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Original Article

Clinico-Epidemiological Spectrum of Childhood Leprosy in Post-Elimination Era: A Multi-Centre, Cross-Sectional Study from West Bengal

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Childhood leprosy is a major concern in the post-elimination era as it reflects active disease transmission. This study aims to analyse the clinico-demographic profile of childhood leprosycases attending two tertiary care centres of West Bengal over a period of 18 months from April 2018 to June 2019. 32 children (<16 years) with histologically confirmed Hansen's disease were subjected to detailed history including contact screening and clinical examination. These comprised of 10.6% (32/303) of all new leprosy cases which were treated at these centres. Findings indicated that thirty-two children with leprosy (mean age 12.53± 3.01 years; M:F 25:7) constituted 10.6% of all new leprosy cases. Borderline tuberculoid (53.1%) was most the frequently seen type, while household contacts were identified in 25% cases, all multibacillary. Patch over hands was the commonest presentation. The ulnar nerve was involved most frequently (47.2%), followed by the common peroneal nerve (18.9%). Lepra reaction (type1>type 2) and disabilities (grade 2> grade 1) were noted in 18.8% children each. Lepra reaction showed a significant association with multibacillary leprosy, while disabilities significantly correlated with the number of skin lesions. Slit skin smear was positive in 21.8% of patients. Clinico-pathological correlation was observed in 2/3rd cases, mostly BT type. The high incidence of childhood leprosy in our set-up suggests active diseases transmission even in the post-elimination era. Thus, active intervention is required to control its transmission and prevent complications in childhood leprosy cases in this part of the country.

Keywords : Leprosy, Childhood, Post-Elimination

Introduction

Leprosy is a chronic infectious disease, primarily affecting the skin and peripheral nerves. Failure of early detection and delayed onset of treatment may result in disabilities, deformities and social

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stigma. Although adults are more commonly affected due to its long incubation period, children are vulnerable, especially in highly endemic areas, due to their weak immunity and exposure to untreated family members. Besides, the magnitude of childhood leprosy has immense epidemiological significance. It reflects the active and recent transmission status of disease and also acts as a tool to assess the impact of leprosy control programmes and community awareness about the disease (Pradhan et al 2020). The World Health Organisation (WHO) achieved global "elimination of leprosy as a public health problem" in 2000, while India achieved the same milestone in December 2005. However, leprosy remains an important health problem in several endemic pockets of the world, especially developing countries like India. According to recent statistics published by the National leprosy elimination programme (NLEP), children constituted 8.7% of the total newly diagnosed cases of leprosy (11,792/135,485) in India, compared to 7.5% globally (NLEP Progress Report for the year 2016-17). While we have achieved the goal operationally (overall prevalence rate <1/10, 000 population) at public health level (Narang & Kumar 2019), complete eradication of leprosy from India remains an unfulfilled target in reality.

As leprosy in children shows continued transmission in the community, we undertook this study to analyze the clinico-epidemiological profile of childhood leprosy in selected tertiary care centres of our state, as leprosy remains endemic in some areas. Prevalence of grade 2 disability was also recorded, as the current WHO strategy aims to reduce the transmission of disease and development of grade 2 disability (G2D) among new child cases to zero, as one of its principle targets (World Health Organization 2016).

Materials and Methods

We conducted a multicentre, cross-sectional study at the Dermatology Department of 2 tertiary care centres, which are among the largest referral hospitals for leprosy in West Bengal. The study spanned for 18 months (January 2018 to June 2019). We included all consecutive children ≤ 16 years, with newly diagnosed and untreated leprosy. The diagnosis was based on suggestive clinical features, and each diagnosis was confirmed by a slit-skin smear and histopathological examination. Indeterminate leprosy, hypopigmented skin lesions without anaesthesia, presence of associated neurologic disease and lack of informed consent/ assent of patient or guardian served as our exclusion criteria. We obtained approval from the Institutional Ethical Committee and conducted our study in accordance with the Declaration of Helsinki (Brazil, 2013).

