RESEARCH PAPER

Normative Data of Infant Pulmonary Function Testing: *A Prospective Birth Cohort Study from India*

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Objective: To develop a normal reference range of Infant pulmonary function test (IPFT) indices for Indian children.

Design: Prospective birth cohort study.

Setting: Division of Pediatric Pulmonology of a tertiary-care institute in India from August 2012 to March 2017.

Participants: All neonates born at the institute during the study period were screened for eligibility.

Measurement: IPFT at baseline and every 6-month until 36-months of age.

Main Outcome Measure(s): Tidal breathing flow-volume loop (TBFVL), Rapid thoracoabdominal compression (RTC), and Raised volume RTC (RVRTC) indices at baseline and follow-up.

Results: 310 newborns were enrolled in the cohort; 281 of them (169 male) had completed 36-months of follow-up at the end of the study period. There was no influence of gender on the baseline IPFT indices. Tidal volume per unit body weight (V_T/kg) significantly increased from baseline to 36 months of age (P<0.001) while the peak ratio (t_{PTEF}/t_E) initially decreased in first 18-months of age (P<0.001), after that returned to the baseline value by 36 months of age. RTC indices did not change significantly from baseline values. In RVRTC, the ratio of forced expiratory volume in 0.5s to forced vital capacity ($FEV_{0.5}$/FVC) was significantly decreased from baseline to 36 months of age (P=0.002).

Conclusions: Normal values for various IPFT indices for TBFVL, RTC, and RVRTC from neonates to the age of 36-month are provided. These data may be used as normative data for healthy neonates and children of Indian origin.

Keywords: *Indices, Rapid thoracoabdominal compression, Tidal breathing flow-volume loop.*

While pulmonary function testing (PFT) is well established for older children (>5 years) and adolescents, it is still evolving for use in infants and preschool children [1]. Sophisticated equipments are now commercially available, which can measure pulmonary function even in premature babies [2].

PFT in infants (IPFT) may contribute to a better understanding of the nature and severity of respiratory illness, progression of the disease, and monitoring response to therapy [3]. Serial measurements of lung function since birth, especially in high-risk infants, may be helpful in recognition of early deviation from the normal pattern of lung development. Longitudinal studies have shown that many of the chronic respiratory disorders have their origin in childhood; hence, intervention at this stage may have an impact on the management of the chronic respiratory disease [4,5].

The measurement of PFT in infants and preschool children is a major challenge [6,7]. The values of pulmonary function indices vary with age, sex, body size, and ethnic groups [8,9]. Currently, there is lack of multiethnic global reference range for IPFT indices, so the development of regional ethnicity-specific normative data is the need of the hour, which will definitively expand its use in clinical practice [6].

Accompanying Editorial: Pages 21-22.

In this birth cohort, we performed IPFT from birth to 36 months of age. The normative data for various indices were generated, which may be used as reference range in a similar population.

METHODS

This prospective birth cohort study was conducted in the Department of Pediatrics of a tertiary-care institute in Delhi, India from August 2012 to March 2017. The study was approved by the Institutional Ethics Committee. Written informed consent was taken from the parents/ guardians. All neonates born at the institute during the study period were screened for eligibility. The inclusion criteria were age ≤4 weeks, full-term (≥37 weeks of

gestation), and appropriate for gestational age (weight 10^{th}- 90^{th} centile) babies [10]. The exclusion criteria were any perinatal insults (*e.g.* birth asphyxia, meconium aspiration, any amount of respiratory distress requiring respiratory support, pathological hyperbilirubinemia or seizure), known major congenital birth defect, required parenteral antibiotic or fluid, neonatal cholestasis, chronic kidney disease or inborn error of metabolism, and mother having antepartum or postpartum hemorrhage, preeclampsia or eclampsia, HIV infection, or parents' refusal for regular follow-up for three years. The enrolled babies were followed-up every 6 months (±8 weeks) and also whenever they had an acute respiratory infection or any other acute condition. The babies were clinically examined, and anthropometric measurements (weight, length, head circumference) were recorded at enrolment and each visit.

The IPFT were performed with Exhalyzer D (Eco Medics AG, Duernten, Switzerland) as per the American Thoracic Society/European Respiratory Society Task Force recommendations [11-16]. IPFT included tidal breathing flow-volume loop (TBFVL), rapid thoracoabdominal compression (RTC), and raised volume rapid thoracoabdominal compression (RVRTC) maneuvers (***Web Fig.* 1**). All the IPFT maneuvers were performed in the Pediatric Pulmonary Function Laboratory, which is well equipped with a central supply of oxygen and resuscitation equipment. The equipment was calibrated daily for atmospheric temperature and pressure and volume with a 100 mL calibration syringe (M30.9011) provided by the manufacturer. Weight and length/height were recorded using standard methods [17]. IPFT was postponed for 2-4 weeks if the child had an acute respiratory infection.

At enrolment and 6 months of age, IPFT were performed either in awake or natural sleep state after breastfeeding. Beyond six months of age, syrup Triclofos (25-50 mg/kg/dose) was used for sedation, whenever required. The maneuvers were performed in the supine position. Baseline TBFVL was completed within four weeks of birth, while RTC and RVRTC were first performed once the child was ≥8 kg as per recommendations of the manufacturer of IPFT equipment. IPFT were repeated at every follow-up visit. The IPFT indices and their physiological interpretation are described in ***Web Table* I**.

