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ORIGINAL ARTICLE

Retrospective Cohort Study

Language and cognitive outcome for high-risk neonates at the age of 2-3 years - experience from an Arab Country

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Abstract

AIM

To investigate the effect of different neonatal risk factors on different language parameters as well as cognitive abilities among Arabic speaking Egyptian children at the age of two to three years of life and to find out which risk factor(s) had the greatest impact on language and cognitive abilities.

METHODS

This retrospective cohort study was conducted on 103 children with age range of 2-3 years (median age 31 mo). They were 62 males and 41 females who were exposed to different high-risk factors in the perinatal period, with exclusion of metabolic disorders, sepsis/meningitis, congenital anomalies and chromosomal aberrations. The studied children were subjected to a protocol of language assessment that included history taking, clinical and neurological examination, audiological evaluation, assessment of language using modified preschool language scale-4, IQ and mental age assessment and assessment of social age.

RESULTS

The studied children had a median gestational age of 37 wk, median birth weight of 2.5 kg. The distribution of the high-risk factors in the affected children were prematurity in 25 children, respiratory distress syndrome

in 25 children, hypoxic-ischemic encephalopathy in 15 children, hyperbilirubinemia in 10 children, hypoglycemia in 13 children, mixed risk factors in 15 children. The results revealed that high-risk neonatal complications were associated with impairment of different language parameters and cognitive abilities ($P < 0.05$). The presence of prematurity, in relation to other risk factors, increases the risk of language and cognitive delay significantly by 3.9 fold.

CONCLUSION

Arabic-speaking children aged 2-3 years who were exposed to high-risk conditions in the perinatal period are likely to exhibit delays in the development of language and impairments in cognitive abilities. The most significant risk factor associated with language and cognitive impairments was prematurity.

Key words: High-risk neonates; Prematurity; Arabic language; Cognition; Child disability

Core tip: The aim of this retrospective cohort study was to evaluate the effect of different neonatal risk factors on different language parameters as well as cognitive abilities among Arabic speaking Egyptian children at the age of two to three years and to find out which risk factor(s) had the greatest impact on language and cognitive abilities. The results revealed that Arabic-speaking children who were exposed to high-risk conditions in the perinatal period are likely to exhibit delays in the development of language and impairments in cognitive abilities. The most significant risk factor associated with language and cognitive impairments was prematurity.

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INTRODUCTION

High-risk neonates are defined as neonates who are more liable to morbidity or mortality due to the exposure to high-risk factors which include preconceptual, prenatal, natal, or postnatal conditions or circumstances that interfere with the normal birth process or impede adjustment to extrauterine growth and development[1,2]. Those risk factors include prematurity, hyperbilirubinemia, hypoglycemia, hypoxic-ischemic encephalopathy (HIE) and respiratory distress syndrome (RDS)[3]. Babies who were exposed to high-risk factors before birth, during birth or during their neonatal periods are likely to have adverse outcomes.They are more liable to an increasing risk of behavioral problems, intellectual deficits and a lag in language acquisition[4]. Advances in perinatal care and establishment of improved neonatal services have increased the survival rates of many high-risk neonates in developing countries. Those neonates can experience significant short-term and long-term sequela.

The first three years of life; when the brain is developing and maturing, is the most intensive period of acquiring speech and language skills. There appear to be critical periods for speech and language development in infants and young children when the brain is best able to absorb language. If these critical periods are allowed to pass without exposure to language, it will be more difficult to learn[5]. Most of the neonatal risk factors cause language and cognitive delays through impairments of the neural development and integrity of the brain functions resulting in affection of the language area and higher functions of the brain.

Language difficulties are prevalent in high-risk children and include expressive language delays that manifest themselves as poor vocabulary and grammar in addition to articulation problems. Difficulties with phonological awareness are also common and predict later poor reading and writing skills. High-risk neonates are likely to have long-term sequalae affecting linguistic development beyond preschool. In addition, such babies are also at an increasing risk of lower IQ scores below 70, attention-deficit-hyperactivity disorders and negative emotionality[6,7]. Developmental delay describes children who present with delays in meeting developmental milestones during early childhood and have lower scores in neurodevelopmental testing. The delay is often in more than one system, including gross and fine motor functions, language, social, communication, and visuo-spatial functions[8,9].

