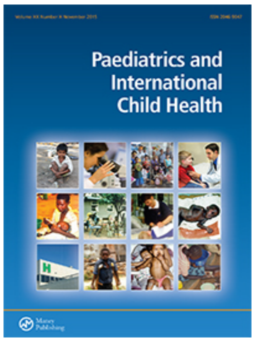

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Beyond survival: 5-year neurodevelopmental follow-up of a cohort of preterm infants in Colombo, Sri Lanka

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Beyond survival: 5-year neurodevelopmental follow-up of a cohort of preterm infants in Colombo, Sri Lanka

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ABSTRACT

Background: There is a lack of information on long-term neurodevelopmental outcome in preterm neonates in low- and middle-income countries.

Objectives: To describe the developmental attainments of preterm neonates followed up for 5 years and to identify the risk factors for impairment.

Method: A prospective descriptive cohort study was undertaken in neonates of 34 weeks gestation born within a period of 12 months at a single tertiary maternity and neonatal unit in Colombo, Sri Lanka. Infants were assessed for neurodevelopment using the Bayley Infant and Toddler III® Assessments at 6, 12 and 24 months of corrected age and school readiness assessment at 5 years.

Results: Fifty-one infants were assessed at least once, 45 were assessed at 2 years and 39 had a final assessment at 5 years. Neurodevelopmental attainment deteriorated significantly in the cognitive and motor composite scores from 6 to 24 months ($p < 0.05$). By 5 years the number of children with delay in cognitive, language and motor domains had reduced significantly from 24 months ($p < 0.05$) but the cognitive skills remained most affected (10/39). At 5 years, 13 of 39 children had a confirmed diagnosis of a neurodevelopmental disorder: eight had attention deficit hyperactivity disorder, three autism spectrum disorder, one cerebral palsy and one visual impairment. Surfactant administration and retinopathy of prematurity were the most significant risks for delayed development at 5 years ($p < 0.05$).

Conclusion: Deterioration of cognitive and motor composite scores over the first 24 months highlights the need for regular surveillance of premature infants. There was a discrepancy between the diagnosis of neurodevelopmental delay at 24 months and at 5 years. But the notable impact on school readiness skills requires public health initiatives to cater for the needs of these children.

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Prematurity; neuro-developmental outcomes; low and middle income countries; risk factors for developmental delay; developmental surveillance; school readiness; Sri Lanka

Introduction

Owing to better perinatal and neonatal care, neonatal survival has improved globally. An estimated 15.1 million infants survive adversities such as prematurity, birth asphyxia and serious infections. These infants are at high risk of acquiring neurodevelopmental morbidities [1–3].

Preterm birth is associated with several acute complications which require advanced interventions [4]. Preterm birth accounts for most neonatal morbidity resulting in diverse long-term neurodevelopmental sequelae such as cerebral palsy, visual and hearing impairment, poor academic performance and social, emotional and behavioural disorders [5,6]. This greater prevalence of neurodevelopmental disorders in these infants is of significant public health concern [1,7]. Some high-income countries have guidelines and protocols for periodically identifying and monitoring such infants [8,9].

Current evidence on outcome in survivors is mostly from high-income settings and describes outcomes in extremely premature and very low-birthweight toddlers to school-age children [6,10–13]. Yet the majority (98%) of such at-risk births are in low-resource settings, i.e. low- and middle-income countries (LMIC) [1–3,6,14].

Until recently, the primary goal in many LMIC was saving the lives of these preterm infants. Now in the twenty-first century the emerging challenge is to look beyond their survival. This is a timely and appropriate goal because an increasing number of these children do survive, thanks to advances in perinatal and neonatal care [1,15,16]. However, the information on outcome and guidelines for follow-up and intervention in such settings is inadequate [6,17].

Such information is useful to predict outcome in preterm newborns and to counsel families with regard to long-term care, and the data will enhance the global

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evidence base on preterm developmental patterns, enabling comparisons between regions.