Statistical analysis: Clinical information during each visit was recorded manually into case record form; data were then entered into Microsoft Access software. IPFT data were automatically stored in software (SPIROWARE, Eco Medics AG, Duernten, Switzerland) after each procedure; data of each individual were extracted and managed in Microsoft Access software. Data were analyzed using Stata software v.13 (Stata Corp, College Station, TX, USA). Quantitative variables were summarized using mean and standard deviation if normally distributed; for skewed distribution, median (interquartile range) was used. Chi-square test was used for the analysis of categorical data. The change in IPFT indices from birth to 36 months of age were calculated with the Wilcoxon sign-rank test. Comparison of IPFT indices between gender and other parameters was analyzed with Wilcoxon rank-sum test (Mann-Whitney Test). A *P*-value of <0.05 was considered significant. For multivariate analysis, mixed-effects linear regression analysis was performed; IPFT indices were taken as the dependent variable, individual subjects as the random effect and gender, weight, length, and age as fixed effect. The LMS chartmaker Pro (Medical Research Council, UK) was used to model the expected median (μ or M), the coefficient of variation (σ or S), and skewness (λ or L) and to smooth the centile curves for IPFT indices against age, utilizing the method described by Cole TJ, *et al.* [18]. The goodness of fit for the model used was tested by the Q curve [18].

RESULTS

A total of 3412 neonates born in our institute from August 2012 to May 2014 were screened for eligibility; 310 neonates fulfilled the inclusion criteria and were enrolled. The median (IQR) age at enrolment was 4^{th} (3^{rd}, 5^{th}) postnatal day. A total of 281 children (90.6%) had completed 36 months of age by 31 March 2017; all IPFT (TBFVL, RTC and RVRTC) at this age were successfully performed in 225 infants (54.5% males) (***Fig.* 1**). The mean (SD) birthweight and length were 2.6 (0.6) kg and 47.7 (6.6) cm, respectively. Other demographic characteristics of enrolled children are summarized in ***Table* I**. TBFVL, RTC, and RVRTC were successfully performed in 1705, 948, and 875 occasions (baseline and follow up visits), respectively. The 5^{th}, 25^{th} 50^{th}, $75^{th,}$ and 95^{th} centile values of TBFVL and RTC as per the age, sex, mean weight and length/height of the enrolled children are described in ***Table* II** and **III**. The same for RVRTC indices are described in ***Table* IV**.

Tidal volume (V_T) per unit body weight (V_T/kg) increased significantly from birth to 36 months of age (P<0.001), which was more prominent in the first 12 months of age (P<0.001). The ratio of time to attained peak expiratory flow to expiratory time (t_{PTEF}/t_E) decreased significantly (P<0.001) from baseline till 18 months of age, then it began to increase (P<0.001) to achieve the baseline value at 36 months of age. V_{PTEF}/V_E

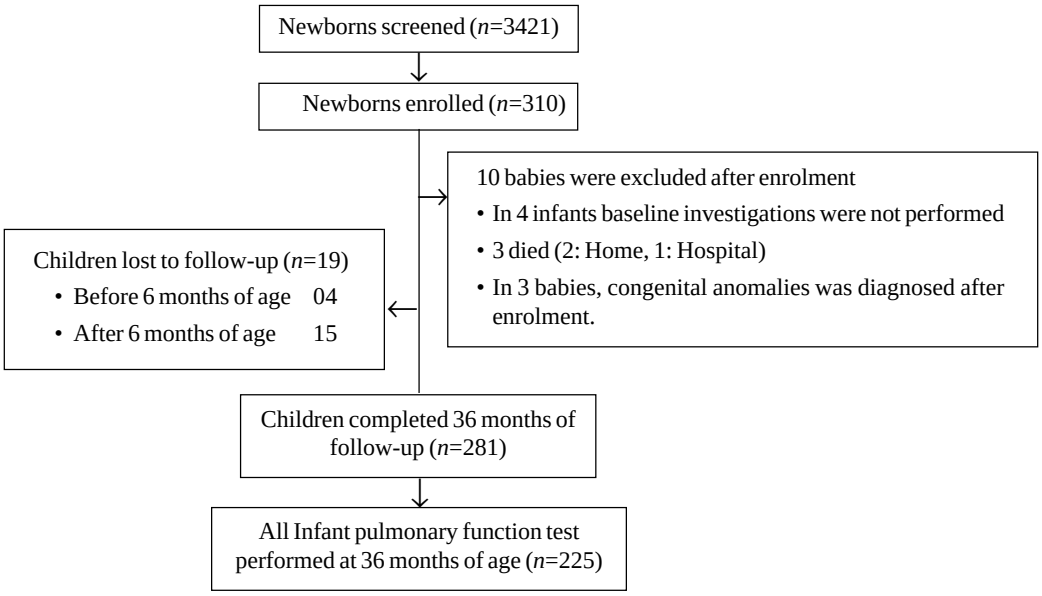

FIG. 1 *Enrolment and follow-up of the study cohort.*

also had decreasing trends from baseline to 18 months (P<0.001) then it gradually increased to achieve the baseline value by 36 months of age. The smoothed centile curves for V_T and t_{PTEF}/t_E are given in ***Fig.* 2** and **3**. At baseline, there was no significant association of gender with IPFT indices. However, on follow up, V_T was significantly more in boys at age of 6 months (P<0.001), 12 months (P<0.001), 18 months (P=0.02) and 36 months (P<0.001). The t_{PTEF}/t_E was significantly more in girls at 6 months (P=0.004) and 30 months (P=0.04) of age; for other ages it was similar in both sex. V_{PTEF}/V_E was significantly greater in girls at 6 months (P=0.004) and 30 months (P=0.02) of age. The t_E/t_{tot} was similar in both sexes at all ages.

