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Risk Factors of Delayed Milestones Among Children Attending Sohag General Hospital

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ABSTRACT

Background: developmental delay occurs when a child exhibits a significant delay in the acquisition of milestones or skills, in one or more domains of development (i.e., gross motor, fine motor, speech/language, cognitive, personal/social, or activities of daily living). **Aim of the work:** the present study aimed to investigate the most common risk factors of delayed development in children under four years attending Sohag General Hospital. **Subjects and Methods:** a case control study was conducted in Sohag General Hospital during the period from January 2015 to June 2016 on children attending Pediatric, Physiotherapy and Phoniatric clinics in Sohag General Hospital, Sohag Governorate. The sample size was 150 cases and 150 controls. One hundred and fifty children (aged 1.5 month to 48 months) diagnosed with developmental delay by a specialist or/and a developmental pediatrician were recruited as cases.

Results: in the logistic regression model, the odds of developing delayed milestones is significantly higher among children with cyanosis (OR=16.391), low birth weight (OR=6.147), parental consanguinity (OR=5.489), 1st birth order (OR=4.048), urban residence (OR=3.702) and history of neonatal jaundice (OR=2.518).

Conclusion: the urban children, first children and from few number of family members were more frequently at risk for developmental delay.

Keywords: Developmental delay, Risk factors, Children, Sohag General Hospital

INTRODUCTION

Developmental delay occurs when a child exhibits a significant delay in the acquisition of milestones or skills, in one or more domains of development (i.e., gross motor, fine motor, speech/language, cognitive, personal/social, or activities of daily living). A significant delay has been traditionally defined as discrepancy of 25 percent or more from the expected rate, or a discrepancy of 1.5 to 2 standard deviations [(1)].

According to the World Health Organization (WHO), about 5% of the world's children who were below 14 years of age suffered from moderate to severe developmental delay (DD) associated disability most of which would have been either prevented or managed, if detected early [(2)].

In Egypt, a retrospective chart review was carried out on all children referred for developmental assessment in the child development center in the National Institute for Neuro-Motor System (NINMS) from July 2001 to April 2002. A total of 1261 patients were identified. Neurodevelopmental assessment did not confirm developmental delay in 165 cases (13.8%). While 350 (28.23%) cases showed mild DD, 398 (31.56%) were moderately delayed and 342 (27.12%) were severely delayed. Positive consanguinity was reported in 43% of cases [(3)].

In a study of risk factors and etiology on developmental delay of 18-month-old children in Beijing, China, Zhou and other researchers [(4)] found that the prevalence rate

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of children with developmental delay is 6.91%. The results showed that the main risk factors included were low-income families, mothers' low educational level, small size for gestational age (SGA) infant, multiple fetuses, serious diseases after birth, congenital malformations and physical retardation.

Aim of the work:

The present study aims to investigate the most common risk factors of delayed development in children under four years attending Sohag General Hospital.

Subjects and Methods

The present study is a matched case-control study. The present study was conducted in Sohag General Hospital on children attending Pediatric, Physiotherapy and Phoniatric clinics. The sample size was calculated by using the EPI Info 2000 statistical package. The calculation was done using the odds ratio of different risk factors of developmental delay (DD) from previous study (3OR) using 95% confidence interval and 80% power of the test and 5% probability of disease at base line. The calculated sample size is 150 cases and 150 controls.

One hundred and fifty children (aged 1.5 month to 48 months) were diagnosed with DD by a specialist or/and a developmental pediatrician were recruited. Patients were referred to the outpatient clinic for etiologic diagnostic evaluation of developmental delay at Sohag General Hospital, which serves as a secondary referral center, serving a region with approximately three million inhabitants. The cases were compared with 150 age and sex matched normally developed children with no evidence of delay as a control group who selected from children who attended the pediatric clinic in Sohag General Hospital for follow up care and vaccination during the same time period.