Sri Lanka is an LMIC in which the government is the principal health-care provider and all health services are free. Over the past decade, the perinatal care services have been improving and most neonatal intensive care units provide tertiary care similar to that in high-income countries. Some of these facilities include surfactant therapy, total parenteral nutrition and positive pressure ventilation. During this study, surfactant was provided as rescue therapy for all eligible preterms in the tertiary care units. Sri Lanka is one of the few countries in the world to have successfully halved its neonatal mortality rate over a decade by primarily reducing premature births to achieve the Millennium Development Goal 4 on child survival [16,18]. Sri Lanka's robust public health system over the past several decades contributed largely towards this success, as have the advanced neonatal services provided by tertiary centres [19,20]. The community-based public health midwife in Sri Lanka plays a major role, monitoring newborn infants at home including developmental screening up to 5 years of age [21]. But the precision and rigour with which these screenings are conducted is unknown, particularly when there are no definitive protocols to monitor high-risk newborns. This is similar to most other LMICs with regard to neurodevelopmental surveillance [22,23].

To create a more robust developmental surveillance system, it is essential to understand the neurodevelopmental trajectories of surviving preterm infants from infancy through to school age.

Such evidence will facilitate early detection and appropriate intervention in infants with developmental delay/impairment [1,6,8]. The findings of this study will contribute to the evidence base from LMIC settings and will inform policy makers on the need for further service development.

The study was conducted in a single tertiary neonatal care unit in Sri Lanka with the aim of describing the developmental attainments of these children from birth to 5 years of age and to identify risk factors for developmental impairment.

Methods

This prospective, descriptive cohort study was conducted to assess neurodevelopmental outcome in preterm neonates admitted to the University Neonatal Unit, De Soysa Maternity Hospital, Colombo. Preterm neonates born between 1 May 2009 and 30 April 2010 were enrolled for the study at the point of discharge. All infants with period of gestation (POG) of 34 weeks or less were eligible. Neonates with apparent congenital abnormalities or dysmorphism and/or families requesting follow-up in peripheral districts were excluded at the point of recruitment. Infants or toddlers who experienced any new central nervous system (CNS) infections subsequent to discharge from the neonatal care unit or who underwent traumatic brain injury or any other acquired neurological condition during the 5-year follow-up period were excluded. Development of seizures at any time during the study was not an exclusion criterion.

All infants meeting the inclusion criteria were scheduled for regular neurodevelopmental assessment until they reached a corrected age (CA) of 2 years. They received mail and telephone reminders to attend for follow-up. Reminders were sent at 5 years of chronological age to return for school readiness assessment.

Data collection

Clinical data were collected from the inpatient daily records, clinic follow-up notes and parent interviews. All data were collected on pre-tested data sheets by clinicians with a paediatric training. Information included details about the antenatal, perinatal and postnatal periods and any significant neurodevelopmental event in infancy or early childhood.

Neonates born during the study period with a POG <34 weeks and who met the inclusion criteria were recruited.

Neonates were subcategorised into prematurity groups according to the World Health Organization definition (POG <28 weeks, extreme prematurity; POG 28–32 weeks, very preterm; POG 32–37 weeks, moderate-to-late preterm) [7]. The upper POG limit for this study was 34 weeks.

The subjects were categorised into three groups according to birthweight as follows: low birthweight (LBW) <2.5–1.5 kg, very LBW <1.5 to 1 kg, and extremely LBW <1 kg [7].

Neurodevelopmental assessment

6-, 12- and 24-month assessment. All subjects underwent developmental assessment using the Bayley Scales of Infant and Toddler Development III® at 6, 12 and 24 months of corrected age [24]. Although this scale has not been validated for Sri Lanka, a similar study was conducted in children aged 6, 12 and 24 months in Sri Lanka and the USA for cognitive and motor scales [25]. To maintain uniformity of assessment, it was undertaken by a single trained evaluator. Raw scores were awarded for five domains – cognitive (Cog), receptive communication (RC), expressive communication (EC) and fine motor (FM) and gross motor (GM) – and converted to scaled scores which were then converted to composite scores. According to the composite scores, children performing <–1.5 SD were categorised as delayed. Because of the small size of the cohort, the delay was not categorised as mild, moderate or severe.

5-year assessment. There are no standardised developmental or psychological tools to assess school readiness in children at 5 years of age in Sri Lanka. Therefore a questionnaire was designed to assess the neurodevelopmental skills of the five main domains (cognitive, language, motor, social, behaviour and attention) required for school readiness using a range of assessments. The ability or inability to perform a certain skill was assessed. To ensure the validity of assessments, all were undertaken by two independent investigators. Because this was a locally designed tool which was not standardised or formally validated, the inter-rater agreement was considered to improve the validity of this assessment.