The aim of this cohort study was to evaluate the effect of different neonatal risk factors on different language parameters as well as cognitive abilities among Arabic speaking Egyptian children at the age of two to three years and to find out which risk factor(s) had the greatest impact on language and cognitive abilities.

MATERIALS AND METHODS

This study was done on 103 Arabic speaking Egyptian children with their ages ranged between 24 to 37 mo (median age was 31 mo). They were 62 males and 41 females. All the studied children were admitted to the neonatal intensive care unit (NICU) at Mansoura University Children's Hospital with history of neonatal high-risk conditions and followed-up at the Phoniatric outpatient clinic at Mansoura University Hospitals in the period from January 2013 to November 2014. Children with a history of neonatal high-risk conditions accompanied with metabolic disorders, sepsis/meningitis, chromosomal aberrations, genetic disorders or multiple congenital anomalies were excluded. All parents/legal guardians provided informed written consent prior to

study enrollment. The study was approved by Institutional Review Board of the Faculty of Medicine, Mansoura University, Mansoura, Egypt.

All patients included in the study were subjected to the following protocol of assessment.

Elementary diagnostic procedures

Parent/legal guardian interview: Parent/legal guardian interviewfor recording information about socio-demographic data of the studied children. The information on child's age, birth order, gestational age, place and mode of delivery, birth weight, presence of neonatal disorders such as neonatal HIE, postnatal hyperbilirubinemia, infections, hypoglycemia, seizures, admission to NICU (causes and duration of admission to NICU and history of assisted ventilation techniques or oxygen supplementation), milestone of development, illnesses of early childhood were recorded. The included cases of Neonatal hyperbilirubinemia in the study were full-term neonates with serum bilirubin level exceeding that is required for treatment by phototherapy according to the guidelines of American Academy of Pediatrics[10]. Neonatal hypoglycemia was defined as a plasma glucose level less than 40 mg/dL.

Assessment of parents-child interaction: A short semi-objective questionnaire was designed to evaluate parent-child linguistic interactions during the first two to three years of child's life. The questions were: (1) Did you spend a substantial time to communicate verbally with your child? (2) Did you wait for your child to communicate? (3) Did you participate and talk to your child during his/her daily activities? and (4) Did you reward your child when pronounced a new word? If the parents responded yes to any of the afore-mentioned questions; it was considered a positive parent-child interaction. The two-point score was assigned where (0) = no parent-child verbal interaction and (1) = positive parent-child verbal interaction.

General, vocal tract and full neurological examinations: General, vocal tract and full neurological examinations were performed for each child.

Clinical diagnostic aids

Formal testing: Formal testing for psychometric evaluation using Stanford Binnet Intelligence Scale 4th Arabic version for determination of IQ[11]. Assessment of social age by Vineland social maturity scale[12] and Language assessment using the Standardized Arabic Language test (Modified preschool language scale) (for determination of receptive, expressive and total language ages)[13].

Audiological evaluations: To evaluate hearing sensitivity through pure tone audiometry, Auditory Brain Stem Evoked Response (ABR) and tympanometry.

Additional instrumental measures

Electroencephalography and computed tomography and magnetic resonance imaging of the brain were done only when indicated.

Statistical analysis

The results were collected, tabulated, and analyzed using SPSS Statistical Package Version 17 (SPSS Inc. SPSS Statistics for Windows, Chicago, IL, United States). Descriptive data were expressed as median/range (Minimum - maximum) for quantitative non-parametric data, Mean ± SD for quantitative parametric data and frequency (number/percent). Mann-Whitney test was used to compare between two groups of numerical (non-parametric) data. Kruskal-Wallis test was used to compare between more than two groups of numerical (non-parametric) data. Inter-group comparison of categorical data was performed by using χ^2 test. Some investigated parameters were entered into a logistic regression model to determine which of the factors would be considered as a significant risk factor and identify its odds ratio. Also, some investigated parameters were entered into forward logistic regression to detect a binary response based on one or more predictor variables (risk factors). All parameters were entered into *post hoc* analysis model. *P* value was consideredstatistically significant if < 0.05.