Each participant was subjected to a detailed history, including demographic parameters, clinical features, duration of disease, source of contact (whether household or extra-familial) and their clinical spectrum with treatment status, drug history and any deformity. Detailed dermatological examination was undertaken to assess the type of leprosy, site, morphology, distribution and number of lesions. The main nerves were examined meticulously to evaluate their function, which included inspection, nerve palpation, sensory examination of the lesional skin, muscle strength testing and neurologic evaluation of the eyes and upper and lower extremities. Each patient was subjected to a slit-skin smear (SSS) from the earlobe and edge of skin lesions and punch biopsy from lesional skin for histological evaluation and confirmation of diagnosis. All biopsy specimens were routinely stained with hematoxylin and eosin (H&E), while

special stains (e.g. Ziehl-Neelsen, Fite-Faraco) were used when necessary.

We classified the cases according to Ridley-Jopling scheme based on their clinical, histological and microbiological findings (Ridley & Jopling 1966). Some patients were classified as pure neuritic leprosy (PNL) when appropriate. For treatment purpose, all patients were classified into 2 operational groups-paucibacillary (PB) or multibacillary (MB) leprosy. We used the WHO criteria-up to five skin lesions and only one nerve trunk involvement (PB) and more than five skin lesions with/without more than one nerve trunk affected (MB) (Pradhan et al 2019).

We also evaluated the degree of physical disability and classified them; all processes being conducted in accordance with standard WHO guidelines and grading system (World Health Organization 1988). Special emphasis was placed to diagnose reactions. Routine haematology and biochemistry panel was done in all patients to rule out any systemic disorder.

Data was entered in a Microsoft Excel spreadsheet and statistically analysed using MedCalc® v17. We used mean and standard deviation for descriptive statistics and proportion for categorical data. Normal distribution of numerical variables was determined using the Shapiro-Wilk test. Chi-square test was used for categorical data while t-test and Mann-Whitney U test were applied for parametric and nonparametric data , respectively. A p -value <0.05 was considered significant.

Results

Overall, 303 untreated leprosy patients attended our out-patient department (OPD) during the study period. Among them, 32 were children, thus accounting for 10.6% (32/303) cases. The children's age ranged from 1 to 16 years with a mean of 12.5 ± 2.9 sd. There was a male preponderance among cases (M:F25:7). Most children were aged above 10 years (25, 78.1%) and hailed from a rural background (18, 56.3%). The duration of lesions ranged from 1-60 months, median (IQR) being 12 (6-24) months. Household contacts were identified in 8 (25%) children (all multibacillary), the index case being a parent in 62.5% (5/8) cases. Almost 3/4th of our patients (24/32) suffered from paucibacillary leprosy. All parameters were statistically comparable with respect to the type of leprosy (paucibacillary / multibacillary) [p>0.05]. Table 1 highlights the clinico-demographic details.

The most common clinical type was BT leprosy in 17 (53.1%) children (Fig. 1), followed by TT (Fig 2),

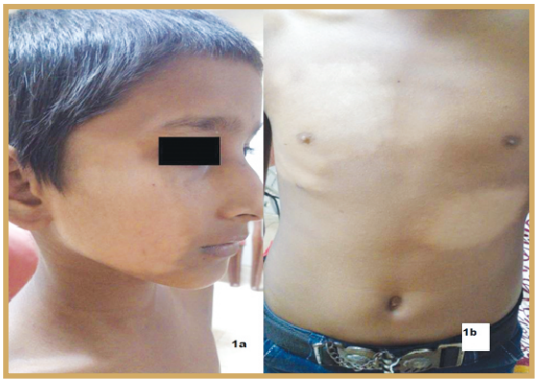

Fig.1 : Lesion of borderline tuberculoid (BT) leprosy in a child (a) face (b) trunk.

