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Paediatrics Section

Effectiveness of Sensitisation Programme on Prazosin Therapy for Scorpion Envenomation at Primary and Secondary Healthcare Level

B RAMESHBABU[1], P PUNITHA[2], E MANOCHITRA[3], K SASIKALA[4], J BALAJI[5]

ABSTRACT

Introduction: Scorpion envenomation is a life-threatening paediatric emergency. Prazosin-an alpha-1 blocker is the gold standard therapy for scorpion envenomation. Many children with scorpion envenomation were under-treated at Primary Healthcare (PHC) and Secondary Healthcare (SHC) level because of lack of awareness about prazosin therapy. If prazosin is started earlier at PHC and SHC level, complications and mortality can be reduced.

Aim: To conduct sensitisation programme for PHC and SHC doctors regarding the management of paediatric emergencies including scorpion envenomation, and to evaluate the effectiveness of sensitisation programme on prazosin therapy for scorpion envenomation at PHC and SHC level.

Materials and Methods: This non concurrent clinical trial consisted of training PHC and SHC doctors at the Department of Paediatrics, Government Dharmapuri Medical College Hospital, Tamil Nadu, India for a period of two years (January 2018-December 2019). After the training, children aged 1 month-12 years with features of scorpion envenomation referred from PHC and SHC to this tertiary care centre, during January 2021-September 2021 were evaluated. The data regarding initiation of prazosin therapy at PHC and SHC level and the clinical profile, complications and outcome at tertiary care level were noted. The present study parameters were compared with previous study on scorpion envenomation, done before the sensitisation programme in the same centre, and the data were compared.

Results: Training was given to 120 medical officers of PHC and SHC. Sixty-two children, with scorpion envenomation referred from PHC and SHC, were included in the study. A total of 7 (10%) children brought to the tertiary care centre directly were excluded. Prazosin therapy was initiated in 43 (69.3%) children at PHC and SHC level before referral. Initiation of prazosin within four hours of scorpion sting was done in 45 (72.6%). Common symptoms were pain {42 (68%)}, diaphoresis {26 (42%)} and salivation {25 (40%)}. Cold peripheries, myocarditis and pulmonary oedema were noted in 24 (39%), 4 (6%) and 6 (10%) children, respectively. Dobutamine and Non Invasive Ventilation (NIV) were needed in 13 (21%) and 11 (18%) cases, respectively. When compared to the observations pretraining, peripheral circulatory failure (76% to 39%) (p=0.019), pulmonary oedema (27% to 10%) (p=0.010), myocarditis (17% to 6%) (p=0.039), ionotrope support (41% to 21%) (p=0.024), and NIV (39% to 18%) (p<0.003) were significantly reduced. There was no mortality.

Conclusion: Following the sensitisation programme, initiation of prazosin for scorpion envenomation at PHC and SHC level significantly improved. Complications like myocarditis, pulmonary oedema, need for inotropes and ventilator support decreased significantly.

Keywords: Complications, Myocarditis, Pulmonary oedema, Scorpion sting, Sting-prazosin interval

INTRODUCTION

Scorpion envenomation is the most common and neglected paediatric medical emergency in tropical and subtropical regions. The case fatality rate of children hospitalised with scorpion sting ranged from 3-22% [1-3]. More than 99 species are identified in India, two of which (*Mesobuthus tamulus* and *Palamnaeus swammerdami*) are more poisonous. *Mesobuthus tamulus* (Indian red scorpion-common in India) is more poisonous and cause fatality, both in adults and children due to cardiac complications. Mortality is higher below five years of age, if not treated properly [4].

Indian red scorpions cause excessive catecholamine release, known as autonomic storm [5]. Autonomic storm is characterised by early transient parasympathetic stimulation followed by prolonged sympathetic stimulation. If not identified and treated, it progresses to myocardial dysfunction and pulmonary oedema, which is the most common complication. Pulmonary oedema starts as early as 30 minutes to three hours, after the sting. So, early identification and treatment of scorpion envenomation reduces the mortality and morbidity significantly. Many regimens used in the past like lytic cocktail, atropine, beta-blockers and insulin have not reduced the mortality significantly and also found to be unhelpful [6]. After starting prazosin as treatment for scorpion envenomation, mortality is significantly reduced [7-9].

