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Factors related to the success rate of pediatric extracorporeal shock wave lithotripsy (ESWL) in Cipto Mangunkusumo Hospital: an 8-year single-center experience

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Abstract

Background: ESWL is still considered as the first favorable therapeutic option for urinary stone disease with acceptable effectivity. However, factors associated with favorable outcome have not been widely studied in pediatrics due to the small number of urinary stone prevalence. The aim of this study is to evaluate the factors associated with the success rate of pediatric ESWL in our center according to immediate stone-free rate and 3-month stone-free rates.

Methods: This is a retrospective cohort study of children less than 18 years who had ESWL for urolithiasis from January 2008 until August 2015. Patient's characteristics including age, gender, BMI, stone location, stone length, stone burden, stone opacity, and number of ESWL sessions were gathered from the medical record. Nutritional status was determined according to the Centers for Disease Control and Prevention BMI curve. The outcome of this study was the factors related to the success rate in pediatric ESWL.

Results: Extracorporeal shock wave lithotripsy was done for 36 patients and 39 renal units (RUs) with mean age of 13.7 ± 4.3 years old, height of 1480 ± 16.0 cm, and BMI of 20.0 ± 3. Of 36 patients included, 39 renoureteral units (RUs) and 46 ESWL sessions were recorded. The mean overall treatment was 1.2 ± 0.5 sessions with mean stone length of 11.1 ± 6.3 mm and stone burden of 116.6 ± 130.3 mm^2. Within 3 months of follow-up, we recorded that the overall 3-month success rate was 100%, while the overall 3-month stone-free rate was 66.7%. Stone length ($p < 0.001$ and $p < 0.001$), stone perpendicular length ($p < 0.001$ and $p < 0.001$), and stone burden ($p < 0.001$ and $p = 0.001$) were found to be significantly associated with immediate success and 3-month stone-free status, respectively.

Conclusions: ESWL is an effective and safe modality to treat pediatric urolithiasis cases. Stone length, stone perpendicular length, and stone burden were found to be associated with immediate success and 3-month stone-free status after pediatric ESWL treatment.

Keywords: Success rate, Stone-free rate, ESWL, Pediatric, Urolithiasis, Urinary stone disease

1 Background

Pediatric stone disease is a somewhat rare condition and often caused by metabolic disturbance [1]. It counts only 2–3% globally with prevalence ranging from 1:1000 to 1:7600 in various geographic regions in the USA alone [1–3]. The incidence of pediatric stone disease has been progressively increasing in these past few decades, with some epidemiological studies refer this phenomenon as

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a "stone wave" [4]. Most of the cases were documented from developing countries including Pakistan, India, Turkey, and certain eastern countries [1, 4] .

Extracorporeal shockwave lithotripsy (ESWL/SWL) is still considered as the first favorable therapeutic option for most cases in both pediatrics and adults due to its minimal invasive nature. First reported by Newman et al. [3], ESWL use for pediatric stone cases was astonishingly effective, with low complication, and shorter length of hospitalization compared to other treatments [1, 3]. ESWL has been reported to be effective for stone sized $\leq$ 20 mm or $\leq$ 300 m^2, with stone-free rate ranging from 67 to 93% (short term) and 57–92% (long term) [5–7]. The reported retreatment rate was 13.9–53.9%, and the rate of treatment needing auxiliary procedure needed was between 7 and 33% [5, 6].

The success of ESWL can be reflected from the stone-free status that is defined as residual stone fragments of less than 4 mm in length in the vertical axis and width in the horizontal axis or the absence of any stone fragments on the follow-up plain abdominal radiograph [8]. Stone-free status after ESWL treatment is usually evaluated periodically for at least 3 months after the first treatment; with the stone-free rate as high as 70–100% [3]. The success rate of ESWL in pediatric is higher compared with its adult counterpart due to the relatively smaller stone volume, softer stone composition, smaller body volume, and higher ureteral compliance to accommodate spontaneous stone passage [4, 6, 7]. Certain factors were reported to affect the success rate of ESWL, including stone burden, lower pole localization, infundibular length, infundibulopelvic angle (more than 45°), and stone hardness or composition [4, 7]. The aim of this study is to evaluate the factors associated with the success rate of pediatric ESWL in our center.