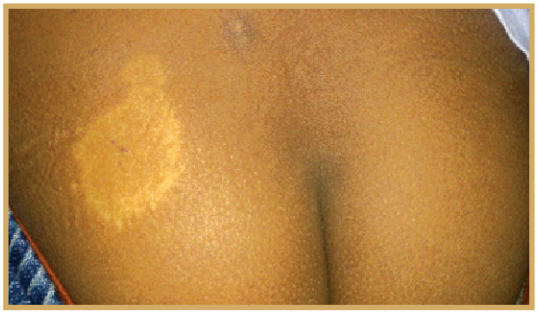

Fig 2 : Solitary, well demarcated lesion of TT leprosy on the buttock.

Table 1 : Clinico-demographic profile (n=32)

Parameters	Type of leprosy (operational classification)		p-value
	Paucibacillary (n=24)	Multibacillary (n=8)	
Age (years)			
Mean (SD)	12.4 (3.05)	12.6 (2.7)	0.9[Â]
Age group			
0-10 years	6 (25)	1 (12.5)	0.6[î]
10-16 years	18 (75)	1 (12.5)	
Gender			
Male	18 (75)	7 (87.5)	0.6[î]
Female	6 (25)	1 (12.5)	
Residence			
Rural	12 (50)	6 (75)	0.4[î]
Urban	12 (50)	2 (25)	
Duration of disease (months)			
Median	186-30,	1211.5-21,	0.5[¶]
IQR, 95% CI	6-24	9.7-24	
Family history			
Present	4 (16.7)	4 (50)	0.2[î]
Absent	20 (83.3)	4 (50)	
Reaction			
Present	3 (12.5)	3 (37.5)	0.1[î]
Absent	21 (87.5)	5 (62.5)	

[Â] t-test, [î] Fisher's exact test,[¶] Mann-Whitney U test

Paucibacillary includes tuberculoid, borderline tuberculoid cases; Multibacillary includes borderline lepromatous, lepromatous and pure neuritic cases; All values expressed in [n(%)] unless mentioned otherwise; SD standard deviation

LL and BL leprosy in 21.9%, 12.5% and 3.1% cases, respectively. One child presented with histoid variety (Fig. 3). Based on the operational classification, PBL outnumbered MBL cases (24, 75% vs. 8, 25%). Three (9.4%, n=32) children presented with pure neuritic leprosy (PNL): [ulnar and common peroneal nerve in 1 case; isolated ulnar nerve in 2 cases] (Table 2).

Twenty-two patients (68.8%, n=32) showed involvement of multiple sites. Hands were the commonest site to be involved in 25 patients, followed by face, legs and trunk in 16, 13 and 10 patients, respectively. Patch was the most common clinical presentation.

Visible deformity (grade 2 deformity) was observed in 5 (15.6%) children (trophic ulcer> ulnar claw hand [Fig 4], while a single child presented with grade 1 disability. No ocular abnormality was observed. We noted a statistically significant association between deformities and multibacillary (MB) leprosy ($p<0.0001$, Chi-square). There was no significant association

with any other parameter like age, duration of lesions, reaction and the total number of lesions ($p>0.05$, logistic regression).

A single nerve was involved in most children (43.8%, 14/32), while 28.1% (9/32) patients presented with involvement of 2 and 3 nerves each; overall, 53 nerves were involved in 32 cases. Ulnar nerve was involved most commonly in 78.1% (25/32) cases. Common peroneal nerve was involved in 31.2% (10/32) cases, while the remaining 18 cases demonstrated variable nerve involvement, including the superficial cutaneous branch of radial nerve, great auricular nerve and posterior tibial nerve.

Six (18.8%) children presented with type 1 reaction and type 2 reaction (3 patients each). There was no statistically significant association between type of reaction (type1/ type 2) and type of leprosy (paucibacillary/ multibacillary) [$p=0.1$, Fisher's exact test]. (Table 1) However, a statistically significant correlation was noted between the occurrence of reactions and a total number of skin lesions ($\rho=0.4$, $p=0.01$, Spearman's correlation).

A positive slit-skin-smear was obtained in 7 (21.9%) children, all multi-bacillary. Clinico-pathological correlation was obtained in 2/3rd cases, mostly BT leprosy.