TABLE I DEMOGRAPHIC CHARACTERISTICS OF ENROLLED INFANTS (N=310)

Characteristics	*Values**
Females	141 (45.5)
*Birthweight, g	2648 (689)
*Length, cm	47.7 (6.6)
*Gestation, d	267.9 (22.6)
Mode of delivery	
Vaginal	185 (59.6)
Caesarean	101 (32.5)
Instrumental	24 (7.8)
#Age at enrolment, d	4 (3, 5)
Age of parents, y	
Mother	26.5 (3.9)
Father	30.5 (4.3)
Family members in house	5.3 (2.8)
Urban accommodation	277 (89.3)
Smoking at home	93 (30)
Pets at home	31 (10)
Family history of allergy	144 (46.4)
Asthma	82 (26.5)
Allergic rhinitis	93 (33.1)
Atopic dermatitis	32 (10 .3)

*All values in no. (%) except *mean (SD) or #median (IQR).*

In RTC, $V'_{maxFRC,}$ $V'_{50,}$ and V'_{70} did not significantly differ from baseline to 36 months of age, while V_{PEF} gradually increased from baseline to 36 months of age (P<0.001). The smoothed centile curves for V'_{maxFRC} are presented in ***Fig.* 4**. $V'_{max,FRC}$, V'_{50}, $V'_{70,}$ and V_{PEF} were similar in both sexes at all ages except at 30 months, where V'_{70} (P=0.01) and V_{PEF} (P<0.001) were significantly higher in boys. In RVRTC, there were minor increases in FVC, $FEV_{0.5}$, FEF_{25-75}, and MEF_{25} from baseline till 24 months of age; after that, there were significant increases till 36 months of age (P<0.01).

PEF initially decreased from baseline to 12 months of age (P<0.001) then remained constant till 24-months of age, increasing again till 36 months of age (P<0.001). $FEV_{0.5}$/FVC was significantly decreased from baseline to 36-months of age (P=0.002), more during baseline to 18 months of age (P<0.001). The smoothed centile curves for $FEV_{0.5}$ and FVC are represented in ***Fig.* 5** and **6**.

TABLE II NORMAL VALUES (PERCENTILES) OF TIDAL BREATHING FLOW VOLUME LOOP INDICES

Indices	*Age, mo*	**Weight (kg)*	**Length/ Height(cm)*	*Boys, percentiles*					*Girls, percentiles*				
				5th	*25th*	*50th*	*75th*	*95th*	*5th*	*25th*	*50th*	*75th*	*95th*
V_T, mL	Baseline	2.8 (0.4)	48.2 (1.7)	5	6	7	9	10	5	6	7	8	10
	6	7.3 (1.1)	66.7(3.8)	10	17	24	49	79	6	13	18	23	60
	12	8.8 (1.0)	73.7(3.4)	35	51	69	92	119	10	28	53	83	109
	18	9.8 (1.2)	78.2(7.2)	35	53	86	121	145	32	52	71	98	130
	24	11 (1.3)	83 (7.5)	52	70	99	134	170	57	77	92	119	144
	30	11.7 (1.6)	86.4 (8.4)	58	94	126	150	184	59	85	120	143	178
	36	12.9 (1.7)	91.4 (7.0)	99	141	157	187	224	71	116	135	158	192
V_T per unit body	Baseline	2.8 (0.4)	48.2 (1.7)	1.6	2.1	2.7	3.1	3.9	1.8	2.2	2.6	3.1	3.6
weight, mL/kg	6	7.3(1.1)	66.7(3.8)	1.4	2.4	3.5	6.1	9.7	0.9	1.9	2.8	3.4	5.6
	12	8.8 (1.0)	73.7(3.4)	4.1	5.5	7.5	10.3	13.1	1.3	3.5	6.1	9.1	12.6
	18	9.8 (1.2)	78.2(7.2)	3.8	5.2	8.3	11.8	15.1	3.9	5.5	8.0	10.7	13.4
	24	11 (1.3)	83 (7.5)	4.5	6.4	8.6	11.2	14.9	5.5	7.3	9.4	11.3	13.2
	30	11.7(1.6)	86.4 (8.4)	4.9	7.5	10.4	12.8	15.6	4.9	7.6	10.9	12.7	15.3
	36	12.9 (1.7)	91.4 (7.0)	7.6	10.5	12.2	14.1	17.4	5.7	8.8	10.8	12.2	15.9
t_{PTEF}/t_E, %	Baseline	2.8 (0.4)	48.2(1.7)	22	32	37	45	56	22	29	36	43	58
	6	7.3(1.1)	66.7(3.8)	16	22	28	37	58	17	25	34	44	62
	12	8.8 (1.0)	73.7(3.4)	14	19	24	32	48	16	20	24	32	49
	18	9.8 (1.2)	78.2(7.2)	12	18	23	30	48	14	19	24	33	49
	24	11 (1.3)	83 (7.5)	15	21	30	40	51	15	21	28	39	58
	30	11.7(1.6)	86.4 (8.4)	19	27	34	44	61	19	29	38	51	65
	36	12.9 (1.7)	91.4 (7.0)	22	32	39	47	62	21	30	41	51	66
V_{PTEF}/V_E, %	Baseline	2.8 (0.4)	48.2(1.7)	20	34	40	46	57	22	30	36	43	55
	6	7.3(1.1)	66.7(3.8)	21	25	31	39	56	22	28	36	44	60
	12	8.8 (1.0)	73.7(3.4)	18	22	27	32	40	20	24	28	32	49
	18	9.8 (1.2)	78.2(7.2)	17	21	26	31	47	18	22	25	33	47
	24	11 (1.3)	83 (7.5)	11	21	32	45	73	16	21	26	39	80
	30	11.7(1.6)	86.4 (8.4)	22	29	36	43	57	22	31	40	48	61
	36	12.9 (1.7)	91.4 (7.0)	24	32	38	45	59	23	31	39	49	60
t_E/t_{tot}, %	Baseline	2.8 (0.4)	48.2(1.7)	47	50	53	55	61	45	49	52	56	60
	6	7.3(1.1)	66.7(3.8)	47	51	53	56	61	47	51	54	56	60
	12	8.8 (1.0)	73.7(3.4)	47	52	55	58	62	48	51	54	58	62
	18	9.8 (1.2)	78.2(7.2)	49	53	56	60	65	49	53	56	58	63
	24	11 (1.3)	83 (7.5)	49	53	56	59	64	49	54	57	59	62
	30	11.7(1.6)	86.4 (8.4)	49	53	56	59	62	47	54	56	58	62
	36	12.9 (1.7)	91.4 (7.0)	52	54	57	60	63	52	55	57	59	62

