Megied *et al.*
Egyptian Pediatric Association Gazette (2023) 71:57
https://doi.org/10.1186/s43054-023-00204-8

Egyptian Pediatric Association Gazette

RESEARCH

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Clinico-laboratory outcomes of plasma transfusion in the Egyptian's pediatric intensive care units—a prospective observational study

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Abstract

Background Despite the paucity of data supporting their indications, plasma transfusions (PT) are regularly administered for critically ill patients (CIP) in pediatric intensive care units (PICU). The aim of this study was to identify the actual indications for PT in the Egyptian's PICUs and determine to what extent it affects the clinic-laboratory outcomes for CIP.

Methods A prospective observational study was conducted for 6 months on 180 CIP in PICUs of Cairo University Hospital who received plasma for at least one time during their length of stay (LOS). Full history, examination, and investigations were obtained from the medical records.

Results Plasma was transfused in 64.4% of the studied population to support moderate and severe critical illness identified by multiple organ dysfunction score (MODS). Meanwhile, subjective-based physician conceptions accounted for 12.8% of all indications for plasma transfusion. PT in CIP was associated with a significant reduction in platelet count, prothrombin time, partial thromboplastin time, and international normalized ratio with p-value < 0.001, while there was a significant increase in hemoglobin level with p-value < 0.001. A statistically positive correlation exists between the time interval between admission and 1st PT and LOS with a p-value < 0.001 being shorter with earlier transfusion. Of the 180 patients enrolled in this study, seventy patients (38.9%) died, while 110 patients (61.1%) survived. A statistically significant increase in mechanical ventilation (MV) ($p = 0.004$), total number of PT ($p < 0.001$), and MODS score ($p < 0.001$) were recorded in dead CIP compared with survivors.

Conclusion Moderate and severe critical illness identified by MODS was the most frequent cause for PT in the Egyptian's PICUs. Early, precise, and objectively based PT has a strong role in improving the outcomes in CIP.

Keywords Critically ill patients, Pediatric intensive care units, Plasma transfusion

Background

Fresh frozen plasma (FPP) is the fluid portion separated from whole blood and frozen for 8 h. It lacks erythrocytes, leukocytes, and platelets but has all coagulation components. It corrects coagulopathy by replacing and providing plasma proteins in patients who have deficient or malfunctioning plasma proteins [1].

The percentages of patients requiring plasma transfusion (PT) were reported to be 22.4%, 21.2%, and

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11.7% due to active bleeding, mild bleeding, and scheduled surgery and treatment, respectively. However, 34.1% of these patients were due to neither bleeding nor any invasive operation [2]. Studied cases with international normalized ratio (INR) > 2.5 at baseline had the greatest improvement after receiving plasma transfusions, suggesting that this treatment is only effective for severe cases of coagulopathy [3].

Plasma transfusion is associated with various risks, including acute lung damage [4], circulatory overload [5], and allergic reactions [6]. Moreover, there may be other risks associated with plasma transfusions than the spread of infections. Many observational studies have shown significant association between plasma transfusion and increased risk of multiple organ dysfunction syndromes (MODS) and death [7].

The reviewed literature revealed heterogeneity in plasma transfusion thresholds and strategies, as two-thirds of pediatric intensivists prescribe plasma transfusion for nonbleeding CIP [2]. As far as we know, there is no study conducted on critically ill patients in the Egyptian's PICUs. Moreover, in spite of the presence of guidelines for the proper transfusion of plasma in children, significant mortality exists. This indicates the presence of hidden factors that require further investigation. From this point, this study was conducted to identify the actual indications for plasma transfusion in the Egyptian's PICUs and assess the impact of plasma transfusion on the clinico-laboratory outcomes for CIP with the hope of reducing the mortality among this age group. We hypothesized that non-adherence to the plasma transfusion thresholds and strategies in PICUs would have undesirable clinico-laboratory outcomes.

Methods

Study setting

This 6-month duration prospective observational study was conducted on CIP who received plasma transfusion for at least one time during their period of admission in the PICUs of the children's hospital of Cairo university.

Study population

This study was conducted on CIP of both sexes, with age ranging from 1 month to 12 years. The included CIP were admitted for active bleeding (with or without coagulation profile defect), hemorrhagic shock, or liver disease. Preterm, full-term neonates, patients with volume overload, patients who died within 24 h of admission, or patients who refused to participate in the study were excluded from the study.