RESULTS

Descriptive data

The current retrospective cohort study was conducted on 103 Arabic speaking Egyptian children with their ages ranged between 24 to 37 mo (median age was 31 mo) with history of high risk conditions to assess their language and cognitive outcomes. The demographic data of the studied children and their mothers are summarized in Table 1. The distribution of the high risk factors in the affected children and the maternal risk factors are summarized in Table 2. Eight children had history of intra-ventricular hemorrhage, 7 children had history of peri-ventricular leukomalacia, 5 had history of retinopathy of prematurity and 5 had history of intra-uterine growth retardation (IUGR). All the children with hyperbilirubinemia were born full term with the serum level ranged between 18-24 mg/dL.

Among the 103 studied children, 68 of them demonstrated delayed language development (DLD) (66%) with underlying different etiological factors (Table 3). The rest of the studied children (n = 35) (34%) demonstrated no language delay.

Reliability of questionnaire for assessment of parents-child interaction

Reliability testing of the questionnaire used for assessment of parents-child interaction using Cronbach's alpha coefficient demonstrated a value of 0.87 which indicated

Table 1 Demographic data of the studied children/their mothers

Demographic data of children	Median	Range	Number	%
Age (mo)	31	24-37		
Gestational age (wk)	37	24-38		
Birth weight (kg)	2.5	0.75-5		
Outcome of pregnancy				
Single			79	76.7
Twin			15	14.6
Triplet			9	8.7
Order of birth				
First			54	52.4
Second			32	31.1
Third			10	9.7
Fourth			7	6.8
Sex				
Male			62	60.2
Female			41	39.8
Demographic data of the mothers				
Maternal age (yr)	25	18-40		
Maternal age groups				
⩽ 18			2	1.9
18-35			95	92.2
⩾ 35			6	5.8
Maternal risk factors[1]				
Yes			48	46.6
No			55	53.4

[1]Maternal risk factors as diabetes mellitus, hypertension, pre-eclampsia, antepartum hemorrhage, chorioamnionitis, premature rupture of membranes, *etc*.

excellent reliability of the questionnaire.

Correlative analysis

A number of correlative analyses were done between gestational age and birth weight *vs* cognitive abilities (IQ and social age) and language parameters (receptive, expressive and total). The results demonstrated statistically significant positive correlations between gestational age and expressive language score, total language age, and social age ($P < 0.05$). On the other hand, no statistically significance correlations were found between the other language parameters and IQ score (Table 4). Statistically significant positive correlations were found between birth weight and receptive language age, expressive language score, expressive language age, total language score, total language age, and social age ($P < 0.05$). On the other hand, no statistical significance correlations were detected between receptive language age and IQ score (Table 4).

Comparison analysis

The association between different peri-natal risk factors regarding the different language parameters and cognitive abilities revealed statistically significant differences in receptive language age, expressive language score, expressive language age, total language age, mental age and social age ($P < 0.05$). On the other hand; there were no statistical significant differences as regard receptive language score, total language score and IQ. *Post hoc* analyses between different peri-natal risk factors and the various language and cognitive parameters were summarized in Table 5.

Table 2 The distribution of risk factors in the studied children and their mothers

	Number	%
The neonatal risk factors		
Prematurity	25	24.3
RDS	25	24.3
Hypoxic-ischemic encephalopathy	15	14.6
Hyperbilirubinemia	10	9.7
Hypoglycemia	13	12.6
Mixed risk factors	15	14.6
The maternal risk factors		
PROM	12	25
Anemia	8	16.70
Pre-eclampsia	10	20.80
DM	10	20.80
Assisted fertilization techniques	8	16.70

RDS: Respiratory distress syndrome; PROM: Premature rupture of membrane; DM: Diabetes mellitus.

Table 3 Underlying causes of delayed language development among studied children

Causes of DLD	Number of children	%
Mental retardation	26	38.2
Environmental deprivation	12	17.6
Below average mentality	10	14.7
Specific language impairment	6	8.8
Cerebral palsy	5	7.4
Hearing impairment	5	7.4
ADHD (inattentive)	2	2.9
ASD - autism	2	2.9

DLD: Delayed language development; ADHD: Attention deficit hyperactivity disorder; ASD: Autism spectrum disorder.