2 Methods

2.1 Patients

This is a retrospective cohort study of 36 pediatric patients (16 boys and 20 girls) who had ESWL for urolithiasis. Pediatric patients were defined as patients with age $\leq$ 18 years [9]. Data from January 2008 until August 2015 were retrospectively analyzed. Sample size was determined pragmatically, on the basis of available patients in the medical records. This study has been approved by Ethics Committee. The authors confirm the availability of, and access to, all original data reported in this study. No particular exclusion criteria were applied for the patients in this study.

Body mass index (BMI) was calculated and categorized using special tools from Centers for Disease Control and Prevention (CDC) and was classified into certain category: underweight, healthy, overweight, and obese [10]. The diagnosis of stone disease was made through pre-ESWL radiologic evaluation using CT-Scan. Stone burden was then calculated by multiplying the stone maximum length by its maximum perpendicular length [11]. We also classified the stone burden into low (< 100 mm^2) and high (> 100 mm^2) stone burden before the measurement [12]. We also include stone opacity, anatomical location, and laterality, determined through pre-ESWL radiologic evaluation. The outcome of this study was the factors related to the success rate of pediatric ESWL.

2.2 ESWL technique

Since 2008, our institution has been using Richard Wolf Piezolith 3000, a third-generation piezoelectric lithotripter with incorporated lithotripter-fluoroscopy (Lithoarm) and ultrasonography. This lithotripter can be adjusted continuously to penetrate up to 165 mm [13, 14]. All stones were then re-evaluated using intra-ESWL ultrasonography or fluoroscopy.

The shockwave power and total shocks were set and adapted according to the patients' age, body weight, comfort, and stone response. The procedures were usually started at power level 1 (0.03 mJ/mm^2) and progressed to the higher power level gradually depending on the desired stone fragmentation response, with a maximum power level of 20 (1.6 mJ/mm^2) [15]. The use of sedations or analgesics was considered necessary depending on the patients' compliance and response to the pain caused. Analgesics used in most cases were suppository Profenid (ketoprofen), although in some cases additional sedations with adjusted dose of propofol were used. Successful ESWL treatment was defined as complete absence of stone fragments in imaging modalities (stone-free status) or presence of clinically insignificant residual fragments sized less than 4 mm [11, 16–18]. Patients requiring repetitive ESWL procedure for the same stone were defined as retreatment [11]. The immediate stone-free rate and 3-month stone-free rate were then calculated to determine the ESWL treatment success rate. Radiological evaluation was done 3 months after ESWL treatments to evaluate the stone-free status. The use of auxiliary supportive and curative procedures was also recorded. These auxiliary procedures include double-J (DJ) stent, ureteroscopy, percutaneous nephrolithotomy (PCNL), etc. [11, 13]. All ESWL procedures were done in an outpatient setting, and patients were usually discharged the same day as the procedures completed.

2.3 Statistical analysis

Patients, stones, and ESWL technical data characteristics and demographics were analyzed using Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive data are presented with mean and standard deviation for normal distribution, while median and minimum–maximum value for abnormal distribution. All categorical data were then analyzed using Chi-square, Fisher exact, and Cramer's V test; while numerical data were analyzed using Mann–Whitney U test and unpaired t-test. p value < 0.05 considered as statistically significant.

3 Results

A total of 36 patients and 39 renoureteral units were treated in 46 ESWL sessions. The demographics and characteristics data of the patients can be seen in Table 1. Stones were commonly found in the renal (23 RUs), with the laterality to the right side (21 RUs) and in the form of radiopaque (27 RUs). The maximum stone length and burden treated with ESWL were 28 mm and 500 mm^2, respectively.

The mean ESWL power and shocks used for all cases were 1.31 mJ/mm^2 and 4274.3 shocks, respectively. Maximum power at level 20 (1.6 mJ/mm^2) with total shocks more than 4000 was recorded in 3 patients with ureteral stone; 1 patient aged less 10 years. Ketoprofen suppositories were considered quite sufficient to control the pain in most cases (29 RUs). There were 2 patients aged less than 12 years old that cooperative enough to undergo the procedure without additional sedation.