Procedure

Based on the mentioned inclusion criteria, 180 patients were chosen. All patients who underwent testing had a thorough medical history, including name, age, sex, weight, place of residence, cause of admission to PICU (respiratory, shock, cardiac, infection, trauma, burn, neurological and emergency surgery), severity of illness as estimated by multiple organ dysfunction score (MODS) (Table 1) [8], LOS in the PICU, and need for respiratory support, as well as its degree and duration. In the current study and according to the calculated total M score, the critical illnesses were sub-graded into no (0–3), mild (4–6), moderate (7–12), and severe (13–24) critical illnesses.

Based on the recorded hematological data, the researcher plotted familial/personal history of coagulation disorders, previous transfusion, type of plasma transfusion whether fresh frozen plasma, frozen plasma or irradiated plasma, the total number of transfusions, volume of plasma per transfusion, time interval among admission and 1st plasma transfusion, laboratory data collection, red blood cells, hemoglobin, platelet count, and bleeding profile especially INR, and outcome.

Data management and statistical analysis

Social Science Statistical Package (SPSS) version 26 was used for data coding and entry. Mean, standard deviation, median, minimum, and maximum were used to represent quantitative data, while frequency and relative frequency (per cent) were used to summarize categorical data. The non-parametric Kruskal–Wallis (KW) and Mann–Whitney tests were used to compare quantitative variables. The Wilcoxon signed rank test was used to compare successive measures taken from same subject. Chi-square test was used to compare the two sets of category information. When anticipated frequency was less than five, an exact test was applied instead.

Table 1 MODS score according to Fuhrman et al. [8]

Organ system	0	1	2	3	4
Respiratory	> 300	226–300	151–225	76–150	≤ 75
Renal (serum creatinine)	≤ 100	101–200	201–350	351–500	> 500
Hepatic (serum bilirubin)	≤ 20	21–60	61–120	121–240	> 240
Cardiovascular	≤ 10	10.1–15	15.1–20	20.1–30.0	> 30
Hematological	> 120	81–120	51–80	21–50	≤ 20
Neurological	15	13–14	10–12	7–9	≤ 6

Results

The enrolled patients involved 104 (57.8%) males and 76 (42.2%) females with male to female ratio 1.37:1, with a mean age of 41.35 ± 44.36 months. One hundred (55.67%) patients were living in urban regions, while the remaining 80 (44.4%) were living in the rural regions. The mean weight for the included patients was 1.42 ± 11.29 kg.

Respiratory conditions like pneumonia and adult respiratory distress syndrome (ARDS) were the most frequent cause for admission to the PICU among the studied CIP accounting for (36.7%), followed by neurological conditions like cerebral palsy and Guillain-Barré syndrome (GBS) (22.8%), infections (20.6%), perioperative (17.2%), and shock (16.7%).

Thirty percent of the studied population received plasma transfusion for moderate illness followed by critical illness (23.3%). Hypoalbuminemia and physician conceptions accounted for 22.8%, and 12.8% of the indications for plasma transfusion in the current study as presented in Fig. 1.

According to the indication for plasma transfusion, there was a significant decrease in PTT after plasma transfusion with p-value = 0.025 being more PTT change in critical illness and transfusion according to physician conceptions as presented in Table 2.

In the studied patients, the mean number of plasma transfusions per patient (2.51 ± 1.75 transfusion), volume of transfused plasma (14.19 ± 2.25 ml/kg), and time interval between admission and time of 1st transfusion (3.24 ± 3.49 days), respectively, are presented in Table 3.

For assessment of severity of illness, the MODS score was computed using the clinical and laboratory data from the first day of admission. The MODS score varied from 2 to 16 with a mean score of 14.56 ± 2.32. Forty-two percent of CIP had PaO_2/FiO_2 in the range of 226–300, platelet count $103/mm^3 > 120$ (60.0%), pressure adjusted heart rate 0–10 (58.3%), Glasgow Coma Scale 13–14 (41.1%), serum creatinine in mg/dl (μmol/L) < 1.1 (51.1%), and serum bilirubin < 1.2 mg/dl (67.2%).