Rather than grading the level of performance, a child's ability (1) or inability (0) to perform a given task was recorded. Some of these items were adopted from a modified Denver development screening test (DDST) used previously in Sri Lanka [26]. All the skills tested were developmentally appropriate for 5 years of age.

Validity of the 5-year assessment. The test items used in the assessment tool were adopted from age-appropriate items in a standardised developmental scale. The items were scrutinised by a team of experts in child health, psychology and education. The team concluded that the items were adequate and appropriate for the study because they were age-appropriate, had been used previously in Sri Lanka and delays were detected [26].

Reliability of the 5-year assessment. The inter-rater agreement between two independent assessors using the assessment tool was 92%.

Statistical analysis

Data were analysed using SPSS-15 software. The significance of relationship to various risk factors using the Bayley composite scores at each assessment was analysed using appropriate inferential statistics. A *p*-value of <0.05 was taken as statistically significant.

Median comparisons of Bayley scores in the three age groups (6, 12, 24 months) and formulation of graphs was undertaken using the R programming language version 3.3.1.

Ethics

Written, informed consent was obtained from the parents of all participants. All invited families consented to participation, and the assessments were undertaken at the outpatient clinics. The Ethics Review Committee of the Faculty of Medicine, University of Colombo granted ethical clearance.

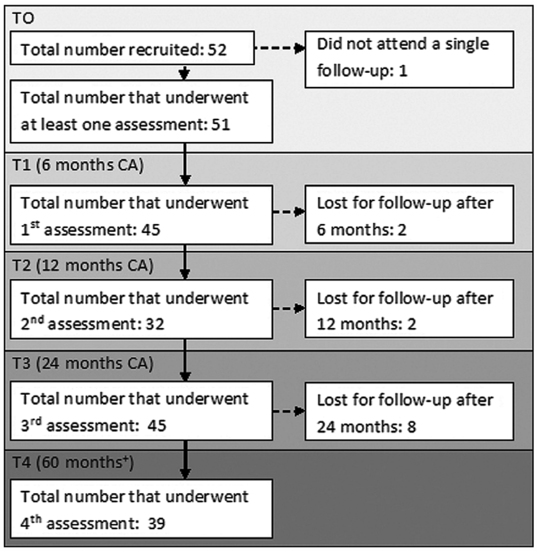


Figure 1. Progression flow chart of the cohort.

Results

Fifty-two infants were enrolled into the study, one of whom did not attend any follow-up and was therefore excluded. The remaining 51 participants attended at least one neurodevelopmental assessment and had a POG of 25–34 weeks. The progress of the study is outlined in Figure 1. Of the 51 infants recruited, 45 (88%) attended the 2-year follow-up and 39 (77%) attended the 5-year follow-up.

Table 1 shows the demographic and clinical data. The majority of neonates (82.3%) were born at a POG of ≤32 weeks (median 31, range 25–34) and 80.4% weighed <1500 g (median: 1400, range 690–2095). Multiple medical complications associated with prematurity were recorded in the majority of infants. All the infants had at least one complication.

Developmental outcomes at 6, 12 and 24 months

The comparison of cognitive language and motor composite scores using the Bayley Scales of Infant and Toddler Assessment at 6, 12 and 24 months CA demonstrated a significant decrease in cognitive and motor scores from 6 to 24 months ($p < 0.05$) (Figure 2). The language scores did not show any significant pattern over the first 2 years.

Developmental attainment at 5 years

Thirty-nine children were assessed at 5 years. Cognitive skills were the most affected at the 5-year school readiness assessment (Table 2). Early literacy skills such as storytelling (15%) and reading the letters of the alphabet (26%) were most affected. The draw-a-man test scores were below the expected for age in 13% of children, and 18% of children did not have the expected numeracy skills at 5 years.

Table 1. Demographic and clinical data at birth for 51 infants.