Prazosin is the gold standard therapy for scorpion envenomation. It is an alpha-1 blocker and it has 1000-fold higher affinity to alpha-1 receptors. As a potent inhibitor of phosphodiesterase, prazosin causes accumulation of cyclic-Guanosine Monophosphate (cGMP) in vascular endothelium and myocardium, and inhibits the formation of inositol triphosphate [10]. As a result of this action, myocardial response to sympathetic stimulation is attenuated. If prazosin is initiated early, above mentioned complications, morbidity and mortality are very much reduced. Most of the studies have proved that mortality and morbidity due to scorpion envenomation is directly related to the sting-prazosin interval (time interval between time of scorpion sting and initiation of prazosin therapy) [6,11-14]. Prazosin therapy for scorpion envenomation is very much underutilised at PHC level because of lack of awareness. This leads to more complications [13]. So, upgradation of knowledge of PHC

and SHC doctors {Taluk Government Hospitals (GH)} on scorpion envenomation and other paediatric emergencies are very much mandatory to prevent the dreadful complications and death.

Many children with scorpion envenomation were referred to this tertiary care centre from PHC and SHC, present in and around this district. Strengthening the primary and SHC level, bridging the gap between primary and tertiary care level are very much mandatory to decrease the under five mortality due to paediatric emergencies.

The aim was to conduct sensitisation programme for PHC and SHC doctors regarding the management of paediatric emergencies including scorpion envenomation and also to evaluate the effectiveness of sensitisation programme on prazosin therapy for scorpion envenomation at PHC and SHC level.

MATERIALS AND METHODS

This non concurrent clinical trial consisted of training sessions for all the medical officers of PHC and SHC of Dharmapuri district, Tamil Nadu, India and to evaluate the effectiveness of the sensitisation programme. The training program was conducted for all the medical officers of PHC and Taluk GH-SHC of this district in the Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamil Nadu, India. Training was conducted with the permission and co-ordination of Head of the tertiary care institute and District authority for PHC Medical Officers and GHs, for the period of two years from January 2018-December 2019. Informed consent from parents and ethical committee clearance was obtained from Institutional Human Ethics Committee (IEC), Government Dharmapuri Medical College, Dharmapuri, vide Reference No.31/2019, dated.12.12.2019.

Training was provided to 120 medical officers from 51 PHC, including urban PHC and from 7 {Taluk Government Hospitals (GH) (SHC)}, in batches. A batch, consisting of 4-6 medical officers, was trained at Department of Paediatrics of the tertiary care centre. For each batch, training was conducted for two weeks. Training included PowerPoint presentations, lectures, and direct demonstration of early identification of critical illnesses. Hands-on training was conducted for assessment of airway, breathing, circulation and disability by using paediatric assessment triangle for all common paediatric illnesses and initial management of all common paediatric emergencies including scorpion envenomation. Periodical review training was also conducted.

After the training programme, all the PHC, SHC (GH) doctors and Paediatric Intensive Care Unit (PICU) of tertiary care centre were linked through phone numbers and a separate WhatsApp group (consisting of PICU, PHC and SHC doctors) was created. While referring a child from PHC and SHC (GH) to tertiary care centre, the details about the case, status of the child, treatment given at PHC or SHC level were informed through telephonic message or WhatsApp message.

The children with features of scorpion envenomation who were referred from the same PHC and SHC to this tertiary care centre, between January-September 2021 were included in this study. The effectiveness of the sensitisation programme on prazosin therapy for scorpion envenomation was then evaluated.

Inclusion criteria: All children, aged 1 month-12 years with history and/or features suggestive of scorpion envenomation, referred from the PHC and SHC were included in this study.

Exclusion criteria: Children with history of unknown bite, features not suggestive of scorpion envenomation, and children who were directly admitted to tertiary care hospital, without referral from PHC or SHC during the above period, were excluded from this study.

Data collection

After admission in the tertiary care centre, the child's basic details like age, sex, residence details were noted. Time of scorpion sting, site of scorpion sting, from which PHC or SHC the patient was referred, initial treatment details given at that PHC or SHC, time taken to reach the tertiary care centre and sting–prazosin interval were enquired in detail and noted in the case sheet. Detailed clinical examination was done and all the clinical features, complications, management and outcome were noted. Prazosin was given in a dose of 30 µg/kg/dose for a case of scorpion envenomation with features of autonomic storm. It is repeated every three hours till peripheries are warm and dry. Maximum three or four doses may be required for a confirmed case of scorpion envenomation with features of autonomic storm [6]. Inj. dobutamine 5-20 µg/kg/min was started, if there was myocarditis and pulmonary oedema. If the child developed respiratory distress due to pulmonary oedema, NIV support was initiated [5].