V_T: Tidal volume, t_{PTEF}/t_E : Ratio of time to peak tidal expiratory flow to expiratory time, V_{PTEF}/V_E : ratio of volume at peak tidal expiratory flow to tidal expiratory volume, t_E/t_{tot}: ratio of expiratory time to total respiratory time.

RVRTC indices were similar in both sexes at all ages except at 36-months, where FEV, MEF_{25}, FEF_{25-75}, $FEV_{0.5}$ and PEF, were significantly higher in boys (P=0.04, 0.01, 0.01, <0.001 and 0.02, respectively). $FEV_{0.5}$/FVC remained similar in both sexes at all ages.

On multivariate analysis, length/height, body weight, gender, and age were significantly associated with V_T. t_{PTEF}/t_E was significantly associated with gender, with values at any point being higher for females in comparison to males, after adjusting length/height and bodyweight.

TABLE III NORMAL VALUES (PERCENTILES) OF RAPID THORACOABDOMINAL COMPRESSION INDICES

IPFTIndices	*Age, mo*	**Weight (kg)*	**Height/ Length (cm)*	*Boys*					*Girls*				
				5th	*25th*	*50th*	*75th*	*95th*	*5th*	*25th*	*50th*	*75th*	*95th*
$V'_{max,FRC}$, mL/s	6	7.3 (1.1)	66.7 (3.8)	–	–	–	–	–	–	–	–	–	–
	12	8.8 (1.0)	73.7 (3.4)	0	0	50	70	125	0	0	40	70	120
	18	9.8 (1.2)	78.2 (7.2)	0	30	55	80	140	0	0	42	65	135
	24	11 (1.3)	83 (7.5)	0	0	50	90	205	0	0	47	75	90
	30	11.7 (1.6)	86.4 (8.4)	0	0	58	95	200	0	0	55	80	110
	36	12.9 (1.7)	91.4 (7.0)	0	0	50	105	180	0	0	60	105	210
V'_{50}, mL/s	6	7.3 (1.1)	66.7 (3.8)	55	80	125	190	335	50	95	105	135	250
	12	8.8 (1.0)	73.7 (3.4)	40	70	95	125	240	40	55	85	112	195
	18	9.8 (1.2)	78.2 (7.2)	45	65	85	125	310	40	60	85	115	235
	24	11 (1.3)	83 (7.5)	45	75	115	170	305	40	70	105	145	220
	30	11.7 (1.6)	86.4 (8.4)	45	80	125	195	315	35	70	103	180	305
	36	12.9 (1.7)	91.4 (7.0)	40	85	125	200	385	30	68	100	175	320
V'_{70}, mL/s	6	7.3 (1.1)	66.7 (3.8)	30	60	80	135	275	20	65	100	135	150
	12	8.8 (1.0)	73.7 (3.4)	25	50	77	105	180	20	55	75	99	140
	18	9.8 (1.2)	78.2 (7.2)	35	55	80	120	255	30	50	75	110	210
	24	11 (1.3)	83 (7.5)	20	60	85	125	210	25	50	80	100	170
	30	11.7 (1.6)	86.4 (8.4)	5	75	105	145	195	0	45	90	115	205
	36	12.9 (1.7)	91.4 (7.0)	0	60	105	150	280	0	55	95	133	270
V_{PEF}, mL/s	6	7.3 (1.1)	66.7 (3.8)	9	13	17	23	35	11	16	19	31	76
	12	8.8 (1.0)	73.7 (3.4)	8	13	18	24	45	8	13	18	27	43
	18	9.8 (1.2)	78.2 (7.2)	9	15	20	27	53	9	15	21	26	56
	24	11 (1.3)	83 (7.5)	9	16	24	37	61	9	16	21	29	42
	30	11.7 (1.6)	86.4 (8.4)	11	21	30	40	72	10	16	23	32	50
	36	12.9 (1.7)	91.4 (7.0)	10	18	31	42	79	10	18	30	37	58

**weight and height in mean (SD), $V'_{max,FRC}$: Maximum expiratory flow at functional residual capacity, V'_{50}: Maximum expiratory flow at 50% of expiration, V'_{70}: Maximum expiratory flow at 70% of expiration. V_{PEF}: Volume to peak expiratory flow; –: Not measured.*