Male (%)	22 (43.1)
Gestation, weeks, mean (SD)	31.01 (2.3)
<28 (%)	9 (17.6)
28–32 (%)	33 (64.7)
32–34 (%)	9 (17.6)
Birthweight, g, mean (SD)	1390 (0.4)
<1000 (%)	10 (19.6)
1001–1500 (%)	31 (60.8)
>1500 (%)	10 (19.6)
Mode of delivery	
Normal vaginal (%)	20 (39.2)
Breech (%)	2 (3.9)
Emergency LSCS* (%)	24 (47.1)
Elective LSCS (%)	5 (9.8)
Medical complications and intervention	
APGAR <6 at 5 min (%)	2 (2.0)
Surfactant administered† (%)	8 (15.7)
Required phototherapy (%)	28 (54.9)
Required blood transfusions (%)	13 (25.5)
Sepsis (%)	22 (43.1)
Seizures (%)	6 (11.8)
Hypotension (%)	20 (39.2)
Hypoglycaemia (%)	9 (17.6)
Hyponatraemia‡ (%)	24 (47.1)
Renal failure (%)	1 (2.0)
Apnoea (%)	5 (9.8)
Necrotizing enterocolitis§ (%)	8 (15.7)
Retinopathy of prematurity (%)	10 (19.6)
Breastfeeding initiation >2 days (%)	37 (72.5)
Hospital stay >2 weeks (%)	36 (70.6)

*LSCS, lower segment caesarean section.
†Surfactant was available for all infants who required it.
‡Hyponatraemia, Na^+<135 mmol/L [27].
§Necrotising enterocolitis, stages IIA–IIIB systemic, intestinal or radiographic evidence as described by Walsh and Kleigman [28].

The second most affected domain was language skills with more than 10% of children performing below the expected level in receptive, expressive and social communication.

At 5 years of age, one child had visual impairment, one had a confirmed diagnosis of cerebral palsy, gross motor function classification system (GMFCS) V, three had autism spectrum disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) V criteria and eight had attention deficit hyperactivity disorder according to the International Classification of Disease (ICD) ten criteria [29–31].

Comparison of the number of children with delay at 24 months and 5 years

At 5 years, there were fewer children with delays in all three main developmental domains than at 24 months of CA. This reduction in the number of children with delay in cognitive, language and motor domains at 5 years was significant ($p < 0.05$) (Table 3).

Risk factors for delay at 2 and 5 years

The risk factors for developmental delay at 2 and 5 years were analysed for the cognitive, language and motor domains (Appendix 1). The risk factors considered were gender, maturity, birthweight (<1000 g), APGAR score <6, administration of surfactant, requiring phototherapy, blood transfusion, sepsis, neonatal seizures, hypotension, hypoglycaemia, hyponatraemia, apnoea, neonatal enterocolitis (NEC), renal failure, retinopathy of prematurity, number of days to establish breastfeeding (>48 h) and number of days in hospital (>2 weeks). Administration of surfactant was a risk factor for cognitive delay across both age groups and motor skills assessed at 5 years ($p < 0.001$).

The risk factors for impairment in behaviour and social skills were analysed at 5 years. In addition to surfactant administration ($p < 0.001$) and retinopathy of prematurity ($p < 0.001$), low birthweight ($p = 0.036$), neonatal seizures ($p = 0.003$) and renal failure ($p = 0.008$) were significantly associated with social skills impairment at 5 years of age (Appendix 2).

Retinopathy of prematurity was a significant risk factor for delay in all domains assessed at 5 years. Most of the risk factors significantly impacted one or more cognitive skills at 5 years of age, except the gender of the infant, low APGAR score and apnoea.