STATISTICAL ANALYSIS

All the parameters were entered in Microsoft Excel software. Descriptive analysis of all parameters was mentioned in percentages. The parameters of present study were compared with previous study (done before the sensitisation programme in the same tertiary care centre) of prazosin therapy for scorpion envenomation at PHC level [13]. Both the results were analysed using Mann-Whitney U Test, using Statistical Package for the Social Sciences (SPSS) version 26.0 software. The p-value <0.05 were taken as significant.

RESULTS

A total of 120 medical officers of PHC and SHC were trained on the management of scorpion envenomation. During the study period, 69 children were admitted for scorpion envenomation at the PICU of this tertiary care centre. Of them, 62 children who were referred from PHC and SHC with features suggestive of scorpion envenomation, were included in the study- 57 (83%) referred from PHC centers, and 5 (7%) from Taluk GHs after initial management. A total of 7 (10%) children were brought to the tertiary care centre directly. Demographic details are shown in [Table/Fig-1].

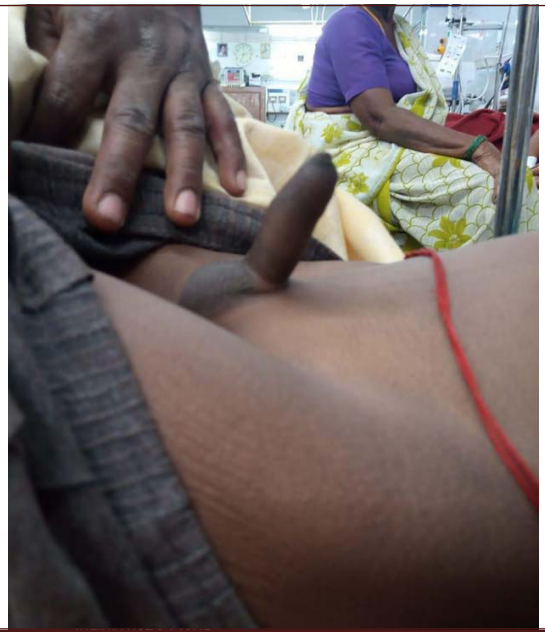
Of the above 62 children who referred from PHC and SHC, 43 (69.35%) children received prazosin at PHC and SHC before referral. Other treatments like analgesics were given to 12 (19.35%) children, 2 (3.2%) children were given antihistamines and steroid, 5 (8.1%) children were not given any treatment before referral [Table/Fig-1].

Pain at sting site {42 (68%)} was the most common symptom noted followed by diaphoresis {26 (42%)}, salivation {25 (40%)} and vomiting {17 (27%)}. The common signs noted were tachycardia {26 (42%)}, followed by cold peripheries {24 (39%)}. Hypertension was noted in 18 (29%) cases. Priapism [Table/Fig-2] was noted in seven cases (11%) [Table/Fig-1].

Complications like shock with peripheral circulatory failure were noted in 24 (39%) children. Pulmonary oedema was seen in 6 (10%) children. Four (6%) children developed myocarditis and none suffered with Multi Organ Dysfunction Syndrome (MODS). Most of these complications were noted in the children who arrived late to this centre or delayed initiation of prazosin. Complications were treated appropriately with inotropes like dobutamine in 13 (21%) children for cardiac dysfunction and shock. Eleven (18%) children needed NIV, none needed invasive ventilation and there is no mortality in this study [Table/Fig-3].

Parameters	Number (%)
Referred from (n=69)	
PHC	57 (83)
GH	5 (7)
Self	7 (10)
Age distribution (n=62)	
<1 Year	5 (8)
1-6 Years	37 (60)
>6 Years	20 (32)
Sex distribution (n=62)	
Male	34 (55)
Female	28 (45)
Prehospital treatment (n=62)	
Prazosin	43 (69.3)
Analgesics only	12 (19.4)
No treatment given	5 (8.1)
Anti-histamines, Steroids	2 (3.2)
Symptoms (n=62)	
Pain	42 (68)
Diaphoresis	26 (42)
Salivation	25 (40)
Vomiting	17 (27)
Drowsiness	13 (21)
Dyspnoea	7 (11)
Incessant cry	3 (5)
Swelling	2 (3)
Signs (n=62)	
Tachycardia	26 (42)
Cold peripheries	24 (39)
Hypertension	18 (29)
Priapism	7 (11)
Tachypnoea	7 (11)

[Table/Fig-1]: Referral details, demographic profile, pre hospital treatment and clinical features of scorpion envenomation.