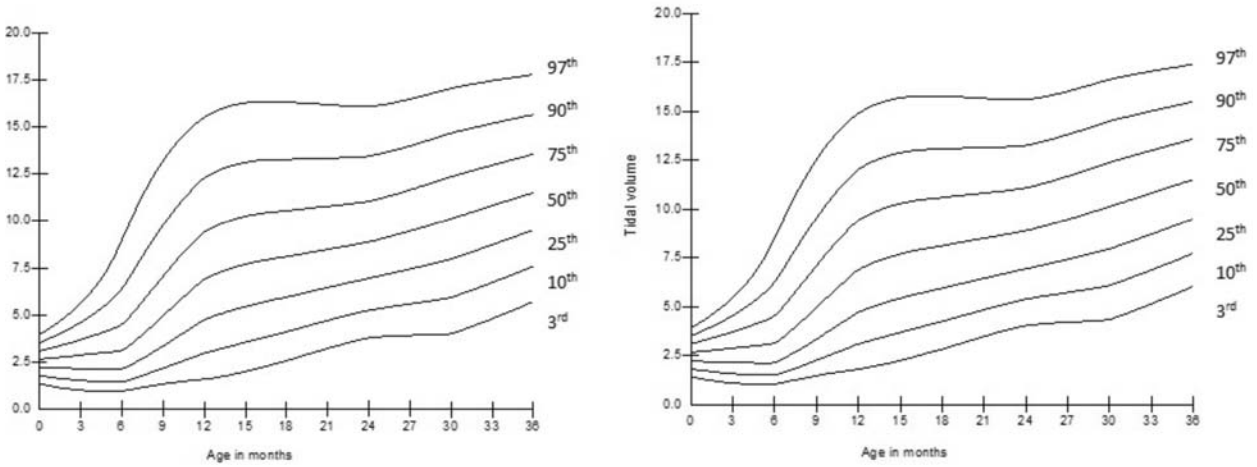

FIG.2 *(a) Change in tidal volume (V_T) with age in girls; (b) Change in tidal volume (V_T) with age in boys.*

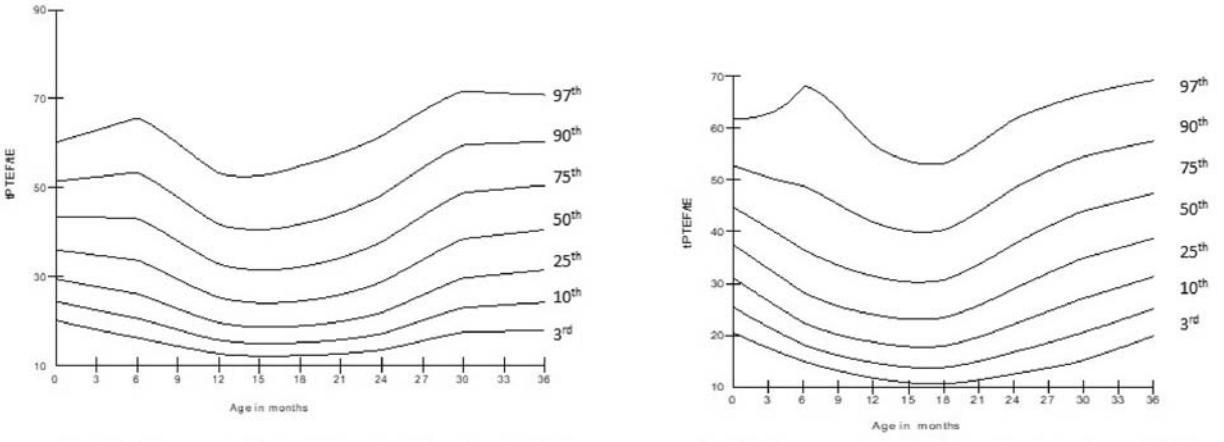

FIG. 3 *(a) Change in ratio of time to attained peak tidal expiratory flow to expiratory time (t_{PTEF}/t_E) with age in girls; (b) Change in ratio of time to attained peak tidal expiratory flow to expiratory time (t_{PTEF}/t_E) with age in boys.*

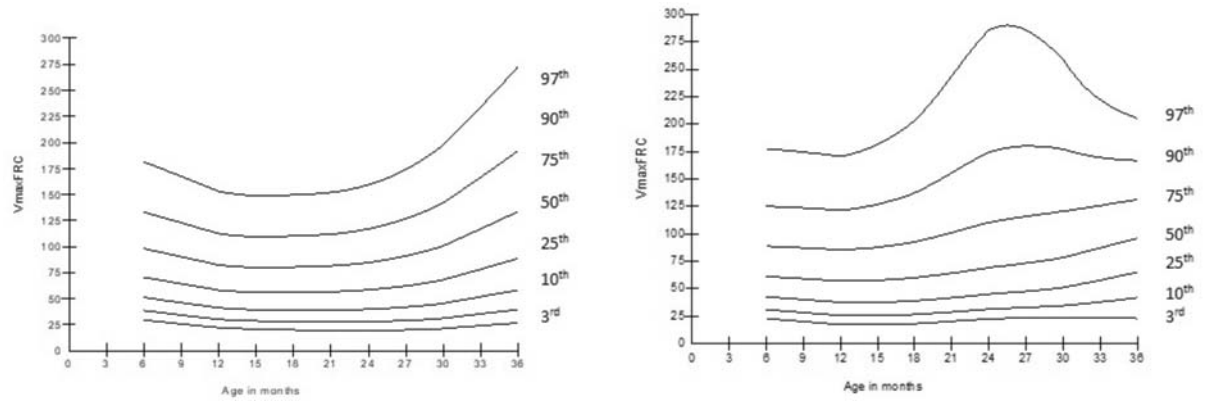

FIG. 4 *(a) Change in maximum expiratory flow at functional residual capacity ($V\dot{c}_{max,FRC}$) with age in girls; (b) Change in maximum expiratory flow at functional residual capacity ($V\dot{c}_{max,FRC}$) with age in boys.*