Table 4 Correlation between gestational age and birth weight of high risk children *vs* different language parameters and cognitive abilities

		Gestational age	Birth weight
Receptive language score	R	0.054	0.112
	P	0.591	0.26
Receptive language age (mo)	R	0.189	0.241
	P	0.055	0.014[a]
Expressive language score	R	0.231	0.309
	P	0.019[a]	0.001[a]
Expressive language age (mo)	R	0.168	0.289
	P	0.09	0.003[a]
Total language score	R	0.192	0.239
	P	0.051	0.015[a]
Total language age (mo)	R	0.197	0.286
	P	0.046[a]	0.003[a]
IQ score	R	0.125	0.178
	P	0.208	0.072
Social age (mo)	R	0.214	0.322
	P	0.030[a]	0.001[a]

[a]$P < 0.05$. R: Spearman's rho correlation coefficient.

No statistically significant differences were detected between the presence or the absence of maternal risk factors regarding all different language parameters, IQ and

Table 5 Association between high-risk factors regarding language parameters and cognitive abilities

	Hyperbilirubinemia	Hypoglycemia	Hypoxic-ischemic encephalopathy	Prematurity	Respiratory distress syndrome	Mixed risk factors	*P*-value
Receptive language score							
Median	76.5	76	53	63	82	72	0.5
Range	51.0-110.0	51.0-110.0	52.0-110.0	51.0-105.0	53.0-115.0	51.0-105.0	
Receptive language age (mo)							
Median	21.5	24	20.0[2]	20.0[2]	30.0[3,5]	20	0.027[a]
Range	1.0-36.0	12.0-39.0	1.0-39.0	1.0-36.0	2.0-43.0	1.0-37.0	
Expressive language score							
Median	58.5	57	52.0	52.0[2]	62.0[5]	53.0[2]	0.049[a]
Range	50.0-105.0	52.0-105.0	50.0-93.0	50.0-78.02	50.0-112.0	50.0-93.0	
Expressive language age (mo)							
Median	21.5	25	16.0[2]	18.00[2]	21.00[4]	15.00[2]	0.037[a]
Range	10.0-35.0	15.0-39.0	1.0-39.0	1.0-36.0	1.0-41.0	1.0-36.0	
Total language score							
Median	57.5	56	50	50	71	51	0.11
Range	50.0-110.0	50.0-124.0	50.0-96.0	50.0-92.0	50.0-117.0	50.0-96.0	
Total language age (mo)							
Median	22	26	18	17.02	24.0[5]	17.0[2]	0.03[a]
Range	4.0-35.0	13.0-39.0	1.0-39.0	1.0-32.0	1.0-39.0	1.0-36.0	
IQ score							
Median	79	85	67	78	74	75	0.38
Range	54.0-90.0	64.0-95.0	54.0-33.0	54.0-94.0	53.0-33.0	29.0-90.0	
Social age (mo)							
Median	30	36	29.0[2]	27.0[2]	31.0[5]	27.0[2]	0.004[a]
Range	24.0-39.0	24.0-41.0	24.0-37.0	19.0-38.0	24.0-44.0	12.0-41.0	
Mental age (mo)							
Median	25.5	24	24	21.0[1]	28.0[4,5]	24.0	0.005[a]
Range	15.0-36.0	18.0-36.0	18.0-36.0	12.0-36.0	17.0-36.0	12.0-34.0	

Kruskal-Wallis test. [a]$P < 0.05$. [1]Significance relative to hyperbilirubinemia; [2]Significance relative to hypoglycemia; [3]Significance relative to hypoxic-ischemic encephalopathy; [4]Significance relative to mixed risk factors; [5]Significance relative to prematurity.

Table 6 Comparison between presence *vs* absence of maternal risk factors regarding language parameters and cognitive abilities

	Maternal risk factors				*P*-value
	Absence		Presence		
	Median	Range	Median	Range	
Receptive language score	66	51.0-115.0	77	51.0-115.0	0.3
Receptive language age (mo)	22	1.0-43.0	22.5	1.0-37.0	0.8
Expressive language score	53	50.0-105.0	53.5	50.0-112.0	0.6
Expressive language age (mo)	20	1.0-39.0	19	1.0-41.0	0.9
Total language score	51	8.0-124.0	52	50.0-117.0	0.7
Total language age (mo)	23	1.0-39.0	19.5	1.0-39.0	0.9
IQ score	78	53.0-133.0	78	29.0-110.0	0.78
Social age (mo)	31	19.0-44.0	28	12.0-41.0	0.008[a]
Mental age (mo)	24	12.0-6.0	24	12.0-6.0	0.3

Test used: Mann-Whitney; [a]$P < 0.05$.

mental age. On the other hand; there was a statistically significant difference with social age ($P < 0.05$) (Table 6).