There was statistically significant positive correlation between total MODS score and total number of plasma transfusion with p-value = 0.001. MODS score for assessment of disease severity among CIP who received plasma transfusion has cut-off point 9 with 88.6%

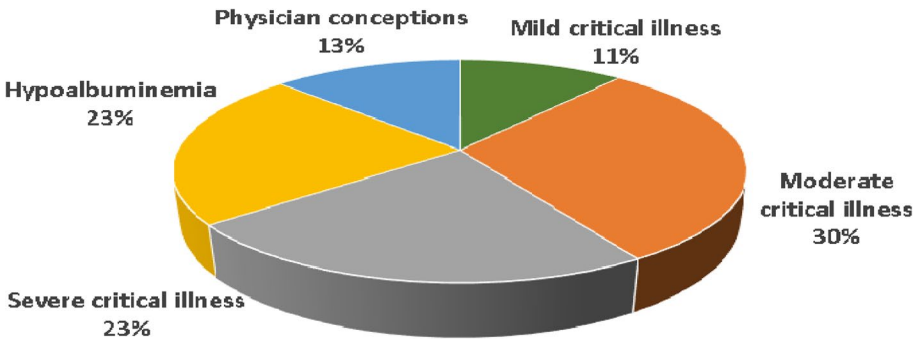

Fig. 1 Indications for plasma transfusion in the study group

Table 2 Change in the bleeding profile after plasma transfusion according to the reason of plasma transfusion

		Reason of plasma transfusion					KW	*P* value
		Mild	Moderate	Critical	Hypo-albuminemia	Physician conceptions		
Change in INR	**Mean**	0.44	0.52	0.64	0.71	0.64	2.293	0.682
	SD	0.43	0.45	0.56	0.67	0.59		
	Median	0.40	0.40	0.45	0.50	0.55		
	Min	0.40	0.10	0.10	0.10	0.30		
	Max	1.80	2.00	2.60	2.60	2.10		
Change in PTT	**Mean**	3.74	6.46	7.83	7.20	8.23	11.173	0.025
	SD	4.60	12.58	5.92	9.88	6.17		
	Median	4.00	5.00	7.00	6.00	6.50		
	Min	7.00	20.00	3.00	12.00	2.00		
	Max	15.00	84.00	20.00	55.00	22.00		

INR international normalized ratio, *PTT* partial thromboplastin time, *SD* standard deviation, *KW* Kruskal–Wallis

Table 3 Data of plasma transfusion in the study group

	Mean	Standard Deviation	Median	Minimum	Maximum
Total number of transfusions	**2.51**	1.75	2.00	1.00	10.00
The volume of transfusion (ml/kg)	**14.19**	2.25	15.00	5.00	20.00
The time interval between admission and 1st transfusion (days)	**3.24**	3.49	2.00	1.00	20.00

kg kilogram, *ml* millimeter

sensitivity, 96.4% specificity, 95%CI, area under the curve = 0.970, and p-value < 0.001 as presented in Fig. 2.

As the respiratory conditions were the commonest reason for PICU admission, it was mandatory to study the need for respiratory support, as well as its degree and duration. Out of the enrolled 180 CIP, 145 required respiratory support either as mechanical ventilation (MV), continuous positive airway pressure (CPAP), or nasal prong. Mechanical ventilation was initiated in 81.1% of the studied patients with mean duration of 8.58 ± 4.64 days. Meanwhile and through-out their LOS, 53.9% and 12.8% of the enrolled CIP were in need for CPAP and nasal prong with mean durations of 2.74 ± 1.42 and 3.41 ± 1.85 days, respectively.

The mean LOS in the PICU was 10.36 ± 5.05 days. There was no statistically significant difference between children with coagulation disorders and children with no coagulation disorders regarding LOS with p-value = 0.605. There was statistically positive correlation between time interval between admission and 1st plasma transfusion and LOS with p-value < 0.001 as presented in Fig. 3.