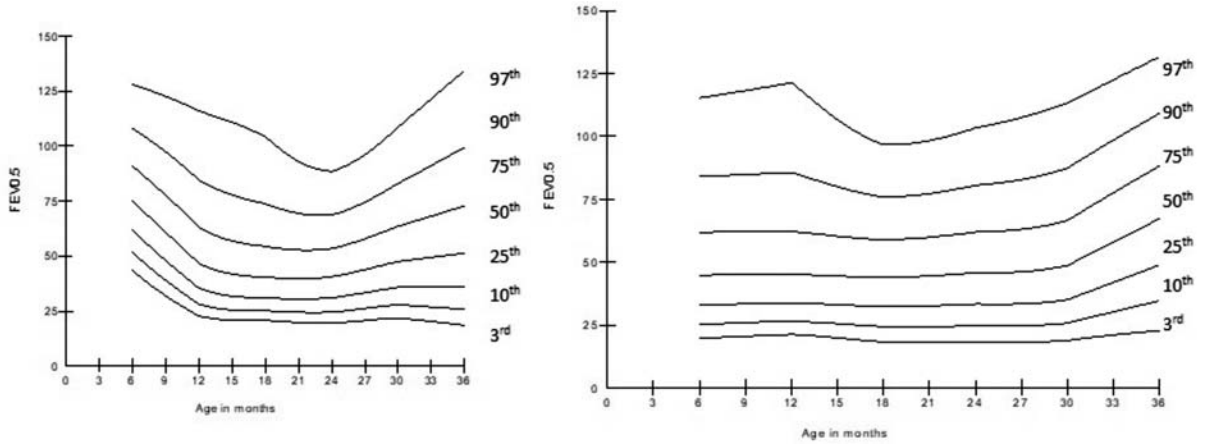

FIG. 5 *(a) Change in forced expiratory volume in 0.5 sec ($FEV_{0.5}$) with age in girls; (b) Change in forced expiratory volume in 0.5 sec ($FEV_{0.5}$) with age in boys.*

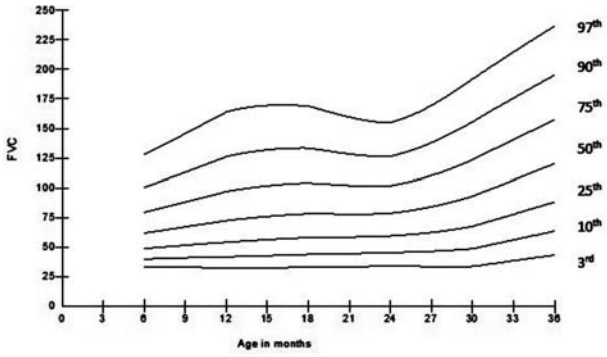

FIG.6 *Change in forced vital capacity (FVC) with age.*

DISCUSSION

IPFT is now widely used in the research context; however, its use in a clinical setting is still restricted by the non-availability of regional and ethnicity-specific reference values. In this prospective birth cohort study, we obtained normative data for TBFVL for neonates to 36 months of age, and RTC and RVRTC from 6 months to 36 months of age.

The major limitation of this study is that subjects were recruited from a single center, which may not be truly representative of the entire population. However, being a tertiary-care institute, subjects were referred from all around the country. Another limitation is that neonates with a family history of smoking or allergy were not excluded in this study, as we considered that they would be normally distributed, though to a different extent, in any given population.

The major strength of this study is the meticulously planned prospective birth cohort design of the study with frequent and regular follow-up. IPFT were performed as per ATS/ERS recommendation. Until one year of age, in the majority of the infants, TBFVL were performed without sedation. As there was a significant difference between genders at a particular age, so gender-specific data have also been presented. Centile curves have been constructed using the LMS method.

In comparison to studies on Caucasian population, V_T/kg was markedly lower at baseline in this cohort; however, it gradually increased with age, and by 12 months it became comparable to global values [19,20]. The rest of the TBFVL indices at baseline were comparable with other studies [19-21]. In this cohort, t_{PTEF}/t_E and V_{PTEF}/V_E were highest at baseline and then gradually decreased until 18 months of age. A study from Switzerland in 342 infants had also observed that t_{PTEF}/t_E gradually decreased in the first year of life [20]. However, a prospective birth cohort study from Taiwan did not observe any significant change in V_T, t_{PTEF}/t_E and V_{PTEF}/V_E from 5 to 26 months of follow-up [7]. Furthermore, in the present study, there was no significant influence of gender at baseline IPFT indices; however, on follow up, many of these indices varied significantly with gender. A study from Norway did not find any significant influence of gender on the baseline tidal expiratory volume; however, they observed that tidal flow and flow ratio were significantly higher in males in comparison to female babies [21]. Another study from Taiwan also did not observe any sex-related difference in IPFT indices [7]. $V'_{max,FRC}$ in this cohort remained similar throughout the follow-up period with no influence of gender. Studies from Taiwan [7], US [22], and a multicentric study from London, Indianapolis, and Boston [23] had observed that $V'_{max,FRC}$ correlates significantly with the height of the children. The measurement of $V'_{max,FRC}$ depends on accurate determination of FRC as a volume landmark, which is highly variable, especially in younger children, and this is a significant limitation in RTC measurement [24]. In this study, jacket pressure was kept fixed at 10 kPa while in other studies, it was used in the incremental range from 2-10 kPa [22,25]. Hence, it might be responsible for the deviation of our finding for $V'_{max,FRC}$ with age from other studies.