The only pre-ESWL and post-ESWL supportive auxiliary procedure recorded was DJ stent insertion, of which was performed for ESWL-related *steinstrasse*. There were 4 patients with history of PCNL procedures and 1 patient with past ureteroscopy procedure few months prior to ESWL treatment that had pre-ESWL DJ stent. Post-ESWL DJ stent insertions were done in most cases with stone burden more than 100 mm^2 (9 RUs). In contrast, none of post-ESWL procedures were recorded within 3 months after ESWL treatment. The overall retreatment rate and overall immediate stone-free rate were 17.9% and 82.1%, respectively. There was one patient needing total three ESWL sessions (two additional retreatment sessions) to achieve a successful result. Within 3 months of follow-up, we recorded that the overall long-term successful rate was 100%, while the overall 3-month stone-free rate was 66.7%. Summary of ESWL technique and outcomes can be seen in Table 2.

The significant factors associated with immediate stone-free rate and 3-month stone-free rate are stone location (kidney or ureter) and burden category ($\leq$100 mm^2 or > 100 mm^2). The immediate stone-free rate was higher for the ureteral stone, reaching up to 100%, while the immediate stone-free rate for the kidney stone was 69.6% ($p = 0.015$). The 3-month stone-free rate significantly decreased in kidney and ureteral stones with the value of 47.8% and 93.8%, respectively ($p = 0.003$). Cases with stone burden of $\leq$ 100 mm^2 had significantly higher immediate stone-free rate and 3-month stone-free rate as compared with stone burden > 100 mm^2, with the value of 96.3% versus 45.5% ($p = 0.001$) and 85.7% vs. 18.2% ($p = 0.001$), respectively.

Subgroup analysis on the stone anatomical location showed no significant difference for stones located on inferior calyx in terms of both immediate stone-free rate and 3-month stone-free rate, but with no statistical difference, reaching up to 100% ($p = 0.128$) and 75% ($p = 0.195$). Moreover, immediate stone-free rate on distal and proximal ureteral stones also showed the same

Table 1 Patients demographics and characteristics

Variables	
Age, mean ± SD	13.7 ± 4.3 years old
Heights, mean ± SD	148.0 ± 16.1 cm
Weights, mean ± SD	44.7 ± 12.8 kg
BMI, mean ± SD	20.0 ± 3.3 kg/m^2
ESWL session(s), mean ± SD	1.2 ± 0.4
Gender, *n* (%) (boys/girls)	17 (43.6)/22 (56.4)
Nutritional status, n (%)	
Obese	4 (10.3)
Overweight	3 (7.7)
Healthy	30 (76.9)
Underweight	2 (5.1)

Table 2 ESWL technique and patient outcomes

Variables	
ESWL power, median (min–max)	1.35 (0.69–1.60) mJ/mm^2
Total ESWL shock, median (min–max)	4000 (2000–6500)
Types of anesthesia/analgesics, n (%)	
Analgesics	29 (74.4)
Additional sedations	10 (25.6)
Pre-ESWL auxiliary procedures, n (%)	
DJ stent	6 (15.4)
No	33 (84.6)
Post-ESWL auxiliary procedures, n (%)	
DJ stent	6 (15.4)
No	33 (84.6)
Retreatments, n (%)	
Yes	7 (17.9)
1 additional session	6 (15.4)
> 1 additional sessions	1 (2.6)
No	32 (82.1)
3 months follow-up, n (%)	
Stone-free	26 (66.7)
CIRF	13 (33.3)

favorable numbers, with the value of 100% on both groups, while the 3-month stone-free rate on the proximal ureteral stones was lower, with the value of 85.7% ($p = 0.242$). The results of the statistical analysis are shown in Tables 3 and 4.

The stone length and stone perpendicular length in the immediate free group were significantly smaller than the not-success group, with the median difference of 13 mm and 9 mm, respectively (both $p < 0.001$); these differences persist until the 3-month follow-up, with the median difference of 9.5 mm in 3-month stone-free status group and 5 mm in the not-stone-free group (both $p < 0.001$). Stone burden on the immediate free group was significantly smaller than the not-success group, with the

Table 3 Factors associated with immediate stone-free rate and 3-month stone-free rate