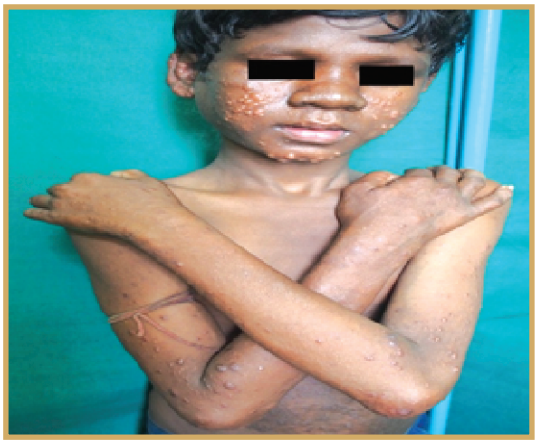

Fig. 3 : Histoid leprosy with lesion on the face and body

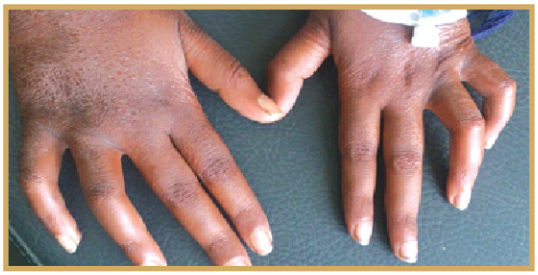

Fig. 4 : Ulnar claw hand of an affected patient.

Systemic examination, including ocular system and serum biochemistry including haemoglobin, total leukocyte count, platelet count, lipid profile,

Table 2 : Spectrum of childhood leprosy (n=32)

Type of leprosy/reaction	Male (n=25)	Female (n=7)
TT	4 (16%)	3 (42.9%)
BT	14 (56%)	3 (42.9%)
BB	0 (0)	0 (0)
BL	1 (4%)	0 (0)
LL	3 (12%)	1 (14.3%)
PNL	3 (12%)	0 (0)

TT: Tuberculoid, BT: Borderline tuberculoid, BB- mid-borderline, BL- Borderline lepromatous, LL- Lepromatous, PNL- pure neuritic leprosy

Table 3 : Comparative analysis of different studies concerning childhood leprosy in the Indian subcontinent

Name of author, place, year	Proportion of new childhood leprosy cases (%)	Sex (male: female)	Contact history positive (%)	Commonest clinical spectrum (%)	Most common type (%)	Most common nerve involved	Reactions (%)	Deformity/dis-ability (%) Most common site/ type of deformity	SSS positivity (%)
Gitte et al (2016), Central India, 2016	16	1.4:1	44.1	-	PB (59.9)	Ulnar	17.6	(17.4), Hands	11.2
Nair (2017), Kerala, India, 2017	6.7	2.15:1	6.7	BT (55%)	PB (81.7%)	Ulnar	5	(5), Ulnar claw-hand	-
Balai et al (2017), Rajasthan, India, 2017	2.3	2.2:1	28.1	BT (46.9)	PB (65.6)	Ulnar	9.4	(25), Ulnar claw hand=trophic changes	36.4
Zia et al (2019), Pakistan, 2019	-	0.8:1	91	BT (37)	PB (55)	Ulnar	18	0	-
Pradhan et al (2020) Odisha, India, 2020	16.4	1.9:1	33.2	BT (59)	PB (71.6)	Ulnar	19.2	(9.3), trophic ulcer	-
Present study, West Bengal, India	10.6	3.6:1	25	BT (53.1)	PB (75)	Ulnar	18.8	(18.8), Trophic ulcer	21.9

SSS Slit-skin smear, BT Bordeline tuberculoid, PB Paucibacillary

liver and renal function tests were within normal limits in all patients.