Regarding the outcome of plasma transfusion in the studied CIP, 110 (61.1%) survived till the time of discharge from the PICU, while 70 (38.9%) died. There was a statistically significant difference among survived and died CIP as regarding the total number of transfusions (being more in children who died later) and

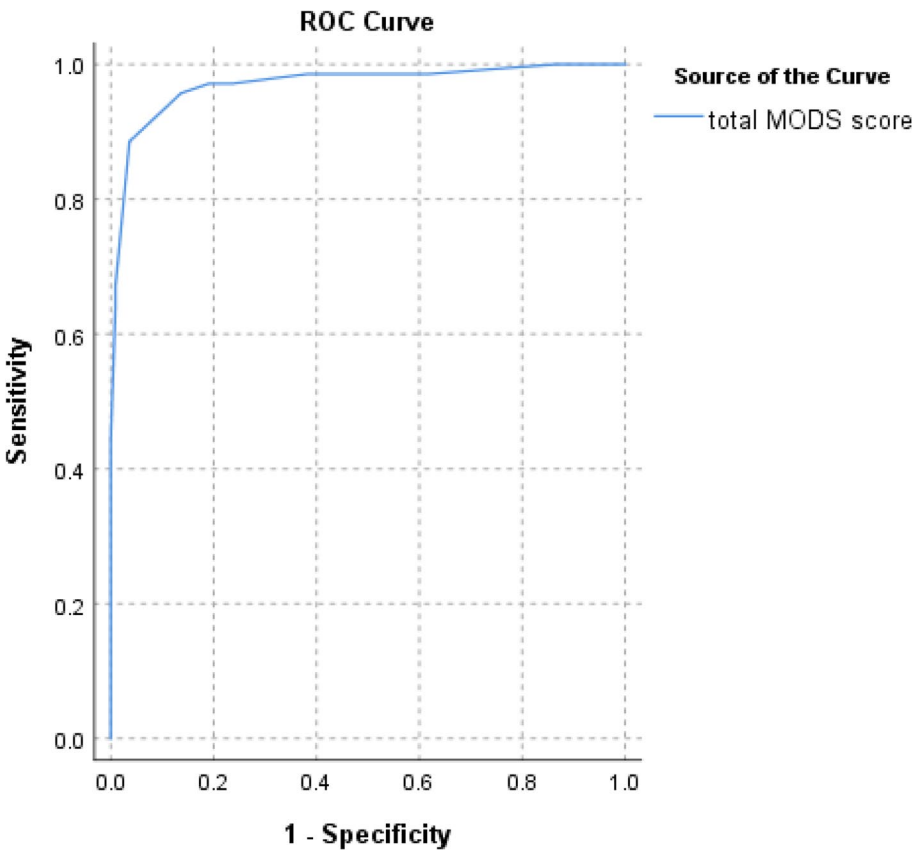

Fig. 2 ROC curve analysis of MODS score in assessment of disease severity in critically ill children who received plasma transfusion

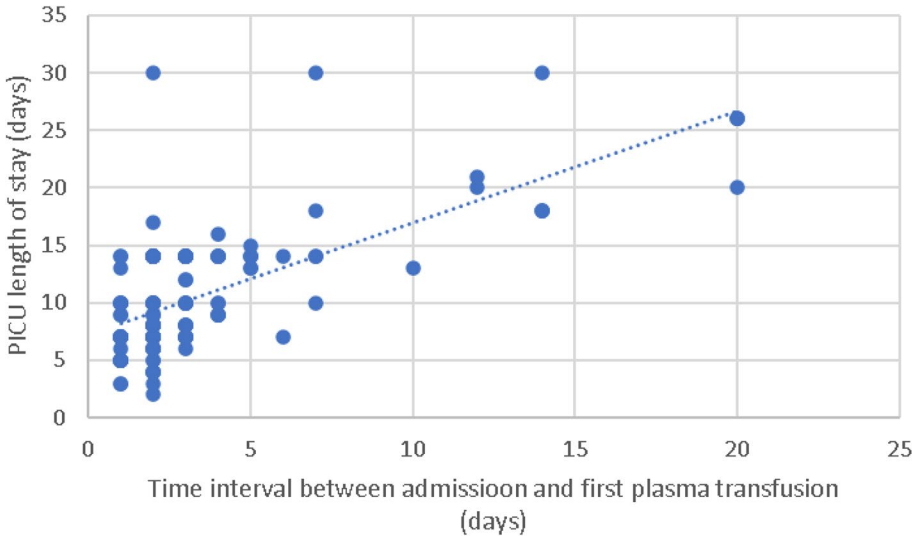

Fig. 3 Correlation between the time interval from admission to the first plasma transfusion and length of stay

volume of transfusion (more in survived children) with *p*-value < 0.001 as presented in Table 4.