Factors	***n* (RU)**	**Immediate stone-free rate, *n* (%)**	***p* value**	**3-month stone-free rate, *n* (%)**	***p* value**
Gender			0.65		0.54
Boys	17	14 (82.4)		11 (64.7)	
Girls	22	18 (81.8)		15 (68.2)	
Health status			0.465		0.131
Obese	4	4 (100)		3 (75.0)	
Overweight	3	3 (100)		3 (100)	
Healthy	30	23 (76.7)		20 (66.7)	
Underweight	2	2 (100)		0 (0)	
Types of anesthesia/analgesics			0.101		0.44
Analgesics	29	22 (75.9)		20 (69.0)	
Additional sedations	10	10 (100)		6 (60.0)	
Stone opacity			0.289		0.134
Radiolucent	12	11 (91.7)		10 (83.3)	
Radiopaque	27	21 (77.8)		16 (59.3)	
Laterality			0.409		0.496
Right	21	18 (85.7)		15 (71.4)	
Left	18	14 (77.8)		11 (61.1)	
Stone location			0.015		0.003
Kidney	23	16 (69.6)		11 (47.8)	
Ureter	16	16 (100)		15 (93.8)	
Burden category			0.001		0.001
$\leq 100\ mm^2$	28	27 (96.3)		24 (85.7)	
$> 100\ mm^2$	11	5 (45.5)		2 (18.2)	

Table 4 Subgroup analysis of stone anatomical location and its association with immediate stone-free rate and 3-month stone-free rate

Factors	***n* (RU)**	**Immediate stone-free rate, *n* (%)**	***p* value**	**3-month stone-free rate, *n* (%)**	***p* value**
Stone anatomical location					
Kidney			**0.128**		**0.195**
Inferior calyx	8	8 (100)		6 (75.0)	
Medial calyx	3	2 (66.7)		1 (33.3)	
Superior calyx	2	1 (50.0)		0 (0)	
Pyelum	10	5 (50.0)		4 (40.0)	
Ureter			–[a]		**0.242**
Distal ureter	9	9 (100)		9 (100)	
Proximal ureter	7	7 (100)		6 (85.7)	

[a] Statistical analysis could not be done because all RUs were successful

median difference of 356 mm^2 ($p<0.001$), while on the 3-month stone-free group showed the same result, with the median difference of 131 mm^2 ($p=0.001$). Statistical analysis result on numerical data is shown in Table 5.

4 Discussion

ESWL treatments in pediatric population have shown a great efficacy, even higher than in adults [19]. Demirkesen et al. [17] found that the overall immediate postoperative success rate for pediatric ESWL was 93%. The result on immediate stone-free rate was lower (82.1%) compared to other study, yet the long-term success rate was considerably high (100%). The 3-month stone-free rate was 67.7%, while the rest were classified as CIRF (23.3%). However, this result is still on the range of current recommendation value (57–92%) [6]. The retreatment rate in our study was 17.9%, which happened due to the relatively low energy delivered to produce minimal pain [3]. It was in accordance with the current recommendation value (13.9–53.9%) [6].

Boys are more likely to have urolithiasis compared to girls, with a ratio of 1.4:1 to 2.1:1 [2]. However, in this study, we found that urolithiasis patients treated with ESWL were predominantly girls, with ratio of 1.25:1. Since our study more concerned on ESWL treatments on pediatric population, our data did not represent the overall actual prevalence of pediatric urolithiasis in our institution.

Various study showed that age was not a significant factor contributing in pediatric ESWL success rate, as well as in our study [20–22]. Aksoy et al. [21] reported that patients aged ≤ 5 years had the most favorable stone-free rate, while those aged 11–14 years showed the poorest stone-free rate. However, Goktas et al. [23] reported that patients aged less than 6 years were significantly had higher stone-free rate after first ESWL session on the renal stones compared to patients aged 7–15 years (67.6% vs. 38.7%, $p=0.004$). Furthermore, recent study from El-Assmy et al. [24] found that age was a significant factor on the formation of steinstrasse, particularly patients aged ≤ 4 years. These population were reported to have more than twofold risk to develop steinstrasse. El-Assmy argued that children aged ≤ 4 years were less active compared to the older population and considered could affect the stone passage [24].

In this study, patients' weight, height, and BMI do not show any significant difference. However, all patients known to be categorized as obese and overweight showed excellent results with immediate stone-free rate and 3-month stone-free rate reaching up to 75–100%. Akca et al. [25] reported that obesity and overweight on pediatric were not significant risk factor affecting the efficacy of ESWL treatment. It has been known that skin-to-stone distance (SSD) represents better and correlated with ESWL success rather than BMI [26, 27]. High efficacy on obese and overweight pediatric population is thought to be caused by the SSD that is still on the lithotripter focal point range [18, 25].