On comparing the delayed language group and non-delayed ones; there was no statistically significant difference regarding age at assessment, gestational age, maternal age, order of birth, outcome of pregnancy, maternal risk factors and consanguinity ($P > 0.05$) (Table 7). On the other hand,there were statistically significant differences as regard all language parameters, IQ and social age ($P < 0.05$) (Table 8).

The results demonstrated statistically significant differences between parent-child interactions and receptive language score, expressive language score, total language score and IQ ($P < 0.05$). On the other hand,there were statistically non-significant differences between parent-child interactions and receptive language age, expressive language age, total language age, and social age ($P > 0.05$) (Table 9).

Regression analysis

Using univariate logistic regression analysis, the presence of prematurity in relation to other risk factors increases the risk

Table 7 Comparison between delayed language development and non-delayed language development groups as regard demographic data

	DLD group *n* = 68		*n* (%)	Non-DLD *n* = 35		*n* (%)	*P*-value
	Median	Range		Median	Range		
Age (mo)	29	24-36		31	24-37		0.17
Maternal age (yr)	25	18-39		25	19-40		0.38
Gestational age (wk)	37	24-38		36.5	27-38		0.2
Birth weight (kg)	2.75	0.75-5		2.5	0.75-4.5		0.027[a]
Sex							
Male			14 (40.0%)			48 (70.6%)	0.003[a]
Female			21 (60.0%)			20 (29.4%)	
Order of birth							
1			20 (57.1%)			34 (50.0%)	0.6
2			10 (28.6%)			22 (32.4%)	
3			4 (11.4%)			6 (8.8%)	
4			1 (2.9%)			6 (8.8%)	
Outcome of pregnancy							
Single			28 (80.0%)			51 (75.0%)	0.8
Twin			4 (11.4%)			11 (16.2%)	
Triple			3 (8.6%)			6 (8.8%)	
Consanguinity							
Negative			27 (77.1%)			53 (77.9%)	0.9
Positive			8 (22.9%)			15 (22.1%)	
Maternal risk factors							
No			19 (54.3%)			36 (52.9%)	0.9
Yes			16 (45.7%)			32 (47.1%)	

Test used: Mann-Whitney; [a]$P < 0.05$. DLD: Delayed language development.

Table 8 Comparison between delayed language development and non-delayed language development groups as regard different language parameters and cognitive abilities

	DLD group *n* = 68		Non-DLD *n* = 35		*P*-value
	Median	Range	Median	Range	
Receptive language score	54.0	51.0-105.0	94.0	76.0-115.0	< 0.001[a]
Receptive language age (mo)	18.5	1.0-37.0	32.0	22.0-43.0	< 0.001[a]
Expressive language score	52.0	50.0-71.0	84.0	50.0-112.0	< 0.001[a]
Expressive language age (mo)	15.0	1.0-36.0	28.0	15.0-41.0	< 0.001[a]
Total language score	50.0	50.0-75.0	89.0	8.0-124.0	< 0.001[a]
Total language age (mo)	17.0	1.0-35.0	30.0	23.0-39.0	< 0.001[a]
IQ score	67.0	29.0-90.0	87.0	74.0-133.0	< 0.001[a]
Social age (mo)	29.0	12.0-40.0	34.0	24.0-44.0	0.002[a]

Test used: Mann-Whitney; [a]$P < 0.05$. DLD: Delayed language development.

of language and cognitive delay significantly by 3.9 fold. The presence of other risk factors, namely hyperbilirubinemia, hypoglycemia, hypoxia and RDS increases the risk of language and cognitive delay by 1.3 folds, 7.8%, 21.9% and 40.1% respectively, but not to a significant level (Table 10).

In multivariate stepwise forward logistic regression analysis, it was found that in step 1 total language score had 0.83 risk (95%CI: 0.78-0.9) ($P \leqslant 0.0001$) which means that the increase in total language score lowered the risk of DLD by 16.3%. On other hand, in step 2 regression; total language score had 0.84 risk (95%CI: 0.79-0.9) ($P \leqslant 0.0001$) and parent-child interactions 0.16 risk (95%CI: 0.02-0.7) ($P = 0.02$) which means that the increase in total language score lowered the risk of DLD by 15.5% and children with positive parents-child interactions had lowered the risk of DLD by 89.4% (Table 11).