[Table/Fig-2]: A child with priapism in scorpion envenomation.

The results of this study were compared with the previous study done in the same institute during January 2013-December 2016 [Table/Fig-3].

Parameters	Pretraining period (as in the published study) (n=262)	Post-training period (n=62)	p-value
Pre-hospital treatment and Sting-Prazosin Interval			
Prazosin given at PHC	7 (3%)	43 (69.3%)	<0.001
Other Drugs at PHC (Anti-histamine, steroid and analgesics)	193 (74%)	14 (23%)	<0.001
Sting-Prazosin Interval <4 Hours	66 (25%)	45 (72.6%)	<0.001
Sting-Prazosin Interval 4-8 Hours	136 (52%)	11 (17.8%)	<0.001
Sting-Prazosin Interval >8 Hours	60 (23%)	6 (9.6%)	<0.001
Complications			
Peripheral circulatory failure	199 (76%)	24 (39%)	0.019
Pulmonary oedema	70 (27%)	6 (10%)	0.010
Myocarditis	44 (17%)	4 (6%)	0.039
Hypotension with MODS	13 (5%)	NIL	0.073
Management			
Dobutamine Support	94 (36%)	13 (21%)	-
Adrenaline Support	13 (5%)	NIL	-
Total Inotrope support	107 (41%)	13 (21%)	0.024
CPAP through Jackson-rees Circuit	77 (29%)	8 (13%)	-
Non Invasive Ventilation	25 (10%)	3 (5%)	-
Total NIV support	102 (39%)	11 (18%)	0.003
Invasive ventilation	5 (2%)	NIL	0.272
Outcome			
Mortality	3 (1%)	NIL	-

[Table/Fig-3]: Comparison of Prazosin therapy at PHC and SHC, complications, management and outcome of scorpion envenomation between the pre and post-training period.

Only 3% (7/262) children received prazosin before referral from PHC and SHC in the previous study. But 69.35% (43/62) children received prazosin for scorpion envenomation before referral from PHC and SHC in this present study. After the training programme, prazosin therapy for scorpion envenomation at PHC and SHC levels were significantly improved (p-value <0.001). A 74% (193/262) children received drugs other than Prazosin in the previous study, but in this present study it was significantly reduced to 23% (14/62) (p-value <0.001). Sting-prazosin interval <4 hours was 25% (66/262) in the previous study, which was significantly improved to 72.6% (45/62) in the present study. Sting–prazosin interval of 4-8 hours was 52% (136/262) in the previous study, which was decreased to 17.8% (11/62) in the present study.

On comparing complications, peripheral circulatory failure was reduced significantly (p-value=0.019) in this study from 76% (199/262) to 39% (24/62). Pulmonary oedema was also reduced from 27% (70/262) to 10% (6/62) in the present study which was also significant (p-value=0.010). Other complications like myocarditis also reduced significantly from 17% (44/262) to 6% (4/62). Hypotensive shock with MODS was noted in 5% (13/262) of cases in the previous study, whereas no child suffered with MODS in the present study [Table/Fig-3].

Ionotrope support was needed in 41% of children (107/262) in the previous study, whereas it was 21% (13/62) in the present study. NIV support was needed for 39% (102/262) children in the previous study, as compared to 18% (11/62) in the present study (p-value-

0.003). Overall, 2% (5/262) of children needed invasive ventilation and mortality was 1.1% (3/262) in the previous study, whereas, no child needed invasive ventilation and there was no mortality in the present study [Table/Fig-3].

DISCUSSION

New diseases with various manifestations, outbreaks or epidemics and new treatment options are emerging every day in the field of medicine all over the world. In any emergency, earlier management will prevent the complications and improve the outcome. So, updating the knowledge for any illness is a must for all the doctors, who are dealing with the patients in day-to-day practice. PHC doctors may not have much idea about management of all paediatric emergencies, as they may have not seen those types of cases during their internship period. Also, there may be a gap between their internship period and joining as a Medical officer at PHC or SHC.

