et al.[12] (Punjab)	486	0.903 (0.873–0.932)		$p = 0.25$			
Popli[13] (Delhi)	145	0.871 (0.806–0.921)		$p > 0.05$			
Muthupandi et al.[14] (Tamil Nadu)	102	0.881 (CI: 0.769–0.992			0.768 (CI: 0.628–0.908)		
Simalti et al.[15] (Delhi)	315	0.905 (CI: 0.844–0.967)					
Patel et al.[16] (Gujarat)	250	0.918		$p = 0.59$			
Patki et al.[17] (Maharashtra)	132	0.923 (0.861–0.964)	1.42 (1.21–1.67)	$p = 0.56$	0.946 (0.890–0.977)	1.25 (1.13–1.38)	$p = 0.72$
Varma et al.[18] (Maharashtra)	723	0.860		$p = 0.63$			
Tyagi et al.[19] (Maharashtra)	350	0.667 (0.605–0.725)	0.9	$p = 0.74$	0.728 (0.674–0.783)	1.06	$p = 0.47$
Sreekrishna et al.[21] (Karnataka)	120				0.867 (0.729–0.980)	1.0	$p = 0.96$

AUROC, area under receiver operator curve; SMR, standardized mortality ratio; HL, Hosmer–Lemeshow test

it (pSOFA-L) and found good discriminating ability for mortality (AUROC-0.925) at a cut-off of 10.5 with sensitivity and specificity of 96.8 and 88.4% respectively.[25]

Changes in the score over PICU stay may be helpful in predicting mortality as the disease progresses, the present study suggests that the use of descriptive scores like pSOFA and changes in the score over time may be better in predicting PICU mortality compared to one-time scores like PRISM III and PIM 2.

The strengths of the study were the prospective study design, the comparison of widely used PRISM and PIM scores with the relatively new pSOFA score and the generation of optimal cut-offs. The limitation was that the study involved a single PICU center and may not be applicable to the other centers as the patient population may differ. Another limitation was that PIM 2 was used in the present study in place of PIM 3 which has shown better discrimination in the Indian population.[26] The reason for using PIM 2 was that it was already being used in the PICU, so the same was continued for the study.

Conclusion

Pediatric sequential organ failure assessment score at admission and at 72 hours performed better than PRISM III and PIM 2 scores for prediction of mortality. Calculation of the descriptive score over time may be better for mortality prediction in the developing countries.

Clinical Significance

This study shows that descriptive score like pSOFA may be used for prediction of mortality, especially when measured over time.

Ethics Approval and Patient Consent to Participate

The study was approved by institutional ethical committee, Maulana Azad Medical College, New Delhi, India. (F.1/IEC/MAMC/(72/07/2019/No.24), Dated: 18.02.2020.

Availability of Data and Materials

The study data is available with the authors, and may be provided if required.

Clinical Trial Registry Number: CTRI/2020/04/024433, dated 20.03.2020.

Previous Presentation

This study was presented at PediCritiCon 2021 on 30-April-2022 as a poster presentation.

Authors Contribution

SA: Data curation, methodology, project administration, formal analysis, writing-original draft, writing-review and editing, validation; MJ: Data curation, Project administration, writing-original draft, validation; RS: Methodology, formal analysis, supervision, writing-review and editing, validation; PP: Formal analysis, supervision, writing-review and editing, validation; UJ: Conceptualization, methodology, resources, supervision, writing-review and editing, validation. All the authors have read and approved the manuscript.

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