DISCUSSION

Children who were exposed to neonatal risk factors, which include prematurity, hyperbilirubinemia, hypoglycemia, HIE and RDS as well as children with history of maternal risk factors, including pre-eclampsia, hypertension, diabetes mellitus, anemia and assisted fertilization technique, are more liable to increase the risk of behavioral problems, intellectual deficits and a lag in language acquision[4]. The present retrospective cohort study evaluated different language parameters (receptive, expressive and total language) and cognitive outcome (IQ, mental age and social age) in 103 Arabic speaking Egyptian children with a history of neonatal risk factors at the age of two to three

Table 9 Comparison between different parents-child interactions regarding language parameters and cognitive abilities

	Parent-child interactions				*P*-value
	Negative (n = 41)		Positive (n = 62)		
	Median	Range	Median	Range	
Receptive language score	58.0	51.0-105.0	82.0	51.0-115.0	0.003[a]
Receptive language age (mo)	20.0	1.0-37.0	24.0	1.0-43.0	0.6
Expressive language	53.0	50.0-78.0	67.5	50.0-112.0	0.02[a]
Expressive language age (mo)	19.0	1.0-35.0	21.0	1.0-41.0	0.3
Total language score	51.0	50.0-90.0	76.5	50.0-124.0	0.009[a]
Total language age (mo)	19.0	1.0-35.0	23.0	1.0-39.0	0.4
IQ score	70.0	53.0-90.0	85.0	29.0-133.0	< 0.001[a]
Social age (mo)	30.0	20.0-40.0	30.0	12.0-44.0	0.6

[a]$P < 0.05$.

Table 10 Univariate logistic regression for different neonatal risk factors

	95%CI for OR			
	P-value	OR	Lower	Upper
Hyperbilrubinemia	0.714	1.307	0.313	5.457
Hypoglycemia	0.799	0.922	0.492	1.725
Hypoxic-ischemic encephalopathy	0.671	0.781	0.25	2.444
Respiratory distress syndrome	0.256	0.599	0.247	1.451
Prematurity	0.023[a]	3.937	1.21	12.813

[a]$P < 0.05$.

Table 11 Forward logistic regression

		B	*P*-value	OR	95%CI for EXP(B)	
					Lower	Upper
Step 1	Total language	-0.178	0.000[a]	0.837	0.783	0.895
Step 2	Total language	-0.168	0.000[a]	0.845	0.793	0.902
	Parents interaction	-2.246	0.019[a]	0.106	0.016	0.695

[a]$P < 0.05$.

years.

There were significant correlations between different language parameters, social ages of the studied children and their gestational age. Similar results were obtained by Gatti *et al*[14], Reidy *et al*[15], and Duncan *et al*[16], who reported a significant association between language delay and a smaller gestational age especially preterm babies less than 32 wk gestation as compared to full term babies. On the other hand, we found no significant correlation between IQ and gestational age in our studied children. This finding did not come in agreement with the Aarnoudse-Moens *et al*[17]'study who reported a significant correlation between high-risk children with a gestational age less than 30 wk and IQ. This could be explained by a higher gestational age of children included in our study (median age 37 wk) relative to children included in the later study.

Another significant correlation was detected between different language parameters, social age and birth weight in our studied children. Similar results were reported by Schirmer *et al*[18], and Foster-Cohen *et al*[19], who also reported impaired cognitive parameters including the IQ. They reported that the presence of white matter abnormalities in such very low-birth-weight babies impairs the integrity of the brain and affects the higher functions resulting in low IQ results. We did not find significant correlation between birth weight and IQ in our studied children which may be due to their higher birth weights (median 2.5 kg) compared to the birth weights of the later studies which were less than 1.5 kg. Moreover, we found no statistically significant association between different neonatal risk factors and IQ in our studied children. Morsing *et al*[20], reported a statistically significant association between high-risk neonates (preterm/IUGR) and cognitive functions as assessed by IQ testing with scores less than 70. Such difference may be attributed to the lower gestational age included in the later study (their median gestational age was 26.9 wk), while in our study it was about 31 wk which might decreased the associated risk on IQ.