Scorpion envenomation is a very important public health problem, which is neglected often, causing significant mortality and morbidity in children. Though, the same amount of venom is injected into children and adults, envenomation is more significant in children due to lesser body surface area [4]. On many occasions, children with scorpion envenomation present as an unknown bite, because scorpion usually hides in shelves, luggage, bags, piles of bricks, wooden materials, firewood, shoes, etc. Many times small infants or school going children were brought to an emergency with features of incessant cry, irritability, altered level of consciousness, which may be due to unnoticed scorpion envenomation. Diagnosis and treatment for scorpion envenomation is very much delayed or missed in this scenario. Many children developed pulmonary oedema and mortality is quite high among them. Prazosin therapy is the standard line of management for scorpion envenomation, as it is a competitive alpha-1 blocker. It decreases the preload, after-load and hypertension without increasing heart rate [4,6,7]. Prazosin should be given as early as possible, as the first dose of the prazosin determines the outcome in many instances. Pulmonary oedema is the main cause of mortality in children due to scorpion envenomation, which can be prevented by early prazosin therapy. In Prasad R et al., study many children who presented after six hours of scorpion sting had significant complications (shock in 53.3%, myocarditis in 42.2%, encephalopathy in 35.5% and pulmonary oedema in 37.8%), the mortality rate was also significantly higher (8.9%) [14]. In Kumar CM and Prasad NSV study, younger age, red scorpion, sting-prazosin interval >8 hours were associated with increased incidence of pulmonary oedema and circulatory failure [12]. In a study by Yadav RK et al., 46.1% of children received prazosin after six hours. Due to this, complications like pulmonary oedema (19.2%) and myocarditis (15.3%) were noted in many children. So, inotrope support (30.7%) and mechanical ventilation (15%) were needed in many children [15]. Bawaskar HS and Bawaskar PH mentioned in their study that prazosin usage at PHC has a very good outcome [9]. In their study, five children developed massive pulmonary oedema and two died, where prazosin was not used in PHC. But, there was no mortality and no massive pulmonary oedema noted in children where prazosin was used in PHC. In Ganesh J and Kumaravel KS study complications were noted less frequently in children who received a dose of Prazosin early, within eight hours of sting [11].

There was no death reported in present study, which was conducted after the sensitisation programme on prazosin therapy for scorpion envenomation. Similarly, there was no death reported in Moruskar AD and Choudhary VV, study, where 82% children received prazosin within six hours [16]. Mortality was quite high in various studies due to complications, where prazosin was not initiated earlier [Table/Fig-4] [14,17-19].

S. no.	Study	Sting -Prazosin interval	Complications	Mortality
1.	Balaji J et al., [13] (n=262) 2017	>4 hours -75%	Peripheral circulatory failure-76% Pulmonary oedema -27% Myocarditis-17% Hypotensive shock -5%	1.1%
2.	Prasad R et al., [14] (n=90) 2011	Mortality more if interval >6 hours	Shock-53.3% Myocarditis -42.2% Encephalopathy-35.5% Pulmonary oedema-37.8% Priapism-31.1%	8.9%
3.	Yadav R et al., [15] (n=52) 2020	>6 hours - 46.1%	Pulmonary oedema-19.2% Myocarditis-15.3% Peripheral circulatory failure-13.4%	1.9%
4.	Moruskar Ad and Choudhary VV. [16] (n=50) 2020	>6 hours - 18%	Peripheral circulatory failure -40% Pulmonary oedema – 16% Congestive heart failure-28% Myocarditis-16%	Nil
5.	Reddy RM and Somaiah G. [17] (n=50) 2017		Peripheral circulatory failure-80% Myocarditis-18% Congestive heart failure -18% Pulmonary oedema 24%	4%
6.	Bosnak M et al., [18] (n=45) 2009		Peripheral-72.4% Pulmonary oedema -46.6% Unconsciousness-48.8%	4.4%
7.	Ramesh P et al., [19] (n=240) 2011.	Majority approached after 6 hours	Myocarditis- 40% Acute pulmonary oedema-18.3% Encephalopathy-12.5%	7.5%
8.	Present study (n=62) 2022	>4 hours-27.4%	Peripheral circulatory failure-39% Pulmonary oedema-10% Myocarditis-6%	Nil

[Table/Fig-4]: Comparison of sting-Prazosin interval, complications and mortality with various studies of scorpion envenomation [14,17-19].