Discussion

We found the proportion of new child cases with leprosy to be 10.6%, slightly higher than the state (West Bengal, 7.48%) (NLEP Progress Report for the year (2016-17) 2016), national (8.7%) (NLEP Progress Report for the year 2016-17 (2016) and global (7.5%) (World Health Organization 2016) figures. However, it is lower than that reported by Pradhan et al (13.1%, Western Odisha) (Pradhan et al 202) and at some areas of Africa (38.25%, Comoros) (Narang & Kumar 2019), and higher than that reported in Cuba (2.6%) (Ruiz-Fuentes et al 2019). Overall, variable prevalence rate of new childhood leprosy has been recorded in different studies conducted in the Indian subcontinent, ranging from 4-34% (Narang & Kumar 2019). This may be attributed to varying upper age limits of the study subjects in different studies (14-19 years); in our study, the upper age limit was 16 years. Proportion of children among newly detected leprosy cases is a strong indicator of active transmission of diseases and awareness in the community and reflects the status of concerned health programmes. Thus, a higher proportion in our study (10.6%), compared to national (8.7%) and state (7.48%) statistics, probably indicates active disease transmission in the present set-up (NLEP Progress Report for the year (2016-17). Table 3 compares the salient findings of some recent studies in the Indian subcontinent concerning childhood leprosy.

More than 3/4th of our patients were aged >10 years, the mean age being 12.5±2.9 years. This data is consistent with most authors, who recorded maximal occurrence between 10-15 years (Pradhan et al 2020, Pradhan et al 2019, Ruiz-Fuentes et al 2019, Zia et al 2019). The possible explanations may belong incubation period of the diseases (3-5 years) (Pradhan et al 2019, Ruiz-Fuentes et al 2019), failure to report in early stages or delayed diagnosis as sensory loss is difficult to elicit in the younger age group. However, Santos et al (2012) reported maximum occurrence in 5-9 year age group (54.5%), while Brubaker et al (1985) reported 91 infants with leprosy, thus suggesting that no age is immune to develop this diseases. Our youngest patient was 1 year old.

Most authors have reported boys to be more commonly affected than girls in childhood leprosy (Pradhan et al 2020, Narang & Kumar 2019) consistent with our finding (boys: girls 25:7). In contrast, a Cuban study reported no sexual predilection (Ruiz-Fuentes et al 2019), while a Pakistani study recorded slight female predominance (Zia et al 2019). Male predilection may be explained by lower detection in girls, possibly due to neglect of girl child and increased chance of contact in boys due to their greater mobility in our society.

Our median duration was 12 months (range 1-60 months), comparable to studies conducted at South India (Nair 2017) (10.7 months), Haryana (Uikey et al 2020) (12 months) and Pakistan (Zia et al 2019) (9 months), but less than a study from Delhi (Mahajan et al (2006) (17 months). This delayed presentation indicates a lack of awareness and urgency of parents, which may be mitigated by conducting regular health camps at the localities and schools. The variable duration may be due to heterogeneous awareness and education levels in different study populations.

For leprosy, the primary mode of transmission is by droplet inhalation through upper airways (Pradhan et al 2020, Ruiz-Fuentes et al 2019). So, children usually acquire leprosy from active household contacts. Thus, it is essential to screen the family members of affected children to detect the index case, which might have been missed. It has been estimated that household contacts

increase the risk of transmission by almost 9 folds, due to continuous and early exposure (Pradhan et al 2019) and this risk is increased (up to 14 folds) if the mother has leprosy or the contact has MB disease (Narang & Kumar 2019). In our study, household contacts were identified in 25% children, all multibacillary; similar to Uikey et al (2020) (25%, Haryana) and comparable to Mahajan et al (2006) (29%, Delhi), Pradhan et al (2020) (33.2%, West Odisha), but higher than Nair et al (2017) (8.7%) and Rao et al (2009) (18%) [both from South India] and much lower than Zia et al (2019) (91%, Pakistan) and almost half of that reported by Gitte et al (2016) (44.1%, Central India). These differences may be attributed to varying sample sizes in different studies. Thus, there is a need for strict contact-tracing activities to eliminate leprosy, especially if the index case is a child.