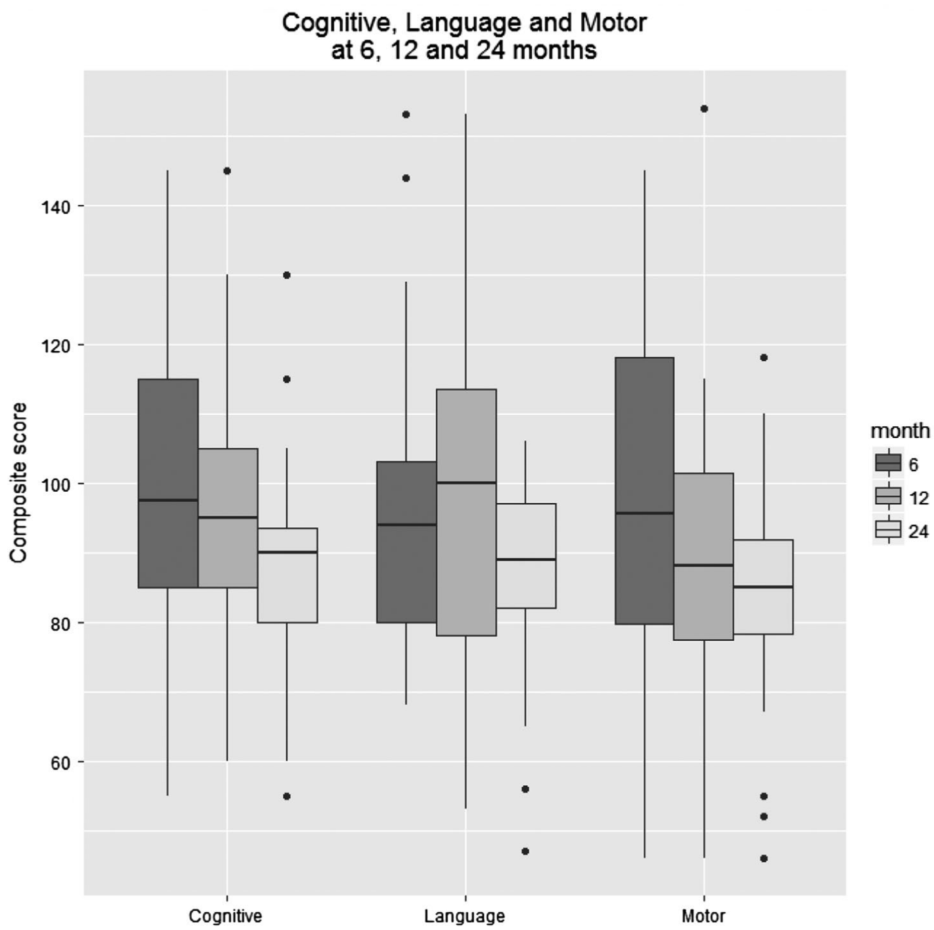
Discussion

The study examined the developmental attainments of a cohort of preterm neonates over a 5-year period.

The results demonstrate the value, for two main reasons, of following up at-risk neonates during the first 5 years of life. Firstly, the developmental scores showed varying patterns over the 5 years of follow-up which confirms the need for surveillance and long-term follow-up. Also, the children displayed impairment of the skills required for school performance at 5 years, emphasising the impact on learning of prematurity and related complications. The developmental trajectories from 6 to 24 months showed a significant decline in scores in the cognitive and motor domains ($p < 0.05$), re-emphasising the value of developmental surveillance until 24 months of age.

This is contrary to the usual practise in LMIC where growth rather than neurodevelopment is the primary concern of regular monitoring in infancy [22]. Also, other challenges such as work overload, lack of training and scarcity of tools may mean that, owing to incomplete surveillance before 2 years of age, primary health-care workers inadvertently discharge too soon, apparently normal neonates who are actually at risk [22,23]. This further underscores the need for more detailed and formal assessment to identify specific delays in infants at risk and the need to ensure that health staff have the necessary skills and knowledge to do so.

Because of previous evidence from Sri Lanka, the increase in the number of children with lower scores in the cognitive and motor domains needs to be viewed with caution. A comparative study was conducted in Sri Lanka and the USA among children aged 6, 12 and 24 months using the Bayley Scales of Infant and Toddler assessments to measure the cognitive and motor



	6m	12m	24m		6m	12m	24m		6m	12m	24m
Range	90	85	75		85	100	59		99	108	72
IQR	30	20	13.5		23	35.5	15		38.25	24	13.5
Median	97	95	90		94	100	89		95	88	85

Figure 2. Cognitive, language and motor developmental trajectories at 6, 12 and 24 months.

domains [25]. The Sri Lankan children showed lower mean composite scores in the two domains at 24 months [25]. This might have contributed to a higher number of children demonstrating delay at 24 months (to score <1.5 SD below the mean) in the present study. However, even at the 5-year assessment the most frequent delay was in the cognitive domain.