The lithotripter that we used was a third-generation piezoelectric lithotripter that can induce a high peak pressure onto a small focal area with remarkably little pain [3]. It is widely known as "anesthesia-free" lithotripter due to its small focus that would reduce the damage to surrounding renal parenchyma [3, 14]. Hence, all the procedures were done in an outpatient setting and did not need any general anesthesia. We used analgesics with ketoprofen suppository and additional sedation with Propofol for particular patients considered too young or not cooperative.

Table 5 Statistical analysis results between numerical variables, immediate success, and 3-month stone-free status

Factors	Immediate stone-free rate ($n=32$), mean ± SD (median)	Not success ($n=7$), mean ± SD (median)	*p* value	3-month stone-free rate ($n=26$), mean ± SD (median)	Not stone-free ($n=11$), mean ± SD (Median)	*p* value
Age (years old)[a]	14.3 ± 4.5 (16)	15.6 ± 1.4 (15)	0.657	14.3 ± 4.5 (16.0)	12.4 ± 4.0 (14)	0.089
Weight (kg)[b]	47.1 ± 11.7 (50)	45.1 ± 7.4 (44)	0.921	47.2 ± 11.7 (50)	39.8 ± 14.6 (41)	0.095
Height (cm)[a]	147.1 ± 17.6 (152)	152.1 ± 7.7 (154)	0.956	149.9 ± 17.3 (155)	144.2 ± 13.8 (150)	0.107
BMI (kg/m^2)[a]	20.0 ± 3.6 (20)	20.0 ± 1.6 (20.2)	0.913	20.6 ± 2.6 (20.3)	39.7 ± 14.6 (41)	0.2
Stone length (mm)[a]	8.9 ± 3.8 (8)	21.1 ± 6.3 (21)	< 0.001	8.3 ± 3.3 (7.5)	16.9 ± 7.2 (17)	< 0.001
Stone perpendicular length (mm)[a]	7.0 ± 3.1 (6)	14.7 ± 4.7 (15)	< 0.001	11.5 ± 5.2 (10)	14.9 ± 4.7 (15)	< 0.001
Stone burden (mm^2)[a]	69.9 ± 61.1 (49)	329.9 ± 162.5 (405)	< 0.001	63.7 ± 60.3 (48.5)	222.3 ± 171.6 (180)	0.001
ESWL power (mJ/mm^2)[a]	1.29 ± 0.2 (1.31)	1.4 ± 0.1 (1.43)	0.192	1.3 ± 0.2 (1.35)	1.33 ± 0.2 (1.43)	0.682
ESWL shock[a]	4256.6 ± 1091.6 (4000)	4357.1 ± 944.9 (4000)	0.76	4373.1 ± 1116.6 (4350)	40,076.9 ± 932.0 (4000)	0.177

[a] Mann–Whitney test

[b] Unpaired *t*-test

In our study, stone opacity did not show any significant difference to ESWL success rate, which is in accordance with other studies [4, 26, 28]. Nevertheless, El-Assmy [26] found that stone density in Hounsfield units (HU) is an important prognostic factor for renal stone clearance on pediatric ESWL. The study reported that stone density > 600 HU was a significant predictor for ESWL failure [26]. Previous study by McAdams et al. [27] also described that a stone attenuation less than 1000 HU significantly predicted the successful outcome of single session ESWL, regardless its size.

Our study showed that stone location was a significant factor associated with pediatric ESWL success rate. Ureteral stone significantly had better results, both in immediate stone-free rate (100% vs. 69.6%, $p = 0.015$) and 3-month stone-free rate (93.8% vs. 47.8%, $p = 0.003$), compared to renal stones. On the contrary, Hammad et al. [29] reported that there was no significant difference between stone-free rates on the ureteral and renal stones; ureteral stones only showed a slight superiority (84% vs 81%, $p = 0.74$). Another study from Badawy et al. [30] showed that renal stones had higher overall stone-free rates at 3 months compared to ureteral stone, although statistical analysis between groups was not conducted (90.4% vs. 76.6%).

