RESEARCH ARTICLE

MOTOR DEVELOPMENTAL DELAY IN 7500 IRANIAN INFANTS: PREVALENCE AND RISK FACTORS

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Abstract

Objective

The purpose of this study was to determine the prevalence and the most common risk factors of motor developmental delay in infants.

Materials & Methods

Following ethical approval, a study was carried out on the prevalence and risk factors of infants with motor developmental delay. The first stage was conducted through a cross-sectional study to determine the prevalence of motor developmental delay on 7500 infants and the second stage was an analytic case-control survey to identify the most common risk factors on 140 infants, aged one month to three years with motor developmental delay. Data was collected using a demographic questionnaire, the Parents Evaluation of Developmental Status questionnaire, the Denver Developmental Screening Test II, a neurological assessment form, and the movement and tone assessment form.

Results

The prevalence of motor developmental delay in 7500 infants was 18.7/1000. The most common risk factors in infants with motor developmental delay were prematurity (25.6%), low birth weight (19.2%), neonatal seizures (7.5%), hyaline membrane disease (6.7%), systemic infections of mothers during pregnancy (5.9%), severe neonatal hyperbilirubinemia (5%) in sequence. Motor developmental delay was significantly correlated with consanguinity of parents (p=0.001), prematurity (p=0.046), abnormal head circumference at birth (p=0.038), and low birth weight (p=0.026).

Conclusion

The prevalence of motor developmental delay appears to be high and further studies should focus on different preventive strategies, controlling the most common risk factors and emphasizing on early detection and treatment of high risk infants.

Keywords: Motor developmental delay, Prevalence, Risk factors, Prematurity

Introduction

The documented prevalence of motor developmental delay (MDD) in the general population is reported to be more than 2-4/1000 (1, 2). In high risk infants, the prevalence of MDD is higher than that of the general population, being up to 73% in periventricular hemorrhagic infarction of prematurity (3).

One of the most important risk factors for MDD is prematurity (3, 4). Bassan et al (2007), investigated neurodevelopmental outcome in survivors of periventricular

hemorrhagic infarction in 30 premature infants. The median adjusted age at evaluation was 30 months. They reported developmental delays involving gross motor, fine motor, visual, receptive and expressive language and cognitive domains in 73%, 59%, 46%, 38% and 50% of infants respectively. In the Ancel et al (2006) study, the prevalence of MDD was investigated in 1954 survivors at age of two years, in children born very preterm, according to gestational age; they reported a prevalence rate of 20% in infants born at 24 to 26 weeks of gestation and 4% in those born at 32 weeks. This study concluded that despite recent improvements in survival rates, MDD remains highly prevalent among very preterm children (4).

Mikkola et al (2005), investigated the neuro-developmental outcome at five years of age in 172 extremely low birth weight infants (ELBW) born between 1996-1997, and demonstrated that the prevalence rate of MDD in infants with ELBW, born at <27 gestational weeks was 19% and that of those born at ≥27 gestational weeks was 9% (5).

In terms of other risk factors, in a study carried out by Wollack and Nichter (1996), the correlation of prevalence of MDD and Apgar score was investigated. Their results demonstrated that the prevalence of MDD significantly increased in children with birth asphyxia, and that in infants with an Apgar score of 0-3 at 1, 5, 15 and 20 minutes of birth, the prevalence of MDD increased by 1.5, 4.7, 16.7, 36 and 57.1%, respectively (6).

Chen et al (2002), conducted a study to determine the underlying diseases and risk factors in children with different functional delays (cognitive, speech, motor, pervasive, global and non-specific developmental delays). The prevalence of MDD in children with motor delays was associated with risk of prematurity or low birth weight (LBW); while in children with global delays, it was associated with risks of genetic defects or congenital anomalies, suggesting suggesting that heterogeneous risk factors and related diseases are associated with different kinds of functional delay (7).

Furthermore, the prevalence of MDD significantly increases with a history of some risk factors such as kernicterus, multiple gestation, intracranial hemorrhage, malformations, severe bronchopulmonary dysplasia, and post hemorrhage hydrocephaly (6).

Obviously determining or highlighting the most important risk factors in any society is of great value since the most common risk factors differ in each society. Considering the increasing prevalence of MDD and that generally, developmental delays seem avoidable, every attempt should be made to prevent and control risk factors in order to reduce the prevalence of MDD.