Among the various risk factors examined in the study, prematurity showed a statistically significant association with language delay in all language parameters. On logistic-regression analysis, prematurity in relation to other neonatal risk factors increases the risk of language and cognitive delay by 3.9 folds. These results come in agreement with most reported literature[5,14,21,22] that had studied the effect of high-risk neonatal conditions on language outcome. They reported that prematurity is significantly associated with language and cognitive delays.

We found no statistically significant association between neonatal hyperbilirubinemia and different language parameters and cognitive outcome in our studied children. However, the presence of hyperbilirubinemia in relation to other risk factors increased the risk of language and cognitive delay by 1.3 folds, but not to a statistically significant level. Johnson *et al*[23] and Bhutani *et al*[24] reported a significant correlation between neonatal hyperbilirubinemia and language delay. Such difference may be due to the small number of cases included in our study and the presence of other risk factors as prematurity in their studies in contrast to ours where all cases of neonatal hyperbilirubinemia were full-term.

In the current study, there was a statistically significant association between neonatal hypoglycemia and expressive language age, total language age and social age, whereas, it was not associated with other language and cognitive parameters. The presence of hypoglycemia in relation to other risk factors increases the risk of language and cognitive delay by 7.8%, but not to a statistically significant level. The receptive language was not delayed in our studied children due to the fact that most of the cases of neonatal hypoglycemia were diagnosed as specific language impairment in which the IQ was more than 90, and in such circumstances; the receptive language is usually intact. These results come in agreement with the results reported by Akçay *et al*[25] who reported that neonatal hypoglycemia causes severe and permanent but preventable neurological sequelae and may lead to poor neurodevelopmental outcome that may causes poor cognitive and language development.

We found no statistically significant association between neonatal HIE and different language and cognitive parameters in our studied children. On regression analysis, the presence of HIE in relation to other risk factors increases the risk of language and cognitive delay by 21.9%, but not to a statistically significant level. Marlow *et al*[26], and Perez *et al*[27], reported in their study a significant association between neonatal HIE and language and cognitive outcomes. Such differences in the outcomes may be due to the severity of HIE in the later studies which were moderate and severe, while our studied children were affected by mild to moderate HIE with only two cases with cerebral palsy and a single case with severe mental retardation. There are some accumulating data that long-term neurodevelopmental outcome depends on the severity of HIE, with rare adverse outcomes in children with mild HIE, more common in children with moderate HIE, and invariably present in children with severe HIE[28,29].

We found a statistically significant association between neonatal RDS and receptive language age and mental age and no statistically significant association with other language parameters and cognitive outcome. Such differential affection of the receptive *vs* expressive language outcomes may be due to the deteriorating effect of brain anoxia on higher brain functions and neural development with consequent mentality affection. Such affection results in impairment of receptive more than expressive language. Regression analysis demonstrated that the presence of RDS in relation to other risk factors increases the risk of language and cognitive delay by 40.1, but not to a statistically significant level. It comes in agreement with Anderson and Doyle[30] who reported that neonatal RDS is associated with a strong possibility of delayed language development, particularly with regards to receptive language skills. Moreover, five out of 25 full-term children with RSD in our study demonstrated moderate sensory neural hearing loss (SNHL). D'Souza *et al*[31], stated that perinatal asphyxia resulted in SNHL by lesions in the dorsal and ventral cochlear nuclei and in the cochlea.

The comparison of the DLD group *vs* the non-DLD group regarding parent-child interactions demonstrated a statistically significant association between language delay and subnormal IQ and lack of parent-child interactions. Moreover, forward logistic regression revealed that the total language score improved significantly by 89.4% in the presence of positive parent-child interaction. This comes in agreement with the results reported by Meijssen *et al*[32] and Stolt *et al*[33], who stated that the quality of mother-child interaction was associated significantly with later language development in high risk children. The importance of parent-child interaction was not only in its existence or not, but by the quality of such interaction which should positively affect language development. Parents of such high risk children should be aware of these interactions to provide a language thriving environment for their children.