Our finding on stone anatomical location subgroup analysis showed that neither kidney stones group nor ureteral stones group were a significant factors related to the immediate stone-free rate and 3-month stone-free rate. Likewise, most of previous studies showed there was no statistically significant result between stone anatomical location and pediatric ESWL success or stone-free rate [3, 16, 19, 26, 29, 30]. Nonetheless, Lu et al. [1] reported a significantly higher stone-free rate in the proximal ureter rather than in middle or distal ureter, while in the various locations of renal stones, no statistical significance was found. El-Nahas et al. [4] also found that the calyceal site of the stone was an independent risk factor for not being stone-free after pediatric ESWL treatment. Although not statistically significant, inferior calyx stones had the most favorable results compared to other locations in kidney, on both the immediate stone-free rate and 3-month stone-free rate. Lower-pole stones have been reported to tend to be more refractory to ESWL and have relatively lower stone-free rate compared to other locations [4, 18, 31]. However, several other recent studies showed that lower-pole ESWL success rate within one session and stone-free rate at 3 months could be considerably high, reaching up to 80% and 85–100%, respectively [15, 23, 32].

Stone size has been reported to be one of the most significant factors predicting success rate of pediatric ESWL [1, 4, 17, 26, 30, 32, 33]. From our results, low burden stone significantly had better stone-free rate, in both immediate (96.3%) and 3-month follow-up (85.7%, $p = 0.01$). Wadhwa et al. [33] reported that stone-free rates for stone burdens ≤ 100 mm^2 were reported reaching up to 94%, while dropped significantly to 70% when the burdens increased to > 200 mm^2.

A recent multivariate analysis study showed that stone length was the most important risk factor for low stone-free rates on pediatric ESWL, compared to the stone location. It is reported that any increase of 1 mm in stone length was associated with an increased risk of residual stone fragments by 1.123-folds. Based on size and location, the study then recommended pediatric ESWL should be done for stone sized up to 24 mm in renal pelvis; up to 15 mm in upper or middle calyceal; and up to 11 mm in lower calyceal [4]. It is in accordance with our results which showed that higher stone length has a significant stone-free rate outcome compared to lower stone length ($p < 0.001$).

Our study has several limitations. First, our study has small sample size relatively compared with the reported prevalence of pediatric stone diseases in the general population. In addition, our study did not document the periprocedural complications, as might be reported in Clavien–Dindo classifications.

5 Conclusions

From our report, we conclude that stone length, stone perpendicular length, stone burden, and stone location were the significant factors related to the success rate of pediatric ESWL based on the immediate stone-free and 3-month stone-free status. The overall immediate stone-free rate and 3-month stone-free rate were 82.1% and 67.7%, respectively. After 3-month follow-up, all of the ESWL procedures were considered successful and none of the auxiliary curative procedures were done. ESWL was shown as a favorable modality to treat pediatric urolithiasis cases.

Abbreviations

ESWL/SWL: Extracorporeal shockwave lithotripsy; BMI: Body mass index; CDC: Centers for Disease Control and Prevention; DJ: Double-J; PCNL: Percutaneous nephrolithotomy; SPSS: Statistical Package for Social Sciences; RU: Renoureteral unit; SPSS: Statistical Package for Social Sciences; SSD: Skin-to-stone distance; HU: Hounsfield units; NCCT: Non-contrast computerized tomography; EAU: European Association of Urology; PNL: Percutaneous nephrolithotripsy.

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Authors' contributions

AIS contributed in gaining ethical approval, data collection, research of literature, draft writing, and manuscript finalization. FA contributed in gaining ethical approval, data collection, research of literature, draft writing, and manuscript finalization. IW involved in protocol development, administration of the study, data analysis, manuscript writing, and manuscript finalization.

AR contributed in conceptualization, administration of the study, funding, data analysis, and manuscript editing and finalization. NR involved in protocol development, study conceptualization, patient recruitment, and manuscript editing and finalization. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated during and/or analyzed during the current study are available on demand.

Declarations

Ethics approval and consent to participate
This study has been approved by Ethics Committee of Cipto Mangunkusumo Hospital–Faculty of Medicine University of Indonesia (No. KET-991/UN2.F1/ETIK/PPM.00.02/2019). Written informed consent was obtained from a parent or guardian for participants under 16 years old.

Consent for publication
Not applicable.

Competing interest
The authors declare that they have no competing interests.

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