Although it is now broadly accepted that periodic developmental assessments are very crucial in early detection of MDD, unfortunately the developmental status of infants is not currently systemically and routinely assessed in Iranian health-care centers and pediatric clinics. Due to lack of resources, it seems difficult to perform developmental assessment for all infants in the country, thus periodic developmental assessments in high risk infants are strongly recommended. It is important to note that such infants usually have a history of one or more prenatal, perinatal or postnatal risk factors.

Considering the critical significance of the prevalence of MDD, addressing the most common risk factors in infants with MDD, and the limited research in Iran in this area, the present study was designed to determine the prevalence and the most common risk factors in Iranian infants with MDD.

Materials & Methods

Following ethical approval from the University of Social Welfare and Rehabilitation Sciences (USWR) Research Ethics Committee, a cross-sectional and an analytic (case-control type) study were carried out to determine the prevalence and the most common risk factors of MDD in Iranian children, aged between one month and three years. Data was collected using a demographic questionnaire, a neurological examination form and a movement and tone assessment form (8). The study was conducted at the Saba Developmental Disorders Center affiliated to the USWR, Tehran, Iran, between March 2004 and November 2005. Since generally Iranian infants refer to health-care centers for routine vaccination and periodical measurements of height, weight and head circumference, this setting was selected for the study. Inclusion criteria were: Age between one month to three years, living in the west, south and southwest of Tehran, willingness of parents

to take part and ability to read and write in Persian (Farsi); exclusion criteria were: Age over three years and lack of interest of the subjects' parents. In infants ≤ 2years, with a history of prematurity, the corrected age was used rather than the chronological age.

A one-day workshop was held to train health-care workers on how to screen gross motor developmental delays by the Parents Evaluation of Developmental Status (PEDS) questionnaire and to refer infants suspected of MDD, to the Saba Center, the only referral center for evaluating such infants.

Over a period of 20 months 7500 normal infants, aged one-month to three years, were referred to the west, south and southwest health-care centers of Tehran Health Network for monthly care and vaccination. About 85% of infants in the region are brought to health-care centers for different health-care purposes as services offered in these centers are provided free-of-charge. These health centers provide coverage to almost 50% of the rural and urban populations of Tehran city, since these areas are highly crowded and almost all infants in the region are brought to health-care centers for different health-care purposes. Hence all families, regardless of their income status, have equal access to the health-care services.

Following referral of infants through health-care workers, all parents were given written information sheets explaining the aims and plans of the research and were asked to sign a consent form if they agreed to take part; however if not, they would receive the usual services provided.

Outcome Measures

Data was collected by a demographic questionnaire including age, sex, consanguinity of parents, type of delivery, number of siblings, family history, and prenatal, perinatal, and postnatal history. Although, the questionnaires were completed by parents, the information given by the parents was double checked with the children's medical records, whenever necessary.

Prenatal risk factors considered in this study were vaginal bleeding, systemic intrauterine bacterial and viral infections (such as rubella, chicken pox, cytomegalovirus and hepatitis B), mother's non-infectious diseases (such as toxemia of pregnancy, diabetes mellitus, asthma, gastrointestinal diseases, significant anemia, thyroid diseases, uterine problems, and cardiac diseases), premature rupture of membrane, multiple gestations, and teratogens; perinatal risk factors taken into account were prematurity, prolonged labour, instrumental delivery, asphyxia, fetal distress, nuchal cord, and placenta previa; postnatal risk factors comprised of LBW, neonatal seizure, hyaline membrane disease (HMD), severe hyperbilirubinemia, sepsis and meningitis, congenital anomalies, neonatal pneumonia, metabolic disorders, congenital heart diseases, urinary tract infections, and severe anemia.

During the study, 190 infants suspected of MDD and referred to the Saba Center, were assessed by a trained pediatrician. Gross motor development was assessed by the Denver Developmental Screening Test II (DDST II) and the neurological examination was performed on the basis of by a neurological examination form that consisted of items such as, primitive and postural reflexes, cranial nerve, sensory and cerebellar assessment. In addition, head circumference was measured and gait assessment was performed. The movement variability, muscle tone and antigravity movements were also assessed by the same pediatrician in eight standard positions (i.e. supine, side lying, prone, pull to sit, sitting, standing, horizontal suspension, and protective reaction). All infants with motor developmental levels, below 75% the normal level according to DDST II, or showed any abnormality in motor neurological examination, were considered infants with MDD, resulting in a diagnosis of MDD in 140 infants.