There was a statistically significant difference between survived and died CIP who received plasma transfusion regarding Hb, PLT, PT, and INR *before* plasma transfusion with *p*-value = 0.016, 0.004, 0.038, and 0.009, respectively. There was a statistically significant difference between survived and non-survived CIP who received plasma transfusion regarding PLT, PT, and INR *after* plasma transfusion with *p*-value < 0.001, 0.004, and < 0.001, respectively. Survived CIP experienced more increase in platelet count and decrease in PT and INR after plasma transfusion than dead children as presented in Table 5.

There was a statistically significant difference between survived and non-survived CIP who received plasma transfusion as regards the total MODS score and duration of MV being more in died CIP with *p*-value < 0.001 and = 0.004, respectively as presented in Table 5.

Discussion

Plasma transfusion remains a common practice in the medical field, in particular for bleeding in emergency and intensive care settings. In less critical clinical conditions, pediatric researchers found an independent link between plasma transfusion and advancement of nosocomial infections [9], acute respiratory distress syndrome [6], multiple organ failure [9], and mortality [10]. Accordingly, it is critical to define when advantages outweigh risks, particularly since previous research showed that plasma transfusions fail to correct mildly abnormal coagulation tests [11].

The current study revealed statistically significant decrease in PLT, PT, PTT, and INR after plasma transfusion, while there was statistical rise in Hb level after plasma transfusion in CIP. This was in concordance with what was reported by Karam et al. [2] which found significant decrease in PT, PTT, and INR after plasma transfusion. However, Atiyyah et al. [12] reported that there

Table 4 Relation of number of plasma transfusion and outcome

	Outcome										*P* value
	Died					Survived					
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	
Total number of transfusion	3.04	2.02	2.0	1.0	10.0	2.16	1.47	2.0	1.0	6.0	< 0.001
Volume of transfusion (ml/kg)	13.64	2.81	15.0	5.0	20.0	14.55	1.73	15.0	10.0	20.0	0.018
Time interval between admission and 1st transfusion (days)	2.80	2.08	2.0	1.0	12.0	3.52	4.13	2.0	1.0	20.0	0.940
Total MODS score	11.70	2.36	12.0	3.0	14.0	4.52	2.13	4.0	2.0	12.0	< 0.001
MV duration (days)	9.86	5.37	8.50	2.00	30.00	7.51	3.65	7.00	2.00	18.00	0.004

MODS Multiple Organ Dysfunction Score, *SD* standard deviation

Table 5 Relationship between the outcome of plasma transfusion and laboratory results in the study group before and after plasma transfusion

	Outcome										*P* value
	Died					Survived					
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	
Hb before	9.51	1.57	9.5	5.2	12.9	10.09	1.87	10.0	6.6	25.0	0.016
Hb after	10.42	1.60	10.5	6.4	14.0	10.73	1.91	10.5	8.0	22.0	0.915
PLT before	232.81	150.98	212.0	19.0	602.0	273.28	121.90	250.0	10.5	567.0	0.004
PLT after	175.68	123.16	150.0	30.0	550.0	219.81	96.09	216.0	23.0	529.0	< 0.001
PT before	22.96	7.64	21.85	12.0	44.0	22.45	19.49	20.0	12.0	210.0	0.038
PT after	17.07	4.67	16.0	12.0	33.0	14.96	2.87	15.0	5.0	28.0	0.004
PTT before	35.86	13.89	33.0	18.0	117.0	32.19	5.58	31.0	15.0	45.0	0.197
PTT after	27.44	6.99	28.0	13.0	50.0	26.41	5.53	27.0	13.0	55.0	0.280
INR before	2.11	1.53	1.80	1.07	10.0	1.65	0.53	1.45	1.0	4.0	0.009
INR after	1.44	1.17	1.10	1.0	8.0	1.11	0.15	1.10	0.8	1.80	< 0.001

Hb hemoglobin, *PT* prothrombin time, *PTT* partial thromboplastin time, *PLT* platelet, *INR* international normalized ratio, *SD* standard deviation

were statistically significant decreases in PTT, and INR only after plasma transfusion.

Our results are contradictory to those reported by Soundar et al. [13]. They found no significant changes in PT and INR before and after plasma transfusion as transfusion of plasma resulted in normalization of PT and INR values in only 15.4% of their studied cases with the remainder showing no development in PT and INR regardless of age, volume of transfusion, or bleeding status. Muntean et al. [14] explained this difference by different normal ranges of bleeding profile according to age.