Developmental assessment of all children was carried out by using the Denver developmental screening test [(5)]. The test is a general screening instrument consists of 125 items divided into four domains: gross motor skills, fine motor/adaptive skills, personal/social, and language skills. Developmental delay is said to exist when a child does not reach developmental milestones at the expected age. Socioeconomic level was calculated by Abd El-Tawab scale [(6)].

Exclusion criteria: Age under 1.5 months and over 4 years. The actual age registered in the birth certificate was used.

Before starting to collect final data, a pilot study was carried out on 30 patients and some modifications were applied on the questionnaire used. SPSS version 16.0 was used for description and analysis of data. The Chi-square test and t-test were used. Statistical significance was set at $p \leq 0.05$. Odds ratios were calculated for risk factors for cases and controls, using Binary Multiple Logistic Regression Analysis.

Ethical statements: Protocol of the study was approved by the Ethical Committee of Assiut Faculty of Medicine. Also, consents to participate in the study were taken from the parents of the participants.

RESULTS

This study included 150 cases and 150 controls. Table (1) shows the personal characteristics of the studied children. The mean age for both cases and controls was 31.02 ± 9.35 and 30.78 ± 10.24 months, respectively. As regards the sex of the children 68.7% of cases and 70% of the controls were males, without statistically significant differences.

Table (1): Personal characteristics of the studied children, Sohag General Hospital, 2016

Variables	Cases (n= 150)		Controls (n= 150)		P-value
	No.	%	No.	%	
Sex:					
Male	103	68.7	105	70.0	0.802
Female	47	31.3	45	30.0	
◦ **Age: (months)**					
Mean ± SD	31.20 ± 9.35		30.78 ± 10.24		0.711
Range	12.0 - 48.0		12.0 - 48.0		
Residence:					
Rural	112	74.7	138	92.0	0.000
Urban	38	25.3	12	8.0	
Birth order:					
1st	94	62.7	58	38.7	
2nd-3rd	31	20.7	48	32.0	0.000
4th-5th	13	8.7	18	12.0	
6th or more	12	8.0	26	17.3	
◦ **Number of family members:**					
Mean ± SD	3.97 ± 1.37		4.35 ± 1.49		0.022
Range	3.0 - 9.0		3.0 - 9.0		

◦ **t-test**

Table (2): Socio-demographic characteristics of the studied children families, Sohag General Hospital, 2016

Variables	Cases (n= 150)		Controls (n= 150)		P-value
	No.	%	No.	%	
Father education:					
Illiterate/ Read & write	13	8.7	6	4.0	0.190
Basic education	28	18.7	33	22.0	
Secondary	23	15.3	32	21.3	
University or higher	86	57.3	79	52.7	
Mother education:					
Illiterate/ Read & write	15	10.0	14	9.3	0.083
Basic education	65	43.3	84	56.0	
Secondary	35	23.3	32	21.3	
University or higher	35	23.3	20	13.3	
Father occupation ●:					
Employee	76	50.7	71	47.3	0.066
Freelancer	32	21.3	21	14.0	
Farmer	19	12.7	18	12.0	
Skilled worker	18	12.0	23	15.3	
Unskilled worker	5	3.3	14	9.3	
Mother work:					
Housewife	136	90.7	145	96.7	0.033
Employee	14	9.3	5	3.3	
◦ **Crowding index:**					
One per room	84	56.0	63	42.0	0.049
Two per room	59	39.3	76	50.7	
More than two per room	7	4.7	11	7.3	
Socioeconomic level :					
Low	29	19.3	26	17.3	0.017
Middle	88	58.7	108	72.0	
High	33	22.0	16	10.7	

● 3 Control children their fathers were dead

Table (2): demonstrates some sociodemographic characteristics of parents of the studied children. The table shows that there are statistically significant differences between the cases and the control regarding the crowding index, mother's work and socioeconomic status (SES); more than half of the cases (58.7%) live in a middle SES followed by high SES (22%) then low SES (19.3%).