For the second part of the study, infants with MDD were considered as the case group while 140 normal matched (gender, age, socio-economical status) infants, referred to the west and southwest health-care centers for monthly care and vaccination, were randomly assigned as the control group. Nineteen infants were excluded from the case group since they either did not meet the inclusion criteria or their parents were not willing to participate in the study, and five participants dropped out from the control group, due to parental unwillingness to take participate. Hence this case-control study finally included the remaining 121 infants with MDD as the case group and 135 normal infants as the control group. The same demographic questionnaire was also completed by

parents of infants in control group.

Data analysis

Data was analyzed by the SPPS software, version 14, using the Chi-square, T test, and two-way analysis of variances (ANOVA) to analyze the data. Statistical significance was set at p=0.05.

Results

In total, 140 infants were diagnosed with MDD, indicating a prevalence of MDD of 18.7/1000 (140 out of 7500) in this study.

Table (1) demonstrates the age distribution of children in the case and control groups. More than half of the infants in both groups were aged<1 year, as this is the age of children more commonly referred to health-care centers for monthly check ups; others are checked every two or three months, as the rate of referral at a higher age is low, compared to that of lower aged infants, for different reasons including parents' willingness.

Some demographic characteristics of samples are given in Table (2); there was no significant difference between the case and the control groups in terms of gender, birth type, presence of five children or more in the family, and a positive family history of MDD. However a statistically significant different was found between the case and the control group, in terms of consanguinity of parents, birth weight, birth head circumference, and gestational age (Table 2).

The prevalence of prenatal risk factors is shown in histogram 1. There was a significant difference between the two groups in terms of intrauterine systemic bacterial infections (P= 0.00), while the rest were not significant (P>0.05). The most common prenatal risk factors in the case group were systemic bacterial infections (5.9%), hypertension (4.2%), diabetes mellitus (2.5%) and viral infections of mother during pregnancy (2.5%), respectively.

The prevalence of perinatal risk factors is shown in histogram 2. There was a statistically significant difference between the two groups only in prematurity (P=0.046), whereas the rest were not significant (P>0.05); prematurity was also shown to be the most common perinatal risk factor in the cases (25.6%).

The prevalence of postnatal risk factors is shown in histogram 3. There was a significant difference between the two groups in terms of LBW (P= 0.026), the rest not being significant (P>0.05). The most common postnatal risk factors in the cases were LBW (19.2%), neonatal seizure (7.5%), HMD (6.7%) and severe hyperbilirubinemia (5.0%).

Table1. Age distribution of infants in the case and the control groups.

		Controls N (%)	Cases N (%)	Total N (%)
Age	<1y	75 (55.6)	64(52.9)	139(54.3)
	1-2y	45(33.3)	37(30.6)	82(32.0)
	2-3y	15(11.1)	20(16.5)	35(13.7)
	Total	135	121	256

N: Numbers

Table 2. Characteristics of infants in the case and the control groups.

		Controls N (%)	Cases N (%)	P Value
Gender	Male	66(48.2)	56(46.3)	0.678
	Female	71(51.8)	65(53.7)	
Birth type	Normal vaginal	59(43.7)	63(52.1)	0.169
	Caesarean section	76(56.3)	58(47.9)	
Consanguinity of parents	First cousin	19(14.1)	31(25.6)	0.001
	Second cousin	16(11.8)	28(23.2)	
	No relationship	100(74.1)	62(51.2)	
Number of childern in the family	≥5	3(2.2)	4(3.3)	0.231
	<5	132(97.8)	117(96.7)	
Family history of MDD	Positive	25(18.5)	19(15.7)	0.507
	Negative	110(81.5)	102(84.3)	
Birth weight (gr)	Normal	100(74.1)	72(59.5)	0.026
	<2500	30(22.2)	45(37.2)	
	>4500	5(3.7)	4(3.3)	
Birth head circumference (cm)	Normal	96(71.1)	78(64.5)	0.038
	Microcephaly	27(20.0)	36(29.7)	
	Macrocephaly	12(8.9)	7(5.8)	
Gestational age	Premature	21(15.6)	33(27.3)	0.046
	Term	114(84.4)	88(72.7)	