In many PHC and SHC centres, drugs like steroids, analgesics and antihistamines are used for scorpion envenomation. They are not at all useful and may rather worsen the situation. In a study by Ramesh P et al., mortality was significantly high (7.5%) with usage of steroid, and antihistamines [19]. In this study, after the sensitisation programme for PHC and SHC doctors, prazosin usage for scorpion envenomation has increased in PHC and SHC level and usage of other drugs decreased from 74% to 23%, which resulted in the good outcome. Recent systematic review and meta-analysis showed that Scorpion antivenom is effective for rapid resolution of symptoms [20]. Pandi K et al., reported that scorpion antivenom with prazosin leads to faster recovery and decreases incidence of myocardial dysfunction [21]. A study by Bawaskar HS and Bawaskar PH showed that, prazosin plus scorpion antivenom hastened the recovery and shortened the hospital stay [22]. But, it is also mentioned that prazosin is very much cheaper than scorpion antivenom. Also,

scorpion antivenom is not widely available in many places in India. But prazosin is cheap, easily available and free from anaphylaxis. If medical officers of all PHC and SHC start using prazosin early for indicated cases of scorpion envenomation (as reported in this present study), complications and duration of stay in the hospitals will be reduced and also the outcome will be improved. Even though scorpion antivenom is not available, if prazosin is used earlier at PHC and SHC level, it will give the same result of prazosin plus scorpion antivenom usage.

Bawaskar HS and Bawaskar PH also concluded that training for the appropriate use of prazosin at PHC and general hospitals have a very good outcome in management of Scorpion sting cases [10]. In one year, 51 peripheral doctors treated 3,522 severe scorpion sting cases with oral prazosin, and among them only 13 (0.3%) patients died. This study found that, after the sensitisation programme for PHC and SHC doctors, there is a positive impact on prazosin therapy at PHC and SHC for scorpion envenomation. Prazosin therapy at PHC and SHC has increased from 3-69% and all the complications and need for ICU care (inotropes and ventilator support) were reduced significantly, when compared to previous study.

India is a country with more villages and rural areas. For any type of illness, the people first go to nearby health facilities like PHC centers only. So, initial management at PHC or SHC is very much important to decrease the complications. Late arrival or delayed treatment is the main reason for mortality in tropical countries like India. In any serious illnesses like scorpion or snake envenomation, dengue shock syndrome and scrub typhus, initial management at PHC or SHC is crucial to reduce mortality, than managing them later in fully equipped tertiary care centres. Present study throw light on this under-treatment for scorpion envenomation at PHC and SHC level and bridges the gap between PHC and tertiary care level by conducting sensitisation programme for PHC and SHC medical officers.

Since, the two studies (before training and after training) were conducted at the same centre, the true impact of the training could be determined.

Limitation(s)

About 10 (8%) doctors were transferred in PHC and SHC after the sensitisation programme, and this may somewhat influence the results.

CONCLUSION(S)

Sensitisation programmes for PHC and SHC doctors, significantly increase the knowledge on prazosin therapy for scorpion envenomation with good outcome. After the sensitisation programme, prazosin therapy for scorpion envenomation at PHC and SHC level has been increased significantly. This reduced the complications like, peripheral circulatory failure, myocarditis and pulmonary oedema. This also reduced the need for ICU care (ionotrope and ventilator support) at tertiary care centres.

Periodical training of PHC medical officers and private practitioners (through Indian Medical Association and Indian Academy of Paediatrics) about all paediatric emergencies including envenomation and tropical fevers are very much important. This initiation will decrease the complications and improve the outcome in children who suffers with severe illnesses and helpful to decrease the under-5 mortality.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor and Head, Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamil Nadu, India.
2. Senior Assistant Professor, Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamil Nadu, India.
3. Senior Resident, Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamil Nadu, India.
4. Assistant Professor, Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamil Nadu, India.
5. Associate Professor, Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. J Balaji,
Associate Professor, Department of Paediatrics, Government Dharmapuri Medical College Hospital, Dharmapuri-636701, Tamil Nadu, India.
E-mail: jbalaji1993@gmail.com

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