Table (3): Prenatal risk factors in cases with developmental delay versus controls, Sohag General Hospital, 2016

Variables	Cases (n= 150)		Controls (n= 150)		P-value
	No.	%	No.	%	
◦ **Maternal age at birth:**					0.502
Mean ± SD	26.12 ± 6.14		26.59 ± 5.89		
Range	17.0 - 44.0		16.0 - 41.0		
◦ **Paternal age at birth:**					0.826
Mean ± SD	33.53 ± 8.28		33.73 ± 6.83		
Range	21.0 - 65.0		20.0 - 67.0		
Consanguinity among parents:					0.000
Yes	98	65.3	65	43.3	
No	52	34.7	85	56.7	
Degree of consanguinity:					0.011
First cousin	33	33.7	35	53.8	
Second cousin	65	66.3	30	46.2	
Gestational age:					0.036
Preterm	8	5.3	1	0.7	
Full term	142	94.7	149	99.3	

Table (3): shows that there is statistically significant difference between the cases and the controls as regards history of parental consanguinity (65.3% versus 43.3%), preterm (5.3% versus 0.7%).

Table (4): Natal and postnatal risk factors in the cases versus the controls, Sohag General Hospital, 2016

Variables	Cases (n= 150)		Controls (n= 150)		P-value
	No.	%	No.	%	
▪ **Mode of delivery:**					0.000*
Normal	70	46.7	97	64.7	
Caesarean	80	53. 3	53	35.3	
▪ **Problem during delivery:**					0.258
Yes	13	8.7	8	5.3	
No	137	91.3	142	94.7	
▪ **Problem after delivery ●:**					
Did not cry directly	25	16.7	1	0.7	0.000*
Cyanosed	19	12.7	1	0.7	0.000*
LBW (less than 2.5 kg)	81	54.0	23	15.3	0.000*
Difficulty breathing	17	11.3	4	2.7	0.003*
▪ **Admission into incubator:**					0.000*
Yes	61	40.7	29	19.3	
No	89	59.3	121	80.7	
▪ **Problems during neonatal period ●:**					
Jaundice	124	82.7	122	81.3	0.764
Recurrent vomiting	65	43.3	31	20.7	0.000*
Non-feeding	40	26.7	9	6.0	0.000*
Convulsions	11	7.3	2	1.3	0.011*

● **More than one problem may be found**

Table (4) shows that cesarean section is represented 53.3% in the cases versus 35.3% of the controls with statistically significant difference. Also, the table shows that there are statistically significant differences between the studied cases and their control in the postnatal medical problems as 12.7% of the cases had a history of cyanosis at birth versus 0.7% of the controls, 16.7% of the cases had a history of delayed crying after birth versus 0.7% of the controls.

Table (5): Distribution of delayed milestone cases, Sohag General Hospital, 2016

Variable	Cases of delayed milestone (n= 150)	
	No.	%
Diagnosis:		
Motor	57	38.0
Speech	95	63.3
Cognitive	3	2.0
The person who diagnosed him first time:		
General practitioner	9	6.0
Pediatrician	119	79.3
Professor (pediatric or phoniatrician)	17	11.3
Neurologist	5	3.3

Table (5) shows that 38% of the cases had motor developmental delay and couldn't perform the movements that should be done according to their ages. The table also shows that 63.3% of the cases had speech delay and 2% of the cases had cognitive delay.