In the present study, BT leprosy was most common in 53.1% of children, followed by TT, LL and BL leprosy in 21.9%, 12.5% and 3.1% cases, respectively. Our finding is consistent with most studies that have indicated BT leprosy to be the commonest type of childhood leprosy in the Indian subcontinent in 37-73% of cases (Pradhan et al 2020, Zia et al 2019, Nair 2017, Mahajan et al 2006, Kumar avel et al 2017). Three (9.4%) children presented with pure neuritic leprosy, much higher than that reported by Pradhan et al (2020) (1.3%). Most authors have reported PB leprosy to be commoner in children compared to MB, due to better immunity than adults (Pradhan et al 2019, Uikey et al 2020, Mahajan et al 2006, Gitte et al 2016). Our findings is also in agreement with this view (PB>MB). In contrast, Zia et al (2019) reported a predominance of MB type in a study conducted in Pakistan.

Almost all authors have reported ulnar nerve to be affected most commonly in childhood leprosy (Pradhan et al 2020, Narang & Kumar 2019, Pradhan et al 2019, Zia et al 2019, Uikey et al 2020), consistent with our findings. We observed polyneural involvement in 28% of patients, compared to 35% and 60% by Pandhi (2011) and Rao et al (2015).

We detected lepra reaction in 18.8% patients at presentation, both type 1 and type 2 reactions showing equal distribution (9.4% each). Our finding is similar to that of other previous studies (Pradhan et al 2020, Zia et al 2019, Gitte et al 2016) but lower than (29%) that reported by Bandeira et al (2019) from Brazil. However, the later study was exclusively focused on childhood leprosy reactions. Two systematic reviews have also reported lower reaction rates in childhood leprosy (1.4% - 33.9%), compared to about 50% in adults (Narang & Kumar 2019, Pradhan et al 2019). Majority develop type 1 reaction, as the most common form is BT (Pradhan et al 2019), in contrast our patients developed type 1 and type 2 reactions in equal proportions. Type 1 reaction is usually associated with neuritis, which needs prompt treatment with systemic corticosteroids to prevent inflammation and nerve damage. We detected a statistically significant correlation only with a number of skin lesions (ρ=0.4, p=0.01, Spearman's correlation), while Bandeira et al (2019) noted significant association with 8-14 year age group, MB disease, $\geq$ 10 skin lesions and borderline or lepromatous forms.

Deformities/disabilities were detected in 6 (18.8%) children (grade 2 disability: grade 1 disability 5:1), the most common being trophic ulcer followed by ulnar claw hand. Several authors have reported a variable deformity rate, ranging from 0.5% to 40.7% in Indian children with leprosy (Narang & Kumar 2019, Pradhan et al 2019). Trophic ulcer was the commonest deformity reported by Pradhan et al (2020), similar to the present study. Some authors have documented several risk factors for reaction like

late diagnosis, multiple cutaneous lesions, MB disease, positive SSS and reaction at presentation (Pradhan et al 2019, Pandhi 2011). However, we failed to detect any such risk factor, except a significant association with MB disease ($p< 0.0001$, Chi-square), this risk can be minimised by early diagnosis and treatment. One of the targets of the global Leprosy strategy is zero new child cases with grade 2 disability by 2020, thus considerable work remains to be done to achieve this target in the form of regular screening and awareness camps.

Limitations: Cross-sectional study design, small sample size and possible selection bias due to hospital-based study were our major limitations. Another shortcoming was the lack of data regarding BCG vaccination, as the later has been reported to have a preventive role in some studies (Zia et al 2019).

Conclusion

To conclude, the incidence of childhood leprosy is still quite high, despite several government strategies to eliminate this disease. The high prevalence of childhood leprosy is a direct indicator of active community transmission and operational shortcomings of the current leprosy control strategies. Thus, more robust control measures should be undertaken that should include proper training of field health care workers to enable early diagnosis and institution of appropriate treatment, contact screening of index childhood cases and generating parental and community awareness by using mass media to identify the disease and report to health care workers at the earliest.

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