In this cohort, most of the RVRTC indices *viz*., FVC, $FEV_{0.5}$, FEF_{25-75}, MEF_{25} and PEF increased minimally until 24 months of age, after that they increased dramatically with age. $FEV_{0.5}$/FVC decreased from baseline until 36 months of age. There was no gender difference in any of the RVRTC indices except at 36 months where it was more significant in boys. A multicentric study from Indiana and Ohio [25] in children from 3 to 149 weeks had also observed that RVRTC indices were highly correlated with growth (height) of the child while $FEV_{0.5}$/FVC decreased with increasing length. They also did not find any influence of gender on RVRTC indices except for FEF_{75}, which was higher in girls [26]. Another study from London has documented that RVRTC indices increase with age [25].

In conclusion, this prospective birth cohort study provides reference values for various IPFT indices from neonates to 36 months of age. The median and centile values for boys and girl have been separately provided. Despite some limitation, the data will be useful as a reference range for Indian children for TBFVL, RTC, and RVRTC. These results will serve as normative data for neonates and preschool children of Indian origin.

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TABLE IV NORMAL VALUES OF RAISED VOLUME RAPID THORACOABDOMINAL COMPRESSION INDICES

IPFT indices,	*Age*	*Weight*	*Height/*	*Boys*					*Girls*				
unit	*(mo)*	*(kg)*	*length (cm)*	*5th*	*25th*	*50th*	*75th*	*95th*	*5th*	*25th*	*50th*	*75th*	*95th*
FEV, mL	6	7.3 (1.1)	66.7 (3.8)	36	47	61	81	102	36	47	61	81	102
	12	8.8 (1.0)	73.7 (3.4)	36	51	75	94	143	37	49	77	100	151
	18	9.8 (1.2)	78.2 (7.2)	43	60	85	104	146	32	54	81	94	135
	24	11 (1.3)	83 (7.5)	40	56	84	113	135	41	56	80	97	132
	30	11.7 (1.6)	86.4 (8.4)	36	67	106	133	171	41	67	91	109	149
	36	12.9 (1.7)	91.4 (7.0)	64	100	128	160	219	37	83	118	144	216
MEF_{25}, mL/s	6	7.3 (1.1)	66.7 (3.8)	30	45	65	110	275	30	45	65	110	275
	12	8.8 (1.0)	73.7 (3.4)	30	45	70	95	365	30	40	70	115	255
	18	9.8 (1.2)	78.2 (7.2)	30	50	70	95	125	20	45	65	90	110
	24	11 (1.3)	83 (7.5)	30	45	75	95	170	30	45	70	90	140
	30	11.7 (1.6)	86.4 (8.4)	30	65	90	140	195	30	50	85	120	150
	36	12.9 (1.7)	91.4 (7.0)	50	105	150	220	450	35	80	110	198	410
FEF_{25-50}, mL/s	6	7.3 (1.1)	66.7 (3.8)	39	51	75	134	273	39	51	75	134	273
	12	8.8 (1.0)	73.7 (3.4)	33	53	75	117	315	39	46	86	124	268
	18	9.8 (1.2)	78.2 (7.2)	33	59	80	116	159	24	53	81	108	161
	24	11 (1.3)	83 (7.5)	35	54	91	126	222	34	54	79	109	160
	30	11.7 (1.6)	86.4 (8.4)	35	71	120	177	253	38	66	106	145	194
	36	12.9 (1.7)	91.4 (7.0)	60	117	178	246	449	33	97	139	214	368
$FEV_{0.5}$, mL	6	7.3(1.1)	66.7 (3.8)	19	36	45	65	84	19	36	45	65	84
	12	8.8 (1.0)	73.7 (3.4)	22	35	45	55	134	23	25	51	64	116
	18	9.8 (1.2)	78.2 (7.2)	22	33	44	59	79	23	34	42	52	78
	24	11 (1.3)	83 (7.5)	19	34	44	60	93	18	32	42	56	75
	30	11.7 (1.6)	86.4 (8.4)	20	32	49	69	111	24	36	48	63	89
	36	12.9 (1.7)	91.4 (7.0)	28	49	68	89	111	20	37	50	74	114
$FEV_{0.5/FEV}$, %	6	7.3 (1.1)	66.7 (3.8)	37	54	71	94	100	37	54	71	94	100
	12	8.8 (1.0)	73.7 (3.4)	38	52	65	79	97	34	55	64	74	86
	18	9.8 (1.2)	78.2 (7.2)	32	46	54	67	80	34	48	58	67	87
	24	11 (1.3)	83 (7.5)	32	48	60	70	92	27	47	56	67	81
	30	11.7 (1.6)	86.4 (8.4)	27	42	53	69	90	32	44	59	68	88
	36	12.9 (1.7)	91.4 (7.0)	27	41	54	70	91	20	36	49	64	88
PEF, mL/s	6	7.3 (1.1)	66.7 (3.8)	65	145	200	275	405	65	145	200	275	405
	12	8.8 (1.0)	73.7 (3.4)	60	100	135	200	435	70	105	148	205	340
	18	9.8 (1.2)	78.2 (7.2)	60	105	150	205	360	70	105	140	190	285
	24	11 (1.3)	83 (7.5)	75	125	175	250	410	70	105	160	205	350
	30	11.7 (1.6)	86.4 (8.4)	95	145	195	285	450	95	140	180	235	355
	36	12.9 (1.7)	91.4 (7.0)	115	200	270	385	505	80	165	245	310	500

IPFT: Infant pulmonary function test; FEV: Forced expiatory volume; MEF_{25}: Maximal expiratory flow at 25% of FEV; FEF_{25-75}: Forced expiratory flow between 25-75 % of FEV; $FEV_{0.5}$: Forced expiratory volume in 0.5 sec, PEF: Peak expiratory flow rate.