Yet at the 5-year assessment the proportion of children identified with a delay at 24 months was significantly reduced ($p < 0.05$) in all three domains, which questions the validity of the diagnosis of delay at 2 years. A study in Victoria, Australia describes this same phenomenon of uncertainty about a diagnosis of cognitive disability at 2 years in a cohort of extremely premature and very low-birthweight children followed up to 8 years of age [12]. Yet the current study identified these children as having a delay (mean SD −1.5) rather than a disability, and these children were more mature (25–34 weeks POG) and had a wider birthweight range (0.690–2.095 kg).

However, the study showed that a considerable proportion of children had cognitive delay even at 5 years (10/39) in contrast with the language and motor domains. Similar studies in high-income countries describe cognitive delays which affect school performance as the most significant neurodevelopmental outcome in survivors of prematurity, supporting similar findings in different settings [1,6,32].

The absence of any patterns of development of language skills is noteworthy. The language assessments used need to capture the local language development patterns and therefore should be more specific and sensitive. Sri Lanka does not have validated tools to assess language development in young children and this is a possible reason for the failure to detect any observable pattern.

The significant associations between the risk factors and the developmental domains were more evident at 5 years than at 2 years of age. Such significant associations were most often observed in cognitive, motor and social skills and less often in the language domain, possibly indicating the need for more context-specific and sensitive tools for assessing language.

Table 2. Neurodevelopmental skills at 5 years in 39 children.

Domain	Assessment parameter	No. (%)
Cognitive skills	Draw a man test: age appropriate score or not	34 (87.2)
	Recites a named nursery rhyme	37 (94.9)
	Relates a simple story	33 (84.6)
	Looks at a story book from beginning to end with interest	37 (94.9)
	Reads all letters of the native alphabet	29 (74.4)
	Counts up to 10	32 (82.1)
	Ability to identify numbers up to 10	34 (87.2)
	Assign the value to any number from 1 to 10	35 (89.7)
Total no. of children with poorer than expected performance		10
Language	Speaks in complex sentences	35 (89.7)
	Follows complex instructions	33 (84.6)
	Communicates in a socially appropriate manner	31 (79.5)
Total no. of children with poorer than expected performance		8
Motor	Holds pencil with a mature grasp	37 (94.9)
	Cuts with scissors	37 (94.9)
	Independent and steady walking	38 (97.4)
	Mature running	38 (97.4)
	Hopping	36 (92.3)
Total no. of children with poorer than expected performance		3
social skills	Independent washing	36 (92.3)
	Independent cleaning	36 (92.3)
	Independent use of toilet	37 (94.9)
	Independent feeding	37 (94.9)
	Plays meaningfully with age-appropriate toys	36 (92.3)
	Plays in a group	36 (92.3)
	Total no. of children with poorer than expected performance	3
Behaviour and attention	Behaviour and attention were assessed using the SNAP IV questionnaire parent version.	
	Total no. of children with positive scores for ADHD	8 (20.5)

Table 3. Number of children with cognitive, language and motor developmental delay at 24 months of corrected age and 5 years.

	24 months, $n = 45$ (%)	5 years, $n = 39$ (%)	p-value
Cognitive	22 (48.9)	10 (25.6)	<0.05
Language	19 (42.2)	8 (20.5)	<0.05
Motor	26 (57.8)	3 (7.7)	<0.05

Surfactant is proven to reduce severe morbidity and mortality in preterm infants during the acute stage of respiratory distress syndrome [4]. The administration of surfactant in this study was significantly related to delay in all domains (cognitive, language, motor, social and behaviour) at 5 years of age. Similarly, in children at 5 years, retinopathy of prematurity was significantly associated with delay in all domains except behaviour. It is assumed that the newborns who required surfactant and later showed evidence of retinopathy of prematurity were more acutely ill and their later neural development most affected. Because of the small numbers, comparison between birthweight and maturity together with other associated risk factors was not attempted. However, the findings reflect those in the WHO report 'Born Too Soon' in reference to Sri Lanka because it is identified as a country which has reduced mortality owing to the survival of preterm infants but with uncertainty about survivors' quality of life [7]. This again emphasises the value of surveillance of this group of neonates to bridge the gap in evidence of the developmental patterns and outcomes of the survivors which will provide feedback for further enhancement of quality of care for the pre-term newborn.

A limitation of the study was the decline in the number of children in the cohort over the 5 years, the most probable reason being a change of residence and telephone number. However, all children with significant delays and disabilities continued to attend clinics. The lack of validated tools to assess neurodevelopmental outcomes was another limitation.