Table (6): Logistic regression of the delayed milestones among the studied children, Sohag Governorate, 2016

Variable	OR (95% C.I.)	P-value
Residence in Urban area	3.702 (1.203 – 11.389)	**0.022***
Birth order (r: 6th or more)		
1st	4.048 (1.450 – 11.299)	**0.008***
2nd – 3rd	1.959 (0.692 – 5.545)	0.206
4th – 5th	1.832 (0.535– 6.272)	0.335
Mother work	4.115 (0.942 – 17.982)	0.060
Consanguinity	5.489 (2.769 – 10.883)	**0.000***
Cyanosed	16.391 (1.453 – 184.939)	**0.024***
LBW	6.147 (3.075 – 12.286)	**0.000***
Jaundice	2.518 (1.166 – 5.440)	**0.019***

* = Significant

Table (6): Logistic regression of the delayed milestones among the studied children, Sohag Governorate, 2016

In the logistic regression model (Table 6), the odds of developing delayed milestones is significantly higher among children with cyanosis (OR=16.391), low birth weight (OR=6.147), parental consanguinity (OR=5.489), 1st birth order (OR=4.048), urban residence (OR=3.702) and history of neonatal jaundice (OR=2.518).

DISCUSSION

This study reveals that 68.7% of cases were males and 31.3% of the cases and were females (Table 1) and this is consistent with previous studies which revealed that girls had better neurodevelopmental outcomes in cognitive development, acquisition of both receptive and expressive communication skills, fine motor and social-emotional development. This finding is partially consistent with the results of previous studies which found that girls tend to perform better than boys on cognitive and language tasks. A Swedish study of more than 1000 children showed significant differences in favor of girls' verbal comprehension and production [(7)].

The results provide evidence that residence is significantly associated with delayed development of the child. This is consistent with the study conducted for comparison of normal developmental milestones among urban and rural children in Madina, Saudi Arabia [(8)].

This study revealed that 19.3% of the cases were of low socioeconomic level versus 17.3% of the controls (Table 2) and this is consistent with a previous study conducted by **Horwitz [(9)]** which reported that children who come from families characterized by a low educational level and poverty are more likely to experience delays and difficulties in expressive language. Certainly, this does not mean that the low socioeconomic level of the family per se directly affects language development, but rather that the mechanisms and conditions that define this level affect the process of language development to an extent. High-educated mothers are more likely to use rich vocabulary and speak in longer utterances when interacting with their children. Thus, children coming from a high socioeconomic background develop the size of their productive vocabulary more than children who come from a lower socioeconomic status.

This study shows that fetal exposure to preeclampsia was significantly associated with development of DD in children from the study (Table 3) and the association was more robust in those pregnancies complicated by severe disease. Preeclampsia was associated with DD primarily in severe presentations that involved placental insufficiency. 10% of the cases were born after pregnancies complicated by pre-eclampsia versus 2.7% of the controls with statistically significant difference. The results of this study are consistent with another study found strong associations between preeclampsia and Autism Spectrum Disorder (ASD) that increased with presentation severity; a significant association between severe preeclampsia and/or placental insufficiency and DD was confirmed [(10)].

As regards the birth order, this study revealed that the first child was common in the cases than the controls (Table 1). This is against studies which revealed that first-born children experience an early social and language environment which is different from that experienced by later-born children, with greater possibilities for communicative interaction with an adult. Birth order has been shown to be a risk factor for vocabulary delay in two-year-old children [(11)].

The findings of this study indicated that having older siblings at home showed a positive impact on cognitive, receptive and expressive communication skills and gross motor (Table 1) which revealed that older siblings provide developmentally more advanced models for younger siblings and help create a stimulating, enriched environment that seems to enhance

younger siblings' development in terms of cognitive, language, and motor development [12]. However, this finding are consistent with studies supporting that, in the presence of an older sibling, younger siblings' opportunities to participate in conversations are diminished. A possible explanation for this finding could be that maternal attention being spread over a couple of children may mean mothers are less responsive to each child's particular needs.

It was found that 9.3% of the mothers of the cases were employed compared 3.3 % of controls. Mechanisms for understanding how early maternal employment might affect children are offered by attachment theory [12/13]. In Greece, there is a possibility for a flexible leave policy for employed mothers in the public sector especially, which allows them to stay at home or reduce the working hours during the first year of a child's life. In few cases, however, mothers returned to work sooner because of various reasons (e.g. self-employed mothers).