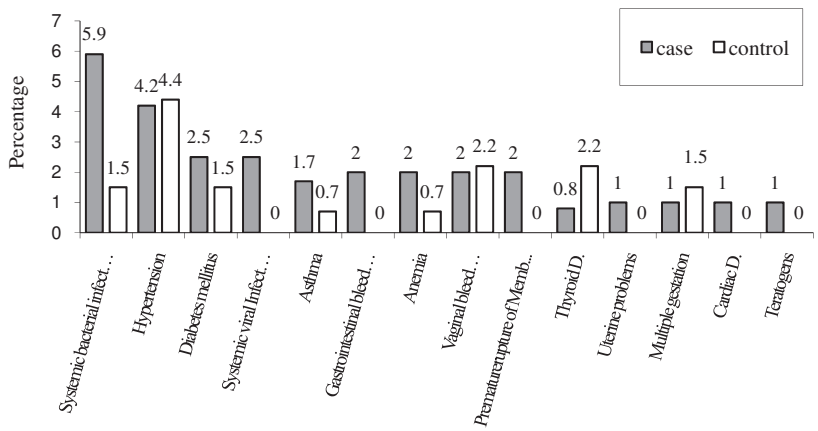

Fig 1: Prevalence of prenatal risk factors in case & control groups

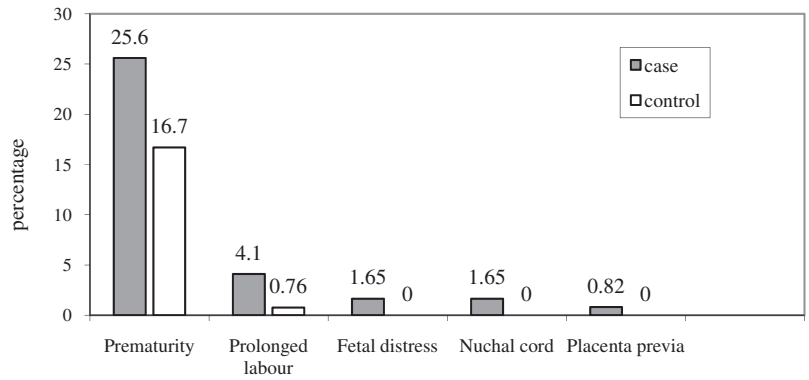

Fig 2: Prevalence of perinatal risk factors in case & control groups

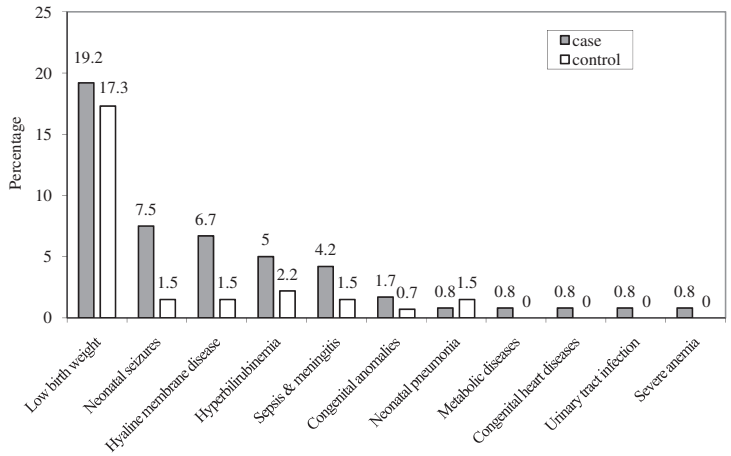

Fig 3: Prevalence of postnatal risk factors in case & control groups

Discussion

In the current study the prevalence of MDD in infants and the most common risk factors for MDD such as prematurity, LBW, and hyperbilirubinemia were studied. According to the results of this study, the prevalence of MDD was 18.7/1000, a figure that appears to be higher than that already reported in current literature (1, 2). The higher prevalence rate in this study may be attributed to:

a) the low to moderate socio-economic status of the population studied (9, 10);
b) the transiently abnormal neurological findings in some cases (8, 11), indicating a longitudinal study is recommended.
c) the coverage of health-care centers was not 100% for all infants born in those areas.