In our study, 61.1% of the CIP who received plasma transfusion survived, while 38.9% died which was similar to what was reported by Atiyyah et al. [12]. They found 74.1% of CIP who received plasma transfusion survived, and 25.9% died.

There was statistically significant difference between survived and non-survived CIP who received plasma transfusion regarding the total number of transfusion (being more in died children) and volume of transfusion (being more in survived children). This is in contrast with what was reported by Karam et al. [9]. They found significant rise in mortality (8%) for each ml/kg of FFP transfused in pediatric studied cases with acute lung injury, after adjusting for severity at admission and coagulopathy.

The same was reported by Philip et al. [15]. They studied 708 patients with history of transfusion of blood product including plasma and revealed significant relationship between number of transfused plasma units and survival.

In the current study, there was significant positive relationship between total MODS score and total number of plasma transfusion. The MODS score for assessment of disease severity among CIP who received plasma transfusion had cut-off point 9 with 88.6% sensitivity, 96.4% specificity, 95%CI, area under curve = 0.970, and p-value < 0.001. This was in accordance with Karam et al. [9] result. They found that the adjusted odds ratio for development of new or progressive MODS related to plasma transfusion was 3.19 (95% CI:1.5506.58, *P*-value 0.002).

In the current study, there was a statistically significant positive correlation between the time interval from admission to the first plasma transfusion and LOS. Our study results are in contrast to those of another study that was conducted by Rajasekaran et al. [16]. The latter retrospectively studied the course of 34 transfused cases and compared them to 45 non-transfused control cases admitted to PICU. They observed that early transfusions in the 1st 48 h were associated with significantly increased ventilator needs, duration, and delayed recovery.

Based on our findings, our hypothesis is accepted as statistically significant differences presented among survived and non-survivors CIP who received plasma transfusion regarding the duration MV ($p = 0.004$), total number of plasma transfusions ($p < 0.001$), and total MODS with p-value < 0.001 being more in dead CIP. It is highly recommended to implement early, precise, and objectively based plasma transfusion strategies especially in resource-limited countries to gain its benefit and eliminate undesirable clinic-laboratory outcomes. In the presence of high MODS score, it is highly recommended to optimize various aspects of management plan, investigations (cultures), nonspecific supportive therapy (as mechanical ventilation), and specific therapy (as culture and sensitivity based antimicrobial therapy) from the first hours of admission.

Conclusion

Moderate and severe critical illness identified by multiple organ dysfunction score (MODS) was the most frequent cause for plasma transfusion in the Egyptian's PICUs. Early, precise, and objectively based plasma transfusion has a strong role in improving the outcomes in CIP.

Abbreviations

ARDS	Adult respiratory distress syndrome
CI	Confidence interval
CPAP	Continuous positive airway pressure (CPAP)
CIP	Critically ill patients
FFP	Fresh frozen plasma
GBS	Guillain-Barré syndrome
HB	Hemoglobin
INR	International normalized ratio
Kg	Kilogram
KW	Kruskal–Wallis
LOS	Length of stay
MV	Mechanical ventilation
ML	Millimeter
MODS	Multiple organ dysfunction score
PTT	Partial thromboplastin time
PICU	Pediatric intensive care unit
PT	Plasma transfusion
PLT	Platelet count
PT	Prothrombin time
ROC	Receiver operating characteristic
SOFA	Sequential organ functional assessment
SPSS	Statistical Package for the Social Science
SD	Standard deviation

Acknowledgements

Not applicable

Authors' contributions

MAA drafted the work and revised it, being the major contributor in writing the manuscript. *LHA* made substantial contribution to the concept and design of the work and interpretation of data. *BSS* contributed to the data interpretation. *YMR* contributed to the data acquisition. *HEM* contributed to the data acquisition. *OSE* contributed to the data interpretation. All authors read and approved the final manuscript. Each agreed both to be personally accountable for the author's own contributions and ensured that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated and resolved and the resolution documented in the literature.

Funding

No fund.

Availability of data and materials

All data are available upon request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Ethical Review Board, Faculty of Medicine, Cairo University, Approval number: MS 354–2019.

Consent for publication

Not applicable (no individual details, images or videos).

Competing interests

The authors declare that they have no competing interests.

Received: 28 June 2023 Accepted: 10 August 2023
Published online: 30 November 2023

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