It can be stated that Arabic-speaking children who were exposed to high-risk conditions in the perinatal period are likely to exhibit delays in the development of language and impairments in cognitive abilities. The multivariate stepwise forward logistic regression demonstrated that the risk of DLD increased with the increase of risk factors affecting neonates and *vice versa*. In general, the neonatal risk factors cause a delay in the total language score by 16.3%. Also when the parent-child interactions increased, the risk of delayed language development decreased. Those findings were in accordance with those of Sidhu *et al*[34]' study who highlighted the complex relationship between risk factors and language outcome in children. They reported that the language quotients of the children decrease as the number of risk factors increase. So the results of our study on high risk Arabic speaking children were consistent with the results of the before-mentioned studies on high risk non-Arabic speaking children which reported that poor language outcomes in young children

are affected by the increased stress of multiple risk factors rather than the nature of any particular risk. Prematurity was found to be the most significant risk factor among the studied risk factors that are associated with such delays. In fact, most, but not all, of the studied children who were exposed to high-risk factors showed delayed language and cognitive developments. This suggests that other factors may modify the effect of such factors which necessitates further studies, *e.g.*, the quality and quantity of parent-child interactions. Moreover, a further study should be planned to follow these patients at school age to check the long term effect and whether they need special teaching and learning strategies on the long run.

Howard *et al*[35], reported that poor expressive and receptive language skills at the age of two years are a significant predictor of poor expressive and receptive language skills at the age of five years. Prevention is one aspect of a Phonetician's/speech language therapist scope of practice in communication disorders that has been neglected in our Arabic countries. Eliminating pre-term birth through adequate prenatal care is one crucial step for preventing efforts. However, even with adequate prenatal care; preterm birth occurs. Many efforts are needed to focus on providing the earliest and proper care, beginning in the NICU, for reducing the risk of language and cognitive deficits. Waiting until a child is two years old for diagnosis and intervention related to their language abilities is not early enough. Awareness of the Pediatricians and parents for early intervention of high risk neonates specifically the premature ones that have potential risk of language and cognitive deficits is warranted.

Limitations of the study

A longer period of follow-up is needed to re-asses the language and cognitive delay *vs* the deficit cases.

Some limitations related to the age of the study group (2-3 years) as we were able to assess only language and cognition, while other abilities were not amenable for assessment as speech disorders and learning disabilities.

In conclusions, Arabic-speaking children who were exposed to high-risk conditions in the perinatal period are likely to exhibit delays in the development of language and impairments in cognitive abilities. The most significant risk factor associated with language and cognitive impairments was prematurity.

COMMENTS

Background

The first three years of life; when the brain is developing and maturing, is the most intensive period of acquiring speech and language skills. There appear to be critical periods for speech and language development in infants and young children when the brain is best able to absorb language. If these critical periods are allowed to pass without exposure to language, it will be more difficult to learn. Most of the neonatal risk factors cause language and cognitive delays through impairments of the neural development and integrity of the brain functions resulting in affection of the language area and higher functions of the brain.

Research frontiers

The aim of this retrospective cohort study was to evaluate the effect of different neonatal risk factors on different language parameters as well as cognitive abilities among Arabic speaking Egyptian children at the age of two to three years and to find out which risk factor(s) had the greatest impact on language and cognitive abilities.

Innovations and breakthroughs

Arabic-speaking children aged 2-3 years who were exposed to high-risk conditions in the perinatal period are likely to exhibit delays in the development of language and impairments in cognitive abilities. The most significant risk factor associated with language and cognitive impairments was prematurity. The presence of prematurity in relation to other risk factors increases the risk of language and cognitive delay significantly by 3.9 fold. The presence of other risk factors, namely hyperbilirubinemia, hypoglycemia, hypoxia and respiratory distress syndrome increases the risk of language and cognitive delay by 1.3 folds, 7.8%, 21.9% and 40.1% respectively, but not to a significant level. We also found that children with positive parents-child interactions had lowered the risk of delayed language development by 89.4%.

Applications

Many efforts are needed to focus on providing the earliest and proper care, beginning in the neonatal intensive care unit, for reducing the risk of language and cognitive deficits. Waiting until a child is two years old for diagnosis and intervention related to their language abilities is not early enough. Awareness of the pediatricians and parents for early intervention of high risk neonates specifically the premature ones that have potential risk of language and cognitive deficits is warranted.

Terminology

High-risk neonates are defined as neonates who are more liable to morbidity or mortality due to the exposure to high-risk factors which include preconceptual, prenatal, natal, or postnatal conditions or circumstances that interfere with the normal birth process or impede adjustment to extrauterine growth and development.

Peer-review

This is a good paper analyzing association between perinatal factors and delay language development in the following life. Manuscript preparation and language are in standard for academic presentation.

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