Early maternal employment initiates a cascade of early starting and long-lasting care by others such as grandparents, other family members, baby-sitters, nursery, etc. A later return to work offers infants the opportunity to establish an attachment relationship with their mothers, which is consequential for later cognitive development and behavior. With a later start of mother's employment research findings show a more mixed picture with some negative, but also positive effects. **Nomaguchi [14]** showed that maternal employment when the child is four years old has a range of positive impacts, including a decreased level of hyperactivity, aggression and anxiety and also more prosocial behavior.

Essentially all intrapartum complications are more common in twin pregnancies [15] and many intrapartum complications are associated with major and minor developmental disabilities and this is consistent with this study which revealed that 6.7% of the cases were twins or multiple pregnancies compared to 0.7% of the controls with statistically significant difference.

The presence of fetal distress during labor was characteristic of the delayed group. This suggests an association with anoxia and/or placental deficiency, evidence of which was found in the cohort study [16].

The simultaneous presence of anoxia before birth has been shown to produce neurological consequences in animal offspring and could therefore be a potential source of injury to neonates. Moreover, most of studies have showed developmental delay was common in children born preterm [17]. Our finding is consistent with these studies where preterm delivery is a significant risk factor for delayed milestones.

Moreover, this study revealed that children with developmental delays more likely experienced the newborn pathological jaundice than the normal group. This is consistent with other studies which demonstrated that free or unbound bilirubin (or bilirubin not bound to protein) is associated with bilirubin-induced neurotoxicity in term or preterm infants [18].

According to its pathogenesis, free bilirubin could cross blood–brain barrier and cause brain injury which may induce the children's motor impairment. The present study also found that LBW (less than 2500 gm.) was significantly associated with an increased risk for all delayed developmental milestones, consistent with a large number of previous studies [19].

The current study revealed a high rate of caesarean deliveries (53.3% among the

cases of the present study) compared with 35.3 % among controls, as suggested by previous studies in Crete and elsewhere in Greece [20], as well. A caesarean section is usually performed in an obstetric emergency, where complications of a vaginal delivery would put the baby's or mother's life or health at risk. In Greece, several medical and non-medical factors have been implicated to this increase in caesarean deliveries such as previous caesarean deliveries dystocia, pathological fetal heart rate [20], fetal distress, breech presentation, maternal body mass, birth weight, following in vitro fertilization, as well as socio-economic factors (e.g. type of delivery hospital, type of insurance) and convenience incentives (i.e. increasing caesarean section rates during the "working" hours of the day for the physicians, etc.).

The preterm deliveries in this study (5.3% for the cases versus 0.7% for the controls) were significantly associated and strong predictors of delayed milestones. This result was in agreement with other studies which stated that the rate of preterm deliveries is ranging between (5-7%) of live births in some developed countries, but are estimated to be substantially higher in developing countries [21].

Del Bono and Ermisch [22] showed that birth weight has significant but very small effects on children's cognitive development at the age of three years old. In this study, consanguineous marriage was found in 65.3% of the cases compared to those born to mothers with no blood relation to their husbands (34.7%). This is consistent with other studies revealed that mild and severe intellectual and developmental disability are present at higher frequency in consanguineous families [23].

CONCLUSION

Developmental delay is associated with children with cyanosis (OR= 16.391), Low birth weight (OR=6.147), Parental consanguinity (OR= 5.489), 1st birth order (OR=4.048), Urban residence (OR=3.702), and History of neonatal jaundice (OR=2.518).

Recommendations

Early identification and referral of children at risk or suspected of disability by primary referral sources (including physicians and other health care providers). Improving the quality of antenatal, natal, perinatal and postnatal care in the health facilities and promotion of breast feeding for improving infant's health outcomes. Also, early diagnosis and proper management of difficulty breathing, cyanosis, low birth weight and neonatal jaundice to avoid their long-term complications. Improvement of socioeconomic conditions of the population to prevent or reduce all negative health outcomes.

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