This study adds to current knowledge of long-term outcome in a cohort of pre-term newborns followed from birth to 5 years in Sri Lanka. The most significant findings were the deterioration of scores during the first 2 years and the significant delay in skills required for school at 5 years of age, the main delay being in cognitive skills. These findings illustrate the importance of long-term surveillance of preterm infants to enable early detection and intervention when there are developmental delays, and the need to design appropriate services to cater for the needs of these children.

Sri Lanka is one of the countries which has achieved improved neonatal care and decreased mortality rates. The results of this study should aid the planning of newborn care and the formulation of health policies for other countries similar to Sri Lanka.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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S P Sumanasena is a principal investigator who is responsible for designing, conducting and writing of the study. She is a consultant pediatrician and senior lecturer with a special interest in developmental pediatrics and childhood disabilities. In addition, her research interests also include developmental surveillance of children at risk and community based qualitative studies on children with disabilities and their families. She published peer reviewed articles on childhood disabilities and published articles in indexed journals on developmental surveillance.

D V Vipulaguna involved in data collection and analysis. He is a registrar in paediatrics with research interests in child development and neurology.

M M Mendis involved in Data collection. He is a student with research interests in medical sciences and childhood disabilities.

N S Gunawardena involved in statistical analysis and input. She is a National Professional Officer (Health Systems Analysis and Evidence) with special interest in statistics and research interests related to community medicine. Her research conducted on various public health concerns and published in refereed journals.

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Appendix 1. Significant associations between risk factors and developmental domains

	Cognitive				Language		Motor	
		5 yrs						
Risk factors	2 yrs	Literacy	Numeracy	Draw a Man	2 yrs	5 yrs	2 yrs	5 yrs
Gender	NS	NS	NS	NS	NS	NS	NS	NS
Maturity <28 wks	NS	NS	NS	0.05	0.004	NS	NS	0.004
Birthweight <1000 g	NS	0.02	NS	0.04	NS	NS	NS	NS
APGAR <6 at 5 mins	NS	NS	NS	NS	NS	NS	NS	NS
Surfactant administered	0.005	0.02	0.008	0.009	0.01	0.002	NS	0.022
Required phototherapy	NS	NS	NS	NS	NS	NS	NS	NS
Required blood transfusions	NS	0.03	NS	NS	0.000	0.02	0.003	NS
Sepsis	NS	NS	NS	NS	NS	NS	NS	0.46
Neonatal seizures	0.01	NS	0.05	0.003	NS	NS	NS	0.01
Hypotension	NS	NS	NS	NS	NS	NS	0.05	0.04
Hypoglycaemia	NS	NS	0.05	NS	NS	<0.0001	NS	NS
Hyponatraemia	NS	NS	NS	NS	0.025	NS	NS	NS
Apnoea	0.04	NS	NS	NS	NS	NS	NS	NS
Necrotising enterocolitis	NS	NS	NS	NS	NS	NS	NS	0.001
Renal failure	NS	NS	0.05	0.008	NS	NS	NS	<0.0001
Retinopathy of prematurity	NS	0.02	<0.0001	0.009	NS	0.035	NS	0.02
No. of days to establish breast- feeding >48 h	NS	NS	0.04	0.003	NS	NS	NS	NS
No. of days in hospital >2 wks	NS	NS	NS	NS	0.04	NS	NS	NS

Appendix 2. Significant associations between risk factors and social skills and behaviour at 5 years

Risk factors	Social	Behaviour
Gender	NS	NS
Maturity <28 wks	NS	NS
Birthweight <1000 g	0.036	NS
APGAR <6 at 5 min	NS	NS
Surfactant administered	<0.001	<0.001
Required phototherapy	NS	NS
Required blood transfusions	<0.0001	NS
Sepsis	NS	NS
Neonatal seizures	0.003	NS
Hypotension	NS	NS
Hypoglycaemia	NS	NS
Hyponatraemia	NS	NS
Apnoea	NS	NS
Necrotising enterocolitis	NS	NS
Renal failure	0.008	NS
Retinopathy of prematurity	<0.001	NS
No. of days to establish breast- feeding >48 h	NS	NS
No. of days in hospital >2 wks	NS	NS