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WHAT IS ALREADY KNOWN?

- Infant pulmonary function test (IPFT) can help in the understanding of natural course and progression of respiratory disease and monitor the response to therapy in infants and preschool children.

WHAT THIS STUDY ADDS?

- This study provides the normative data of IPFT indices in healthy Indian children, and the data can be used as reference range for infant pulmonary function test in Indian infant and preschool children.

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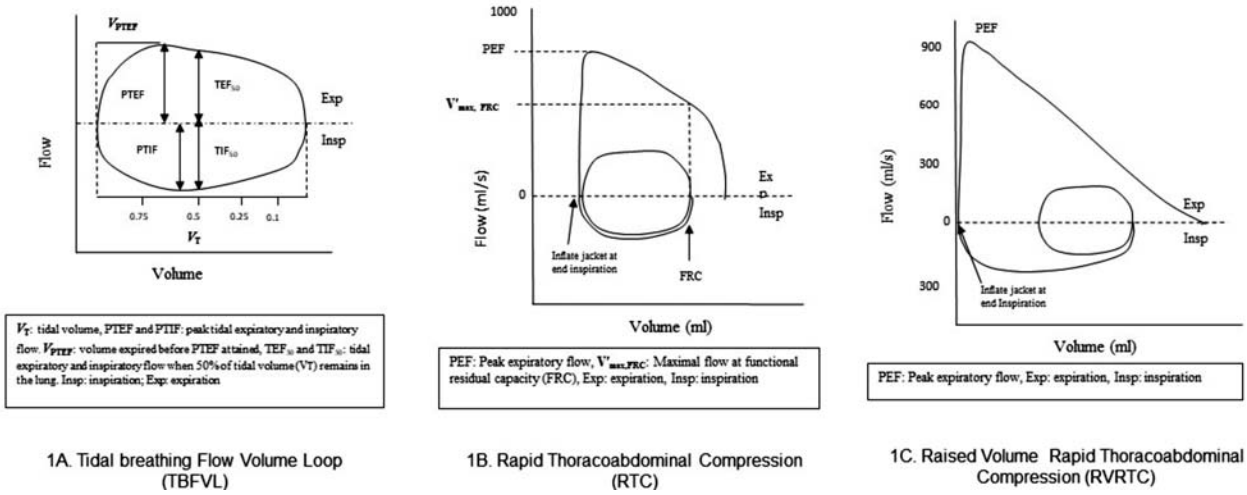

WEB FIG.1 *Normal infant pulmonary function test graphs; (a) Tidal breathing flow Volume loop (TBFVL); (b) Rapid thoracoabdominal compression (RTC); and (c) Raised volume rapid thoracoabdominal compression (RVRTC).*

WEB TABLE I INFANT PULMONARY FUNCTION TEST INDICES AND THEIR PHYSIOLOGICAL INTERPRETATION

Indices	*Unit*	*Physiological interpretation*
Tidal breathing flow volume loop		
• Inspiratory time (t_I), Expiratory time (t_E), Total respiratory time (t_{tot}), time to peak tidal inspiratory or expiratory flow (t_{PTIF} or t_{PTEF})	s	Time taken to complete individual maneuvers
• Tidal volume (V_T), Inspiratory or Expiratory tidal volume (V_I or V_E)	mL	Tidal lung volume
• Peak tidal inspiratory or expiratory flow (PTIF or PTEF)	mL/s	Flow rate
• Mid tidal inspiratory or expiratory flow (MTIF or MTEF)		
• Tidal expiratory flow (TEF) at 75, 50, 25 or 10% of tidal expiratory volume still have to be expired (TEF_{75},TEF_{50}, TEF_{25} or TEF_{10})		
• Ratio of inspiratory or expiratory time to total respiratory time (t_I/t_{tot} or t_E/t_{tot}), inspiratory to expiratory time(t_I/t_E),	%	Represent airway resistance
• Peak ratio: time to PTEF to t_E (t_{PTEF}/t_E)		
• Ratio of exhaled Volume to PTEF to tidal expiratory volume (V_{PTEF}/V_E)		
• Ratio of TEF_{75},TEF_{50}, TEF_{25} or TEF_{10} to Peaked tidal expiratory flow (PTEF)		
Rapid thorocoabdominal compression		
• Maximum expiratory flow at functional residual capacity ($V'_{max,FRC}$)	mL/s	Flow rate
• Maximum expiratory flow at 50% or 70% of expiration (V'_{50} or V'_{70})		
• Volume to peak expiratory flow (V_{PEF})	mL	Lung volume at partial expiratory flow- Airway resistance
Raised volume rapid throocoabdominal compression		
• Forced expiratory volume (FEV), FEV at 0.5, 0.75 or 1.0s of the forced expiration ($FEV_{0.5}$/$FEV_{0.75}$/$FEV_{1.0}$)	mL	Forced lung volume at given time period
• Maximum expiratory flow at 25% or 10% of FEV (MEF_{25} or MEF_{10})		
• Forced expiratory flow between 25% and 75% of FEV (FEF_{25-75})	mL/s	Forced flow rate –representing airway resistance.
• Peak expiratory flow (PEF)		
• Ratio of forced expiratory volume at 0.5 s to total forced expiratory volume ($FEV_{0.5}$/FEV)	%	Airway obstruction

IPFT: Infant pulmonary function testing, TBFVL: Tidal breathing flow volume loop, RTC: Rapid thoracoabdominal compression, RVRTC: Raised volume rapid thoracoabdominal compression.