The history of consanguinity in parents of children with MDD was significantly higher than those of the control group. Consanguinity in turn may contribute to MDD by expressing autosomal recessive disorders. Most inborn errors of metabolism (IEM), usually inherited as autosomal recessive, are considered to be one of the causes of MDD in infants. Consanguinity of parents causes IEM in infants, whereas they are easily preventable (12). Nasir et al (2004) investigated the probable causes of specific childhood disabilities in eastern Afghanistan and demonstrated that 46% of disabled children were born to parents who were first degree relatives (13). It seems that the difference between the findings of this study and those reported by Nasir et al (2004) might be due to the small sample size of the study conducted in Afghanistan. It also appears that the cultural differences of the population investigated might significantly influence the study results.

The large number of children in a family did not seem to be a risk factor in the current study, as there was no significant difference between the two groups; Although this result might be flawed due to the lack of families with more than 2-3 children in this study; this finding supports the results of previous studies, like that carried

out by Kinsbourne and Graf (2000), in which no correlation was reported between the number of children and prevalence of MDD (14).

A history of developmental delay or MDD in the family and close relatives of the infant did not contribute to the occurrence of MDD. Stoll et al (2004) proposed that the presence of some genetic developmental diseases with specific inheritance (such as Mandelian autosomal and X-linked recessive) in the family, help in the diagnosis of the disease in infants (12).

Compared to the control group, prenatal risk factors were more prevalent in the case group although this difference was not statistically significant; the most common prenatal risk factor in the case group was systemic bacterial infection in the mother. In one study (15), intrauterine infection, maternal pyrexia, and the presence of thrombophilic disorders have been identified as major risk factors for subsequent MDD. The interactions of viral or bacterial infections during pregnancy in addition to normal or abnormal fetal cytokine responses as antenatal causes of the neuropathology of MDD are now areas of priority in future research.

In some studies prenatal factors such as teratogenic drugs, radiation, vaginal bleeding and important diseases related to the mother, in particular diabetes and hypertension (pre-eclampsia and eclampsia), were also highlighted as major causes of high risk pregnancies resulting in the birth of high risk infants. However these factors can directly contribute to the occurrence of MDD by causing asphyxia and injuries to the developing brain (6).

Due to the multiplicity of factors in this study, namely 14 factors, future studies with larger samples are recommended to determine the effect of each factor on the prevalence of MDD.

In this study, the prevalence of perinatal risk factors was significantly higher in the case group. Prematurity and asphyxia have been the most common addressed risk factors in different studies. Generally different causes of prematurity can themselves be considered as potential threats for MDD; on the other hand, due to different premature organs, a premature infant is exposed to various problems such as HMD with the final outcome of decreased oxygen supply to the brain, which in turn contributes to MDD. An infant with a lower gestational age will have more problems (1, 14).

Stoelhorst (2003), investigated the effect of prematurity on developmental outcomes at the corrected age of 18 and 24 months and concluded that, at 18 and 24- months corrected age, 40% of very prematurely born infants suffered from either delayed mental or psychomotor development, or both (16). In another study conducted on 200 children with MDD, in different rehabilitation centers in Tehran, prematurity was one of the most significant risk factors of MDD (17).

Postnatal risk factors are important in causing MDD in infants. The most common factors were LBW (less than 2500 gram), neonatal seizures, HMD and severe hyperbilirubinemia requiring exchange transfusion. Factors causing intrauterine growth retardation (IUGR) can also be influential in developing various problems such as hypoglycemia, asphyxia, polycytemia, hypothermia and dysmorphology in the neonatal period (14).

In the study carried out in Tehran on 200 cases with MDD (17), LBW and severe hyperbilirubinemia played a detrimental role in causing MDD. The combination of severe prematurity and IUGR are followed by serious developmental handicaps including MDD, blindness, deafness, and mental retardation, which predispose to physical and developmental delays (18).

Another study reported the association between fetal growth restriction and a rise in the risk of poor neurological outcomes. Increase in the risk of MDD in infants with>32 weeks' gestation is one of the poor neurological outcomes mentioned in the Yanney and Marlow (19) study.

In general, according to the results of this study, the most common risk factors in infants with MDD were prematurity, LBW neonatal seizure, HMD, systemic bacterial infections in mothers during pregnancy, and severe hyperbilirubinemia, respectively. Therefore, further studies focusing on strategies in order to control and prevent such risk factors and on early detection and intervention in high risk infants are highly recommended.

Limitations

Some other risk factors such as congenital disorders were not included. Also due to limitations in assessing

sensory deficits (sight, and hearing) or communication deficiencies, these developmental delays were not included in the study.

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